Anesthesia
UNIVERSITY OF TORONTO

ANESTHESIA FOR MEDICAL STUDENTS

A Concise Clerkship Manual for Medical Students

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Third Edition

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Section 1

COURSE OBJECTIVES

In this section:

- Goals
- General Competencies
- Educational Core Objectives
- Textbooks/Learning Resources

Goals

Upon completion of the Anesthesia Clerkship Rotation, third year medical students will understand the implications of pre-existing disease for patients undergoing anesthesia. They will demonstrate competency in basic airway management and acute resuscitation, and will be able to discuss pain management in the perioperative period.

General Competencies

Medical Expert/Skilled Clinical Decision Maker

The third year medical student will be able to:

1. Demonstrate the ability to assess a patient in the preoperative period and formulate a basic management plan.
2. Demonstrate the ability to take a focused history and physical examination, including anesthetic history and airway exam.
3. Develop a plan for preoperative investigations and interpret these investigations.
4. Understand and explain the risks and benefits associated with regional versus general anesthesia.
5. Develop an approach to acute resuscitation, including appropriate fluid therapy.
6. Develop an approach to perioperative pain management.
7. Demonstrate competency in airway management and other procedural skills relevant to the perioperative period.

Communicator/Doctor-Patient Relationship

The third year medical student will be able to:Communicate effectively and empathetically with patients and their families, and recognize their level of anxiety.

1. Communicate their level of training and involvement in patient care.
2. Communicate risk with high risk patients and their families.
3. Communicate effectively with the perioperative team, noting anesthetic-related concerns.
4. Present a complete preoperative assessment in a clear, concise, and timely manner.

Collaborator

The third year medical student will be able to:

1. Establish and maintain effective working relationships with colleagues and health care professionals.
2. Consult effectively with physicians and other health care professionals.
3. Participate effectively on health care teams, namely the Anesthesia Care Team (ACT), Acute Pain Service (APS), and Cardiac Arrest and/or Trauma Teams.
4. Understand the high level of collaboration (anesthesia, surgery, nursing, pharmacy, anesthesia assistants and respiratory therapists) required for the effective management of the patient in the perioperative period.

Manager

The third year student will be able to:

1. Demonstrate appropriate and cost-effective use of investigations in an evidence-based manner.
2. Understand the prioritization of the surgical emergency patient to minimize the risk of negative outcome.
3. Develop an understanding of the factors contributing to resource issues in the perioperative period.
4. Understand the role of physicians in developing the health care system and promoting access to care (Anesthesia Care Team).

Health Advocate/Community Resources

The third year student will be able to:

- Understand the risk factors that lead to increased perioperative risk and how anesthesiologists can assist in modifying these risks in the perioperative period, including:
  - Smoking cessation
  - Weight loss Alcohol use
  - Recreational drug use

Scholar

The third year medical student will be able to:

1. Retrieve information from appropriate sources related to the anesthesia curriculum
2. Assess the quality of information found, using principles of critical appraisal
3. Develop an approach to self-directed learning

Professional

The third year medical student will be able to:

1. Interact with patients in a compassionate, empathetic, and altruistic manner
2. Recognize his or her limitations and seek appropriate help when necessary
3. Maintain patient confidentiality
4. Understand the current legal and ethical aspects of consent for surgery, anesthesia and blood transfusion
5. Understand full and honest disclosure of error or adverse events
6. Understand initiatives, such as the Operating Room Checklist, which have been undertaken to ensure patient safety and to minimize medical error in the perioperative period
7. Fulfill all obligations undertaken, including educational obligations

Educational Core Objectives

Skills

At the completion of the Anesthesia Clerkship rotation, the third year medical student will be able to demonstrate basic proficiency in the following skills. These skills may be acquired during the clinical rotation, seminars or simulation day.

Technical Skills

One of each of the following must be attempted or completed:

1. Airway insertion
2. Cardiac monitor lead placement
3. Endotracheal intubation
4. Laryngeal mask insertion
5. Video Laryngoscopy
6. Mask ventilation
7. Peripheral IV insertion

Interpretive Skills

One of each must be completed:

1. Capnography
2. Cardiac Monitor
3. Pulse Oximetry

Problem-based encounters

Upon completion of the Anesthesia clerkship rotation, the third year medical student will be able to demonstrate an approach, including the differential diagnosis and management as appropriate, for the following patient encounters. These may be based on either real or simulated encounters.

Required

One encounter of each is required:

1. Hypotension/shock (observe and manage with faculty or resident - simulated acceptable)
2. Hypoxia/apnea (observe and manage with faculty or resident - simulated acceptable)
3. Pain management (observe and discuss management with faculty)
4. Preoperative assessment (complete independently and discuss with faculty)

Other encounters:

1. Altered consciousness/coma
2. Anaphylaxis
3. Anemia
4. Arrhythmia
5. Cholinesterase deficiency
6. Complex regional pain syndrome
7. Cyanosis
8. Delirium
9. Difficult airway
10. Hypercarbia

11. Hypothermia
12. Malignant hyperthermia
13. Nausea/vomiting
14. Obstetrical pain management
15. Pediatric resuscitation
16. Regional anesthesia
17. Trauma

Textbooks/Learning Resources

Students are provided with an anesthesia course manual that contains the core objectives. Chapters in the manual are authored by our faculty. The following are suggested textbooks but are not required for this course.

1. Ottawa Anesthesia Primer, Dr. Patrick Sullivan; Echo Book Publishing 2012
2. Understanding Anesthesia: A Learner's Guide, Dr. Karen Raymer (free download at www.understandinganesthesiology.com)

Section 2

DETAILED OBJECTIVES AND STUDY GUIDE

In this section:

Medical Expert (Revised June 2016)

Preoperative Assessment

- Take a pertinent history, including co-existing disease, medications, allergies, previous anesthetic problems, and family history of problems with anesthesia.
- Identify important factors which may influence the perioperative period in patients with significant co-morbidities, including respiratory and cardiovascular disease, endocrine abnormalities and obesity.
- Explain how to assess fluid status and the need for patient optimization.
- Perform an appropriate physical exam, including assessment of the airway, respiratory and cardiovascular systems.
- Summarize the indications for laboratory testing and special investigations.
  Describe the rationale for pre-operative fasting, NPO guidelines, and pharmacological prophylaxis for aspiration.
- Describe the presentation, pharmacological implications, and management of malignant hyperthermia and cholinesterase deficiency.
- Explain the importance of early disposition planning.

Airway Management

- Perform a full airway assessment.
- Determine which patient populations are at risk for difficult mask ventilation and difficult intubation.
- Interpret the difficult airway algorithm.
- Describe the indications and contraindications for the use of the laryngeal mask airway.
- Summarize the goals/utilities of intubation.
- List the risk factors for aspiration.
- Demonstrate rapid sequence induction, explain its purpose, and describe its indications.
- Summarize the requirements for safe extubation.

Pharmacology

Summarize the main indications and common side effects for the following:

- Medications that work on the autonomic nervous system.
- Benzodiazepines such as midazolam and lorazepam.
- Propofol, ketamine, and etomidate.
- Nitrous oxide, desflurane, and sevoflurane.
  - Explain the concept of minimum alveolar concentration (MAC).
- Opioids such as morphine and fentanyl.
  - Convert IV morphine dose for oral administration.
- Ondansetron, dexamethasone, haloperidol, and dimenhydrinate.
- Succinylcholine and rocuronium.
  - Distinguish between non-depolarizing and depolarizing blockade.
  - Describe the concept of reversal and how to evaluate the degree of neuromuscular block.
- Lidocaine, bupivacaine, and ropivicaine.
  - Calculate the maximal permissible dose for a patient of given weight.
  - Describe the signs and symptoms of local anesthetic toxicity and its management.

Resuscitation

Respiratory

- List a differential diagnosis for hypoxemia and hypercarbia and describe the management of both.
- Summarize the indications for mechanical ventilation.
- Describe the initial management of an apneic patient.
- Describe the different devices available for administering supplemental oxygen and their effect on inspired oxygen.
  - Recognize the significant features of the self-inflating resuscitation bag (Laerdal, Ambu) and demonstrate its use (Covered on Simulation Day).

Cardiovascular

- Describe the determinants of cardiac performance.
- Summarize the signs, symptoms, and differential diagnosis of shock.
- Recognize common cardiac arrhythmias and apply the ACLS guidelines.
- Describe the presentation and management of anaphylaxis.

Fluid Therapy & Transfusions

- Summarize the principles of fluid management.
- List the commonly used crystalloids and colloids. Explain their role in fluid management.
- Describe the guideline for RBC transfusion in the perioperative period.
- Discuss the various blood products, their indications, and potential complications.

Regional Anesthesia

- Distinguish between epidural and spinal anesthesia. Describe the contraindications and complications of both
- List the common peripheral nerve blocks, the indications for their use, and potential complications

Obstetrical Anesthesia

- Summarize the physiological changes of pregnancy.
- Explain the significance of aortocaval compression syndrome and its management.
- List the pharmacological and non-pharmacological methods of pain relief available for labour.

Pediatric Anesthesia

- Contrast the paediatric airway anatomy with that of an adult.
- Demonstrate the initial steps of neonatal resuscitation.
- Apply the Apgar scoring system. Evaluate and manage fluid status in the paediatric patient.

Acute Pain Management

- Assess the adequacy of postoperative pain control.
- List the physiological consequences of poor postoperative pain control.
- Summarize the WHO pain ladder.
- NSAIDs: List the available routes of administration, their major side effects, and contraindications to their use.
- Opioids: List the available routes of administration, contraindications to their use, and major side effects.
    - Describe the management of an opioid overdose.
    - Convert oral to parenteral dosages.
- Discuss PCA, epidural analgesia, and the role of an Acute Pain Service (APS).
- Recognize the importance of multidisciplinary management for patients with chronic pain and list the various modalities for therapy.
- Describe the management of Chronic Regional Pain Syndrome (CRPS).

Post-Operative Management

- List the common causes and describe the management of the following post-anesthetic complications:
    - Respiratory: airway obstruction, hypoventilation, and hypoxemia.
    - Cardiovascular: hypotension, hypertension, tachycardia.
    - Neurological: weakness, delayed recovery, and delirium.
- List the risk factors of postoperative nausea and vomiting and describe its management.

Patient Safety (see professional section for more details)

- Recognize the importance of the operative checklist in promoting patient safety.
- Summarize initiatives to decrease medication error in the perioperative period.
- Discuss standard precautions and initiatives that aim to decrease needle stick injuries.

Skills

Perform the following:

- Intravenous Lines:
    - Intravenous setup
    - Insertion

- Airway management
    - Airway assessment
    - Ventilation assessment
    - Bag/mask ventilation
    - LMA insertion
    - Intubation
    - Advanced airway management (GlideScope, FOB) –observe +/- perform Monitoring (Interpretation)
- EKG
- SaO2
- Capnography

Communicator

Anesthesia highlights the impact of effective communication in a high stakes environment. Through effective communication between health care professionals, critical events can be managed in an optimal manner, thereby improving patient outcome. With high risk patients, communicating risk with patients and their families during the preoperative and perioperative periods is of utmost importance.

MCC Objectives

- Tailor your interview to the clinical context (1.3)
    - During your preoperative assessment of the patient, you should strive to complete and present a succinct and precise assessment of the patient's relevant medical and anesthetic history in a timely manner.

During your anesthesia rotation, you should strive to establish good rapport with patients and their families, and to be able to communicate information effectively to patients and health care providers. The effects of appropriate communication in a high stakes environment will be demonstrated on Simulation Day.

Collaborator

The delivery of safe Anesthesia care requires a high degree of collaboration between health care professionals. The operating room, ICU and labour floors are dynamic environments that necessitate the integration of many health care providers. Managing a patient effectively preoperatively involves close communication between anesthesiologists, surgeons, intensivists, family doctors, nurse practitioners and medical specialists. Managing patients in the operating room involves collaboration between surgeons, nursing, anesthesia assistants and respiratory therapists. In the postoperative period, the pain management team involves collaboration between anesthesia, nursing and pharmacy.

MCC Objectives

- Consult effectively with physicians and other health care professionals (2)
    - Preoperative assessment clinic
        - Optimizing patients preoperatively with appropriate consultation
        - Pharmacy involvement with multiple medications
    - Perioperative
        - Ensure other members of the OR team are aware of anesthetic issues (surgical checklist)
    - Participate effectively on health care teams (3)
        - Anesthesia Care Team (ACT)
        - Cardiac arrest and trauma teams

- Acute Pain Service (APS)

During your Anesthesia rotation, you should have a good understanding of collaboration and its impact on access to care and improving outcome. Collaboration will be highlighted during Simulation Day.

Manager

Anesthesiologists play a key role in optimizing efficient use of operating room time and thus access to patient surgery. Emergency patients are prioritized to minimize the risk of negative outcome. Investigations preoperatively should be ordered in an evidence based manner.

MCC Objectives

- Allocate health resources (human, diagnostic and therapeutic) prudently (2.1)
  - Operating room access
  - Preoperative investigations
- Manage scarce health care resources in an ethical and informed manner, balancing individual and societal needs
  - Ethics of cancelling elective surgery at the end of the day due to time constraints

During your anesthesia rotation, you should develop an appreciation of appropriate use of health care resources during the perioperative period.

Health Advocate

While Anesthesiologists generally see patients later in their disease, there are certain lifestyle changes that we have taken an active role in advocating on behalf of the patient. The smoking cessation program is a recent initiative. International health initiatives are evolving.

MCC Objectives

- Identify the important determinants of health and the risk factors for illness, including: lifestyle issues (1)
- Smoking cessation
  - Alcohol use
  - Weight loss
  - Recreational drug use

During your Anesthesia rotation, you should be aware of risk factors that lead to increased perioperative risk and how we can help modify those risks.

Scholar

Throughout your career, you will be required to develop a plan for personal continued education. This rotation is an ideal forum to learn many aspects of patient care through self-directed learning.

MCC Objectives

- Develop a plan for continued personal education (1)
- Retrieve information from appropriate sources (2.2)
- Assess the quality of information, using principles of critical appraisal (2.3)

During your anesthesia rotation, you will be assessed on self-directed learning. There is an expectation that you will read around the cases that you are involved with.

Professional

- An exemplary level of professionalism is an expectation of all medical students and physicians. In Anesthesia, we encounter patients in a very fragile state. Many have been diagnosed with life-altering or -ending illnesses. It is our responsibility to act in a compassionate, empathetic and altruistic manner.

Honesty and integrity with full disclosure of adverse events is fundamental to this competency. There are many components to professionalism, with major overlaps with other competencies.

MCC Objectives

- Accept responsibility of ensuring continuity of care (2.2)
  - Ensure appropriate transfer of care when receiving patients from the emergency department and ICU and when transferring postoperative patients to the recovery room or ICU
- Maintain patient confidentiality (2.3)
  - Written and verbal consent and disclosure (2.4)
  - Disclosure to patients of level of training and role Blood
  - product consent
  - Procedural consent (regional) Procedural
  - risk disclosure
- Medical Error and Patient Safety (2.5)
  - Operating room checklist (overlap with Communicator role and Collaborator role) Body
  - substance precautions
  - Full, honest disclosure of error or adverse events

During your Anesthesia rotation, you will come in contact with many patients who are experiencing life-altering and emotional events. Altruism, compassion and respect for patients are expectations of every student (please keep this in mind when learning skills on patients: refer to IV guidelines).

Section 3

INTRAVENOUS LINE INSERTION GUIDELINES

The purpose of these guidelines is to allow medical students the opportunity to learn the technique of peripheral intravenous catheterization (IV) while providing the best possible patient care, which includes patient safety and comfort.

An IV line insertion may be attempted when there are at least two or more viable sites for an IV of appropriate size (gauge) to be inserted. IV lines will be deferred to a senior respiratory therapist (RT), anesthesia assistant, anesthesia resident, fellow, or staff when there are less than two viable sites for the insertion of an appropriate sized (gauge) IV or when there are concerns regarding the successful insertion of the IV and/or patient comfort.

Factors such as surgical procedure, surgical site, patient complexity, and history (e.g., difficult line access, extensive cardiac history, etc.) must be considered when IV attempt(s) are being made by a medical student. Not all patients will be suitable for attempts at IV catheterization by a medical student and as such, students will only be given the opportunity to attempt IV access at the discretion of the anesthesia staff.

Medical students must be directly supervised by a member of the Anesthesia team while attempting IV access. The team may include anesthesia assistants, anesthesia residents, fellows, and staff. Students may be given one or two attempts at obtaining IV access on any given patient at the discretion of the supervisor. Should the first attempt fail, ensure that your supervisor is aware before you try again. You may refer to the NEJM video on Peripheral Intravenous Cannulation for an overview of indications/contraindications and technique.

General exclusion criteria for inserting peripheral IV catheters by medical students:

- Patient refusal
- Patient's OR is on hold (or in question)
    - Non-compliant patient
    - Previous surgery at puncture site
    - Signs of infection, haematoma, or swelling at puncture site
    - Patient is receiving anticoagulant medications
    - Patient with significant coagulopathy or thrombocytopenia
    - Hemodialysis patient
    - Arm with an arterial-venous graft or a fistula
    - Arm on side of a mastectomy/axillary node dissection
    - Arm with diminished sensations or paralysis

***Avoid areas above or below a traumatized vein (phlebitis, cellulitis, bruised or interstitial).**

Chapter 1

PREOPERATIVE ASSESSMENT

Sections:

1. **Preoperative Assessment of the Patient with Cardiac Disease**
2. **Preoperative Assessment of the Patient with Respiratory Disease**
3. **Anesthetic Risk: Morbidity and Mortality**

Section 1.1

Preoperative Assessment of the Patient with Cardiac Disease

Amelie Dallaire & David T. Wong. Department of Anesthesia, Toronto Western Hospital

Introduction

Major cardiac complications following non-cardiac surgeries account for most of the deaths in the perioperative period. Cardiac complications also result in substantial morbidity, prolonged hospitalization and increase in health care costs. The role of the anesthesiologist during the preoperative assessment is to effectively identify patients at risk of experiencing cardiac events in the perioperative period. Using a detailed history and a careful physical examination, comorbid cardiac conditions need to be determined. The risk stratification principles and management are based on the 2014 American College of Cardiology/ American Heart Association (ACC/AHA) Guidelines on Perioperative Cardiovascular Evaluation for Non-cardiac Surgery[1].

Evaluation of comorbid conditions

Ischemic heart disease/Coronary artery disease (IHD/ CAD)

The preoperative history taking should assess the severity, stability and functional limitations imposed by CAD. CAD should be suspected in patients presenting with risk factors: male gender, increasing age, hypercholesterolemia, hypertension, smoking, diabetes mellitus, obesity, sedentary lifestyle and positive family history. Symptoms such as angina and dyspnea should be looked for. **Angina** should be characterized by its **severity** (amount of exercise precipitating angina) and its **stability** (changes or stability in pattern). These symptoms may be absent at rest. It is therefore particularly important to evaluate and question the patient's response to various physical activities. Patients with good functional capacity (>/= 4 METs) may undergo surgery without further evaluation. Patients presenting with angina and **poor functional class** (<4 METs) may be at increased risk of perioperative cardiac events, and necessitate delay in elective surgery. **Further stress test** including exercise stress testing (treadmill, stress echocardiography, stress nuclear scan) may be required to determine the likelihood of significant CAD.

TABLE: EVALUATION OF THE FUNCTIONAL STATUS USING METS (METABOLIC EQUIVALENTS)[2]

1 MET	Eat, dress, use the toilet Walk indoor around the house Walk a block or two on ground level at 2 to 3 mph (3.2 to 4.8 kph)
4 METs	Do light work around the house (dusting, doing dishes) Climb a flight of stairs or walk up a hill Walk on level ground at 4 mph (6.4 kph) Run a short distance Do heavy work around the house (scrubbing floors, lifting or moving heavy furniture)
10 METs	Participate in moderate recreational activities (golf, bowling, dancing, double tennis, throwing a football or a baseball)

History of **myocardial infarction (MI)** is important. Acute MI (1 to 7 days previously), recent MI (8 to 30 days previously) and unstable angina carry high risk of cardiac perioperative event. Elective surgery should be delayed at least 30 days following a MI. The presence of cardiac revascularization with percutaneous coronary intervention (PCI) and stent placement or CABG should be determined. After stent placement, dual antiplatelet therapy is routinely administered. It is recommended to delay elective surgery 6 weeks after PCI with bare metal stent placement and up to 1 year after drug-eluting stent placement.

It is reasonable to obtain preoperatively an **electrocardiogram (EKG)** for patients with a history of CAD, significant arrhythmia, peripheral arterial disease, cerebrovascular disease or other significant structural heart disease. EKG abnormalities like arrhythmias, pathological Q-waves, LV hypertrophy, ST depressions, QTc interval prolongation and bundle-branch blocks can be looked for. Changes in EKG suggestive of CAD or MI (**new ST changes or Q waves**), particularly in a patient with limited or unknown exercise tolerance should be considered for further cardiac testing or cardiology consult.

Risk stratification

For patients with ischemic heart disease in stable condition undergoing elective non-cardiac surgery, six independent predictors of major adverse cardiac events (MACE: death, ventricular fibrillation, complete heart block, acute MI, pulmonary edema) have been identified and included in the Lee Revised Cardiac Risk Index. These six predictors are: high-risk surgery (suprainguinal vascular, intraperitoneal, intrathoracic surgery), history of coronary heart disease, congestive heart failure, diabetes mellitus (type I or type II requiring insulin use), renal insufficiency (creatinine > 175mmol/L) and cerebrovascular disease. The presence of 0-1 risk factors represent a risk of MACE </=1 %; 2 risk factors = 4-6% of MACE; and >/=3 risk factors = 9-11% of MACE. Patients with higher risks based on the Lee criteria

system must continue their chronic beta-blocker and statins therapies as part of a risk mitigation strategy. The risk of MACE should be provided for patients for them to weigh the risk/benefit of surgical intervention.

Hypertension

Preoperative evaluation of patients with essential hypertension should determine the adequacy of blood pressure control. **End-organ damage** like angina pectoris, left ventricular hypertrophy, congestive heart failure, cerebrovascular disease, stroke, peripheral vascular disease and renal insufficiency should be looked for preoperatively. There are no universally accepted guidelines for postponement of elective surgery in hypertensive patients in whom blood pressure control is not optimal. Home-measured values of a **systolic blood pressure > 180 mm Hg** and/or a **diastolic blood pressure > 110 mm Hg** on multiple occasions is often used as criteria for postponement. Postponement is also justified in the presence of non-controlled end-organ damages or if further evaluation is required. To ensure optimum blood control management in the perioperative period, most antihypertensive drugs (except ACE inhibitors and ARB) should be continued the morning of surgery.

Congestive Heart Failure (CHF)

Patient with a history of CHF are at significant risk for perioperative complications. History taking should include symptoms evaluation using the New York Association Functional Classification of Heart Failure (see table 3). Clinical findings like peripheral edema, jugular venous distension, crackles, third heart sound or presence of pulmonary edema should be looked for. In the presence of recent clinical exacerbation, surgery should be postponed and cardiac condition optimized prior to surgery. **Echocardiogram** reports should be reviewed to determine the type of heart failure (systolic and/or diastolic) and to evaluate left ventricular ejection fraction (LVEF). Patient with a LVEF < 30% are at higher risk of perioperative complications. Patients with heart failure should continue their medication (including diuretics) in the perioperative period to avoid decompensation.

NYHA CLASSIFICATION

NYHA Class	Description
I	No limitation- symptoms of heart failure only at activity levels that would limit normal individuals
II	Slight limitation-symptoms with ordinary levels of activity
III	Marked limitation- symptoms with less-than-normal levels of activity
IV	Symptoms of heart failure at rest- very poor prognosis

Valvular disease

Significant valvular heart disease increases cardiac risk for patients undergoing non-cardiac surgery. Presence of valvular disease should be suspected in the presence of a heart murmur during cardiac auscultation. Valvular disease can also present with cardiac dysrryhmias; atrial fibrillation being very

common with mitral valve disease. Angina pectoris can occur with aortic stenosis even in the absence of coronary heart disease. Evaluation of functional status is essential. Patients with suspected valvular heart disease should undergo **echocardiography** to quantify the severity of stenosis or regurgitation and obtain systolic function prior surgery. The most significant conditions with impact on perioperative management are **severe aortic stenosis and mitral stenosis**. Patients with known valvular disease should undergo preoperative echocardiography if there has been no prior echocardiography within the last 1 or 2 years or if there has been a significant change in clinical status since last evaluation. In the presence of severe valvular disease meeting surgical criteria, replacement or repair of the affected valve should be done before elective surgery to reduce perioperative risk.

Implantable Cardiac-Devices

Patients with an implantable cardiac device need special attention perioperatively. During preoperative assessment, it is important to determine if the device is a pacemaker or an implantable cardioverter-defibrillator (ICD). The reason for implantation and whether the patient is dependent on pacing should be assessed. The date of the last device's interrogation should be documented as well as proper functioning. The risk of implantable cardiac device malfunction may be high during certain types of surgeries owing to electromagnetic interferences. Preoperative re-programmation of pacemakers to asynchronous mode may be necessary. In the case of ICDs, the anti-tachyarryhthmia function (defibrillation) may be suspended for surgery with frequency electromagnetic interference (interpreted as VF/VT therefore leading to repeated shocks) using a magnet or a re-programing.

Conclusion

Cardiac complications are frequent in the perioperative period. Cardiac comorbid conditions like coronary heart disease, congestive heart failure, arrhythmias, valvular disease and hypertension should be thoroughly evaluated prior to surgery. The most important part of the evaluation is a precise targeted history and obtaining reports of previously performed cardiac testing. Patients having stable cardiac conditions and able to perform >/=4 METs can generally undergo surgery without further evaluation. Those with poor functional status (<4 METs), suspected of CAD or significant valvular disorder may necessitate further evaluation and intervention to decrease their perioperative cardiac risk.

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Section 1.2

Preoperative Assessment of the Patient with Respiratory Disease

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Introduction

Patients can present for anesthesia with acute or chronic lung diseases or both. Chronic respiratory problems include obstructive and restrictive lung diseases and obstructive sleep apnea. The most common obstructive lung diseases encountered in anesthesia are reactive airway disorders (asthma) and chronic obstructive pulmonary disease (COPD).

The goals of the preoperative assessment of these patients are:

1. To identify their disease, its severity and adequacy of management;
2. To optimize the management of their disease before the operation;
3. To plan their management during and after the operation;
4. To intervene and minimize the risk of post-operative pulmonary complications.

Ideally, the patient's respiratory disease should be stable and optimized preoperatively. As a general principle, patients with acute lung problems should not undergo elective surgery, since the risk of respiratory complications (pneumonia, bronchospasm, laryngospasm and atelectasis) is increased. However, for emergent or urgent surgeries, the risk of delaying surgery may outweigh the benefits of optimizing respiratory conditions and minimizing the risk of pulmonary complications.

Asthma

Asthma is a common chronic respiratory disease affecting 3-5% of the population and characterized by bronchial hyper-responsiveness and airflow obstruction. Clinically, it presents with intermittent symptoms of bronchonstriction (cough, wheezing, chest tightness, shortness of breath). Asthma severity is classified based on symptoms, degree of airflow obstruction on pulmonary function tests and amount of treatment required1.

In the perioperative period, asthmatics are at risk for life-threatening acute crises of bronchoconstriction (i.e. bronchospasm), particularly around the time of airway manipulations (such as during endotracheal intubation). A recent respiratory infection (e.g. bronchitis, pneumonia, viral upper respiratory tract infection) may increase this risk. In these patients, it is prudent to delay elective surgery for at least 6 weeks after such infection.

During preoperative assessment, the adequacy of asthma control needs to be assessed. Even patients with severe asthma can present to the preoperative clinic with little to no symptoms. It is essential to elicit a thorough history of the disease including triggering factors, previous exacerbations, need for hospital admissions, current asthma medications, use of "rescue" short-acting bronchodilators, etc. A previous history of severe exacerbations, particularly if requiring intensive care admission or intubation, is indicative of patients at increased risk. Clues to poorly controlled asthma potentially requiring optimization and postponing elective surgery include frequent symptoms, limitation of normal activities, frequent use of short-acting bronchodilators, frequent exacerbations in last year (see ref. 1). Signs and symptoms of acute exacerbation or active respiratory infection should be ruled out during the preoperative assessment.

TABLE 1 - PRINCIPLES OF PERIOPERATIVE MANAGEMENT OF ASTHMA[2]

Preoperative

- Continue chronic bronchodilator medications /inhalers as per usual on day of surgery
- Administer short-acting inhaled bronchodilators (e.g. salbutamol) prior to anesthesia

Intraoperative

- Consider using local / regional anesthesia (e.g. spinal, nerve block) when appropriate
- If general anesthesia required, consider less invasive airway manipulations (laryngeal mask airway or mask anesthesia) over endotracheal intubation when appropriate
- Avoid medications that may release histamine and trigger bronchospasm (e.g. morphine, atracurium, rapid injection of vancomycin)
- Preferentially use agents that promote bronchodilation (propofol, ketamine, sevoflurane, intravenous lidocaine)
- If airway instrumentation is required, it should be performed at deep levels of anesthesia to decrease airway reflexes
- During mechanical ventilation, set ventilator parameters to allow enough expiration time
- Treatment options for acute bronchospasm: short-acting inhaled ß2 agonists and anticholinergics, glucocorticoids, inhalational anesthetics, ketamine, magnesium, supportive therapy with oxygen and mechanical ventilation

Postoperative

- Consider extubation in deep planes of anesthesia ("deep extubation")

Chronic Obstructive Pulmonary Disease (COPD)

COPD is a common disease affecting 5-8% of the population and characterized by pulmonary airflow limitation that is not fully reversible with bronchodilators, with airways that are chronically inflamed and hyper-reactive. By far the most important risk factor for COPD is the amount and duration of cigarette smoking. Other risk factors include environmental or occupational exposures, genetic causes (α-1 anti-trypsin deficiency, various gene polymorphisms) and childhood illnesses (neonatal bronchopulmonary dysplasia). COPD encompasses a broad spectrum of pathophysiological mechanisms including chronic bronchitis (chronic lung inflammation with excessive secretions) and emphysema (heterogeneous destruction of lung parenchyma, bullae). Severity of COPD is based on results of pulmonary function tests (Table 3).

TABLE 3 – CLASSIFICATION OF SEVERITY OF COPD BASED ON POST-BRONCHODILATOR FEV1 % OF PREDICTED IN PATIENTS WITH FEV1/FVC < 0.7

Mild	FEV1 > 80%
Moderate	50% < FEV1 < 80%
Severe	30% < FEV1 < 50%
Very severe	FEV1 < 30%

See Ref. 3: FEV1 = Forced Expiratory Volume in 1 second. FVC= Forced Vital Capacity

The general management of COPD includes a combination of non-pharmacological interventions (e.g. smoking cessation, pulmonary rehabilitation, vaccination, long-term oxygen therapy), pharmacotherapy and surgical options (e.g. lung transplantation). Pharmacotherapy generally includes short and long acting inhaled bronchodilators (anticholinergics and β2 agonists), oral bronchodilators (theophylline), inhaled glucocorticoids and/or oral phosphodiesterase-4 inhibitors (e.g., roflumilast).

Preoperative clinical history and physical examination evaluates the patient's baseline symptoms and functional capacity and assesses current respiratory status. Signs and symptoms of COPD exacerbation or active respiratory infection are sought. Reports of new or worsening dyspnea not previously investigated, changes in cough and sputum volume or character, symptoms of upper respiratory tract infection, low oxygen saturation, systemic signs of infection (e.g., fever, chills), active wheezing or use of accessory respiratory muscles require further investigation. In these cases, strong consideration is made to postponing elective surgery and optimizing the patient's condition.

Preoperative arterial blood gas (ABG) analysis will not change perioperative management in the majority of COPD patients but may be useful in patients with known or suspected hypoxemia or hypercapnia such as those with severe or very severe disease. Indeed, certain COPD patients develop chronic compensated CO_2 retention (i.e. $PaCO_2$ > 45mmHg at rest with normal pH from renal compensation). This has significant perioperative implications as some of these "chronic CO_2 retainers" are at increased risk of worsening hypercapnia when given supplemental oxygen during spontaneous ventilation. Various mechanisms are involved in this phenomenon: exacerbated ventilation/perfusion mismatch, decreased hypoxic ventilatory drive and the Haldane effect (see ref.4). Increases in $PaCO_2$ beyond baseline may lead to respiratory acidosis and associated cardiovascular changes (tachycardia, arrhythmias, hypo or hypertension, pulmonary vasoconstriction) as well as depressed levels of consciousness ("CO_2 narcosis"). Therefore, if COPD patients become hypoxemic, supplemental oxygen should be carefully titrated to target oxygen saturations close to the patient's baseline. Moreover, the cerebral blood vessels of chronic CO_2 retainers have a shifted the CO_2 reactivity curve and trying to reach a normal $PaCO_2$ may lead to significant cerebral vasoconstriction.

Preoperative work-up should also include recent pulmonary function testing in patients with changes in symptoms and those undergoing thoracic surgery. It is also reasonable to obtain a chest X-ray in COPD patients exhibiting changes from baseline status, those with other known cardiorespiratory comorbidities and those over the age of 50 years-old undergoing intrathoracic or major intraabdominal surgery. Chest radiologic examinations should be reviewed and features with specific perioperative concerns noted. For example, some COPD patients develop cystic air spaces in the lung parenchyma

known as bullae. These bullae are often asymptomatic but are associated with increased risk of complications such as rupture, tension pneumothorax and broncho-pleural fistula, particularly during positive pressure ventilation. Therefore, attention should be paid to minimizing airway pressures during mechanical ventilation of these patients and adequate expertise and equipment should be immediately available to manage these complications with a chest tube and lung isolation, as needed. Also, nitrous oxide is contraindicated in patients with bullae as it diffuses into the bullae more quickly than the less soluble nitrogen diffuses out of it, thereby increasing the risk of rupture.

Particular attention should also be paid to patients with long-standing severe COPD and hypoxemia, as these patients may have developed pulmonary hypertension and right ventricular dysfunction. Signs and symptoms of this phenomenon (exertional syncope, dyspnea out of proportion to pulmonary function, elevated jugular venous pressure, peripheral edema) should be sought for and a preoperative echocardiogram may be warranted for further evaluation.

The preoperative assessment of a COPD patient should lead to a clear strategy to optimize the patient's respiratory status as time permits and to reduce the perioperative risk. In addition to general measures to reduce the risk of postoperative pulmonary complications (see last section of this chapter), Table 4 summarizes some of the key elements in the specific perioperative management of COPD patients.

TABLE 4 – PERIOPERATIVE MANAGEMENT OF COPD PATIENTS

Preoperative • Optimize poorly controlled COPD • Delay elective surgery for 6 weeks after an acute respiratory infection • Promote smoking cessation (counselling, nicotine replacement therapy…) • Initiate pulmonary rehabilitation and chest physiotherapy program • Continue chronic COPD medications /inhalers and consider short-acting inhaled bronchodilators (e.g. salbutamol) prior to anesthesia
Intraoperative • Consider using local / regional anesthesia (e.g. spinal, nerve block) when appropriate • If positive-pressure ventilation is required, be aware of expiratory airflow limitation and risks of breath stacking/dynamic hyperinflation and bullae rupture/pneumothorax • Opt for a lung-protective ventilation strategy with permissive hypercapnia and allow sufficient expiratory time (avoid high tidal volume, increase expiratory time) • Avoid targeting lower than baseline $PaCO_2$ in chronic CO_2 retainers • Treat bronchospasm as previously described (see Asthma section) • Titrate short or intermediate acting neuromuscular blockers judiciously, ensure complete reversal of neuromuscular blockade at the end of surgery
Postoperative • Carefully titrate supplemental O_2 to reach baseline oxygen saturation • Optimize pain control while minimizing opioids and sedatives (favour acetaminophen, non-steroidal anti-inflammatories, epidural analgesia, nerve blocks…) • Consider higher levels of postoperative monitoring (intensive care or step-down units, serial arterial blood gas analysis…)

Obstructive sleep apnea

Obstructive sleep apnea (OSA) is characterized by recurrent episodes of apnea or reduced inspiratory airflow caused by functional collapse of upper airways during sleep, leading to abnormal gas exchange (hypoxemia and hypercapnia) and inadequate sleep. By far the most important risk factor for OSA is obesity but other risk factors include advancing age, male gender and upper airway abnormalities (e.g. adenotonsillar hypertrophy, micrognathia). With the recent obesity epidemic, the prevalence of OSA has significantly increased and ranges from 5 to 15% in women and 15 to 30% in men. Clinical manifestations commonly include heavy snoring and daytime sleepiness. The diagnosis is confirmed by polysomnography or other forms of sleep studies and treatment involves weight loss and use of contin
uous positive airway pressure devices (CPAP) during sleep.

Specifically in the perioperative period, OSA has been associated with increased risk of cardiac and respiratory complications, particularly oxygen desaturations and need for mechanical ventilation. Additionally, these patients are at increased risk of difficult airway management and have significantly enhanced sensitivity to respiratory depressants such as opioids and benzodiazepines. Unfortunately, a significant proportion of patients present for surgery with undiagnosed OSA. Therefore, preoperative screening tools have been developed, the most studied being the STOP-BANG questionnaire (Table 5).

TABLE 5 – STOP-BANG SCREENING QUESTIONNAIRE

Criteria	**Question**
Snoring	Do you snore loudly?
Tired	Do you feel tired or sleepy during the day?
Observed	Has anyone observed you stopped breathing/choking during sleep?
Pressure	Do you have high blood pressure?
BMI	Body Mass Index > 35 kg/m^2?
Age	Age > 50 years?
Neck circumference	Shirt collar more than 17in for men? More than 16in for women?
Gender	Male gender?
Scoring criteria – Risk of	

OSA	
Low risk	Yes to 0-2 questions
Intermediate risk	Yes to 3-4 questions
High risk	Yes to 5-8 questions

Consideration should be given to delaying elective high-risk surgery in undiagnosed patients at high risk of OSA or in patients with moderate to severe OSA inadequately managed. In particular, patients with evidence of obesity hypoventilation syndrome or pulmonary hypertension (hypoxemia when awake, elevated serum bicarbonate, signs and symptoms of right ventricular dysfunction) should be thoroughly evaluated with a sleep study, arterial blood gas analysis and echocardiography. The preoperative evaluation should also determine whether the procedure can be performed on an outpatient basis or if the patient should be admitted to the hospital postoperatively for closer monitoring based on the following criteria: severity of sleep apnea, use of CPAP, other comorbidities, invasiveness of procedure and expected impact on cardiorespiratory physiology, type of anesthesia, expected need for postoperative opioids and other sedatives. Table 6 summarizes some of the key elements of perioperative management in these patients. (Table 6).

TABLE 6 – PERIOPERATIVE MANAGEMENT OF OSA PATIENTS

Preoperative

- Review sleep study or screen patient for OSA
- Screen and investigate for OSA-related comorbidities and adequacy of treatment
- Evaluate and plan airway management options
- Consider delaying elective surgery for evaluation and initiation of treatment, especially if evidence of obesity hypoventilation syndrome or pulmonary hypertension
- Determine safety of outpatient surgery

Intraoperative

- Consider using local / regional anesthesia (e.g. spinal, nerve block) when appropriate
- During moderate or deeper sedation, maintain high index of suspicion for airway obstruction and use continuous capnography monitoring
- Minimize use of respiratory depressants: favour shorter-acting anesthetic agents and opioids, ensure complete reversal of neuromuscular blockade at the end of surgery
- Extubate awake, in head-up position

Postoperative

- Carefully monitor in the PACU for adverse respiratory events (desaturations, bradypnea, apnea) and pain-sedation mismatch that may warrant prolonged monitoring
- Resume CPAP therapy during all moments of sleep, including in the PACU
- Consider initiating CPAP therapy in patients not previously receiving it
- Titrate supplemental oxygen to avoid hypoxemia
- Optimize pain control while minimizing opioids and sedatives (favour acetaminophen, non-steroidal anti-inflammatories, epidural analgesia, nerve blocks…)
- Assess adequacy of discharge to unmonitored setting, taking into account underlying risk and adverse respiratory events in PACU
- Instruct discharged patients to rigorously use CPAP during all periods of sleep until no longer taking opioids

Restrictive and Interstitial lung diseases

A restrictive lung physiology is characterized on pulmonary function testing by decreased lung volumes but preserved forced expiratory volume in 1 second to forced vital capacity ratio (FEV_1/FVC). This pattern can be caused by diseases of the lung parenchyma (e.g. interstitial lung diseases), extrinsic problems affecting the pleura or chest wall (e.g. pleural effusions, scoliosis, severe obesity) or disorders causing weakness of the muscles of breathing (e.g. myasthenia gravis, Guillain-Barré syndrome).

Interstitial lung diseases (ILDs) are a heterogeneous group of disorders characterized by inflammation and fibrosis of the lung parenchyma affecting the alveolar-capillary unit. They are usually discerned from other restrictive lung diseases by an impaired diffusion capacity of the lungs for carbon monoxide (DLCO). The most common identifiable causes are related to exposure to occupational or environmental agents (e.g. silica, asbestos), drug related toxicity (e.g. bleomycin, amiodarone) or radiation induced lung injury. However, for a significant proportion of patients, a specific cause is never identified (e.g. idiopathic pulmonary fibrosis). Confirmation of the diagnosis can be difficult and is usually made from a combination of clinical, radiologic, physiologic and pathologic evidences by a multidisciplinary team.

The goals of the preoperative consultation are to assess the severity of the disease, to optimize medical management before surgery and to plan perioperative care. It is useful to involve the patient's respirologist in this process. Preoperative evaluation should seek evidence of pulmonary hypertension or right ventricular dysfunction that may be associated with chronic hypoxemia. Other specific perioperative concerns of ILD patients include potential adverse effects from anti-fibrotics (e.g. hepatic toxicity, gastrointestinal side effects) or immunosuppressive medications (e.g. adrenal suppression, increased infection risk), high incidence of gastro-esophageal reflux disease and overall increased risk of respiratory complications.

Postoperative pulmonary complications

The incidence of postoperative pulmonary complications (PPCs) is usually estimated to be around 3-6%. The definition of PPCs generally includes atelectasis, respiratory infections, exacerbation of underlying pulmonary disease, hypoxemia and need for invasive (i.e. endotracheal intubation) or non-invasive (i.e. CPAP or BiPAP) mechanical ventilation.

These clinically significant complications often share a common pathophysiologic pathway related to the patient's comorbidities and the effects of anesthesia and surgery. The residual effects of anesthetics, neuromuscular blockers, opioids and other respiratory depressants, combined with the pain, splinting and diaphragmatic dysfunction caused by surgery lead to reduced functional residual capacity, vital capacity and tidal volumes and reduced ability to clear respiratory secretions. These phenomena eventually result in atelectasis, V/Q mismatch, hypoxemia and increased risk of respiratory infections. Many risk factors associated with PPCs have been identified (Table 7). Patients with pulmonary hypertension are another population at high risk of pulmonary and cardiac complications, with significantly increased perioperative mortality.

TABLE 7 – RISK FACTORS ASSOCIATED WITH PPCS

Patient-related risk factors • Age > 50 years old • COPD • Smoking (especially current smoking) • OSA • Heart failure • American Society of Anesthesiologists' Physical Status class ≥ 2 • Functional dependence • Low serum albumin
Surgery-related risk factors • High-risk surgical site (intrathoracic, intraabdominal, head and neck, neurosurgery) • Duration of surgery > 3 hours • Emergency surgery
Anesthesia-related risk factors • General anesthesia • Long-acting neuromuscular blockers and residual neuromuscular blockade • Postoperative epidural analgesia (protective against PPCs)

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Section 1.3

Anesthetic Risk: Morbidity and Mortality

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Introduction

"So Doctor, I am going to have surgery soon. What are my risks with the anesthetic?"

Patients generally believe that anesthesia is safe.[1] They assume that they will go to 'sleep' in the operating room, and then 'wake up' after what will hopefully be a successful operation. This perception is generally correct, largely because of impressive safety improvements in the field.[2] Indeed, the risk of mortality solely due to anesthesia decreased by almost 15-fold between the 1970s and 2000s, with deaths where anesthesia care was contributory decreasing by 8-fold over the same time period.[3] In high-income countries, contemporary estimates place the risk of death directly attributable to anesthesia to be 25 events per million, while the risk of death where anesthesia is contributory to be 85 events per million.[3] Nonetheless, it is important to remember that surgery remains a high-risk activity. In a cohort study of about 45,000 surgical procedures across 27 countries worldwide, 0.5% of patients died in-hospital (i.e., 5000 events per million) while 17% experienced one or more postoperative complications.[4] While the safety of anesthesia care has improved considerably, patients undergoing surgery are increasingly older, frailer, and have more comorbid disease, especially in high-income countries.[5] These same individuals are at increased risk for anesthesia-related morbidity and mortality. Anesthesia management has the potential to influence many of these other non-anesthesia-related causes of perioperative morbidity and mortality.

Anesthesia-Related Mortality

The overall risk of mortality after surgery is not low, especially in emergency surgery. In a cohort study of almost 45,000 elective surgical procedures across 27 countries worldwide, 0.5% of patients died in-hospital,[4] while in another cohort study of almost 22,000 patients undergoing major noncardiac surgery in 13 countries, 1.1% of patients died within 30-days after elective surgery.[6] By comparison, the risk of 30-day death after urgent or emergent surgery was 3.1%.[6] The proportion of these deaths that is attributable, directly or partially, to anesthesia is much lower. Nationwide data from the United States suggest that the risk of death related to anesthesia care is only 8.2 per million surgical hospital admissions, but this estimate is limited by its reliance on potentially insensitive diagnostic codes in hospital discharge abstracts.[7] By comparison, a nationwide survey of anesthesia-related mortality in France estimated this risk to be about 0.005% (54 deaths in 1,000,000 anesthetics).[8]

It is important to remember that these estimates represent average risks. The risk of anesthesia-related mortality increases in elderly patients (especially those aged 85 years or older), [7] as well in those with significant comorbid disease. As shown in Table 1, the risk of anesthesia-related mortality varies with patients' American Society of Anesthesiologists Physical Status (ASA-PS) scale.[8] Among anesthesia-related deaths, approximately 31% are due to respiratory failure, 30% were due to hypovolemia, and 38% were due to cardiac-related causes (arrhythmias or cardiogenic shock).[8]

TABLE 1: VARIATION IN ANESTHESIA-RELATED MORTALITY WITH ASA PHYSICAL STATUS.[8]

ASA Physical Status	Risk of Anesthesia-Related Death
Average	54 per million
I	4 per million
II	50 per million
III	270 per million
IV	550 per million

Anesthesia-Related Morbidity

There are several complications, both life-threatening and non-life-threatening, that might be related to anesthesia care. Several of these complications are listed below:

1. **Anesthesia-Related Cardiac Arrest**

Intraoperative cardiac arrests are very uncommon, occurring in 7.2 per 10,000 procedures in the setting of noncardiac surgery,[9] while cardiac arrests that are due to anesthesia-related factors are even rarer, with an estimated risk between 0.6 to 1.1 per 10,000 anesthetics.[10,11] These cardiac arrests are usually related to airway complications that occurred primarily with induction, emergence, or in the post-anesthesia care unit,[11] as well as overdoses of anesthetic medication or hypovolemia.[10]

2. **Anesthesia-Related Airway Complications**

Major airway management complications during anesthesia (i.e., death, brain damage, emergency surgical airway, unanticipated critical care unit admission) occur in 46 per million general anesthetics.[12] The main issues relating to anesthesia airway management include difficult or impossible mask ventilation (1.5% risk), [13] difficult mask ventilation and difficult endotracheal intubation (0.4% risk),[13] as well as aspiration of gastric contents (0.03% risk in elective surgery, and 0.1% risk in emergent surgery).[14] While most patients with clinically apparent aspiration have no important sequelae,[14] aspiration events still account for more than 50% of airway-related deaths in anesthesia care.[12]

3. **Anesthesia-Related Neurological Complications**

Many patients fear that they might 'wake up during anesthesia'. Fortunately, this complication, which is termed 'awareness under anesthesia', is rare. When it occurs, it typically involves being able to explicitly recall events during surgery, but without pain. It is certainly one of the most distressing events that patients can suffer during surgery.[15] In a nationwide survey in the United Kingdom, the overall risk of awareness under general anesthesia was 0.005%, but the risk was higher among patients receiving neuromuscular blockade (0.01%) or undergoing Caesarean section (0.15%). [16] Strategies that might help prevent awareness under anesthesia in high-risk patients include specialized level of consciousness monitors (e.g., bispectral index or BIS monitor) especially during total intravenous anesthesia (TIVA),[17] and automated alarms to indicate low expired anesthetic gas concentrations.[18,19]

In-vitro models show that anesthetics can also induce injury in developing neurons, with confirmation of this neurotoxicity in the non-human primate brain.[20] The clinical implications of these findings in humans are controversial. Based on findings in animal studies, as well as observational studies in humans showing a modest risk of impaired neurodevelopment after anesthesia and surgery exposure (especially multiple exposures) in childhood,[21,22] the Food and Drug Administration in the United

States issued a warning in 2016 against repeated or lengthy use of general anesthetic and sedation drugs in children younger than three years. Conversely, two large Canadian cohort studies found that the risk of developmental impairment associated with early childhood anesthesia exposure was very small,[23,24] while a multicentre randomized trial comparing general versus regional anesthesia in 722 infants found no difference in neurodevelopmental outcomes at two years of age.[25] Issues pertaining to anesthesia-related neurotoxicity also apply to older patients, where the concern is postoperative cognitive dysfunction, which is defined as cognitive deterioration after surgery. A prospective cohort study of more than 1200 patients aged 60 year or older found that almost 10% showed cognitive dysfunction at three months following major noncardiac surgery. Nonetheless, most evidence indicates that these early cognitive changes generally do not persist over the long term,[26] with some research suggesting that persistent postoperative cognitive declines are largely attributable to pre-existing trajectories of cognitive decline prior to surgery.[27]

Neuraxial anesthesia or analgesia, which involves spinal or epidural nerve blocks has the potential, albeit very small, for causing nerve damage. Based on a nationwide audit in the United Kingdom, the risk of permanent nerve injury related to neuraxial blockade was estimate to range from 2.0 to 4.2 cases per 100,000 and the risk of death or paraplegia was estimated to be 0.7 to 1.8 cases per 100,000.[28] In a cohort study of about 88,000 patients who underwent elective noncardiac surgery in Ontario,[29] the risk of spinal decompression laminectomy (which may indicate significant neurological complications) within 30-days after perioperative epidural analgesia was 18 in 100,000 and no different from patients who did not receive epidural analgesia.

4. **Postoperative Nausea-and-Vomiting**

Although seemingly a minor complication, postoperative nausea and vomiting (PONV) is very common after anesthesia, occurring in more than 30% of patients.[30] Furthermore, it results in considerable patient dissatisfaction.[15] Patients who are at increased risk for PONV include younger patients, women, non-smokers, and patients with a history of PONV or motion sickness.[31,32]

5. **Dental Damage**

Laryngoscopy and endotracheal intubation involve the potential for dental damage. The overall risk is approximately 0.02% (i.e., 20 cases per 100,000 anesthetics); when damage does occur, the upper incisors are the most commonly involved teeth.[33]

Perioperative Complications that are Modifiable by Anesthesia Management

Surgical patients are at risk for important postoperative complications that are not directly attributable to anesthesia. About 17% of patients experience one or more postoperative complications after major elective surgery.[4] Nonetheless, anesthesia management has the potential for preventing several of these important causes of postoperative morbidity. Some of these potentially preventable complications are listed below:

1. Cardiovascular Complications

Major cardiovascular complications (e.g., myocardial infarction, non-fatal cardiac arrest, cardiac death) are not uncommon after elective non-cardiac surgery. For example, contemporary estimates suggest that, among patients aged 45 years or major noncardiac surgery, 3.9% experience myocardial infarction, 0.2% experience nonfatal cardiac arrest, and 0.7% experience symptomatic heart failure.

Although most of these complications are not attributable to anesthesia, anesthesiologists may play an important role in modifying the risk for perioperative cardiac events, through preoperative testing, stable management of intraoperative hemodynamics, and maintenance of normothermia.[34–37]

2. Respiratory Complications

The major anesthesia-related respiratory complications, namely aspiration and failure to intubate, are relatively uncommon. It is important to be aware of the overall importance of postoperative

respiratory complications. Major respiratory complications include respiratory failure, which occurs in 3.4 to 4.7% of patients, and postoperative pneumonia, which afflicts 1.5% to 2.4% of patients.[38–41] Anesthesiologists can intervene to prevent major respiratory complications, by avoiding long-acting paralytic agents intraoperatively,[42] using postoperative epidural analgesia,[43] and perhaps applying select lung-protective mechanical ventilation strategies.[44]

3. Neurological Complications

In older adults, postoperative delirium is a relatively common postoperative complication that is associated with increased cost, length-of-stay, complications, and mortality.[45] The reported incidence of postoperative delirium varies widely based on patient (i.e., demographics and comorbidity) and surgery characteristics.[46] Following major elective noncardiac surgery, the risk of postoperative delirium among patients aged 50 years or older is approximately 9%.[47] Anesthesiologists can help potentially mitigate the risk of this complication by avoiding excessively deep levels of anesthesia,[48,49] avoiding specific medications, such as meperidine and long-acting benzodiazepines,[50,51] or using dexmedetomidine for postoperative sedation in select patients.[52,53]

4. Surgical Site Infections

Postoperative wound infections occur in 14% of patients after major elective surgery.[54] These infections are associated with increased hospital length of stay, cost, and re-admission after hospital discharge.[55] Anesthesiologists have the potential to help reduce the risk of postoperative wound infections by adhering to recommended dosing intervals for perioperative antibiotic prophylaxis and maintaining normothermia.[37,56,57]

Summary

1. Mortality and major morbidity after major surgery are reasonably common.

2. Severe perioperative complications that are attributable to anesthesia are rare.

3. Nonetheless, apparently minor anesthesia-related complications (e.g. nausea and vomiting) can still cause considerable distress.

4. Anesthesia management has the potential to reduce other important postoperative complications.

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Chapter 2

AIRWAY MANAGEMENT

Sections:

1. **Airway Management**

Section 2.1

Airway Management

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Learning Objectives

1. Perform a full airway assessment and recognize its limitations
2. Determine which patient populations are at risk for difficult mask ventilation and difficult intubation.
3. Interpret the difficult airway algorithm.
4. Understand the importance of pre-oxygenation and how this can be optimized.
5. Describe the indications for elective and rescue use of a supraglottic airway.
6. Summarize the indications for tracheal intubation.
7. List the risk factors for aspiration.
8. Demonstrate rapid sequence induction, explain its purpose, and describe its indications and limitations.
9. Summarize the requirements for safe extubation.

Airway Anatomy

The anesthesiologist must be familiar with the patients airway from the nose and mouth to the small airways. Our anatomical survey must assess nasal patency, evidence of visible (or invisible lingual) tonsillar hyperplasia, the integrity of the native teeth, the presence of dental prostheses, the size and compliance of the tongue, neck circumference, cervical and temporomandibular mobility and identification of the cricothyroid membrane and cricoid cartilage.

Such familiarity is required since the anesthesiologist assumes responsibility for the patients airway if unconsciousness is induced or paralytic agents are administered. We must be assured of our ability to provide a patent airway and maintain ventilation and oxygenation. Failure to do so can very quickly result in tragic consequences.

Anatomical and functional concerns regarding the digestive tract relate to the relative risk of regurgitation or aspiration.

The nasopharynx serves as a heat and moisture exchanger. Three large turbinates protrude into the nasopharynx like vascular scrolls. The turbinates, nasopharyngeal mucosa or adenoid tissue, can be damaged by the insertion of a nasal airways.

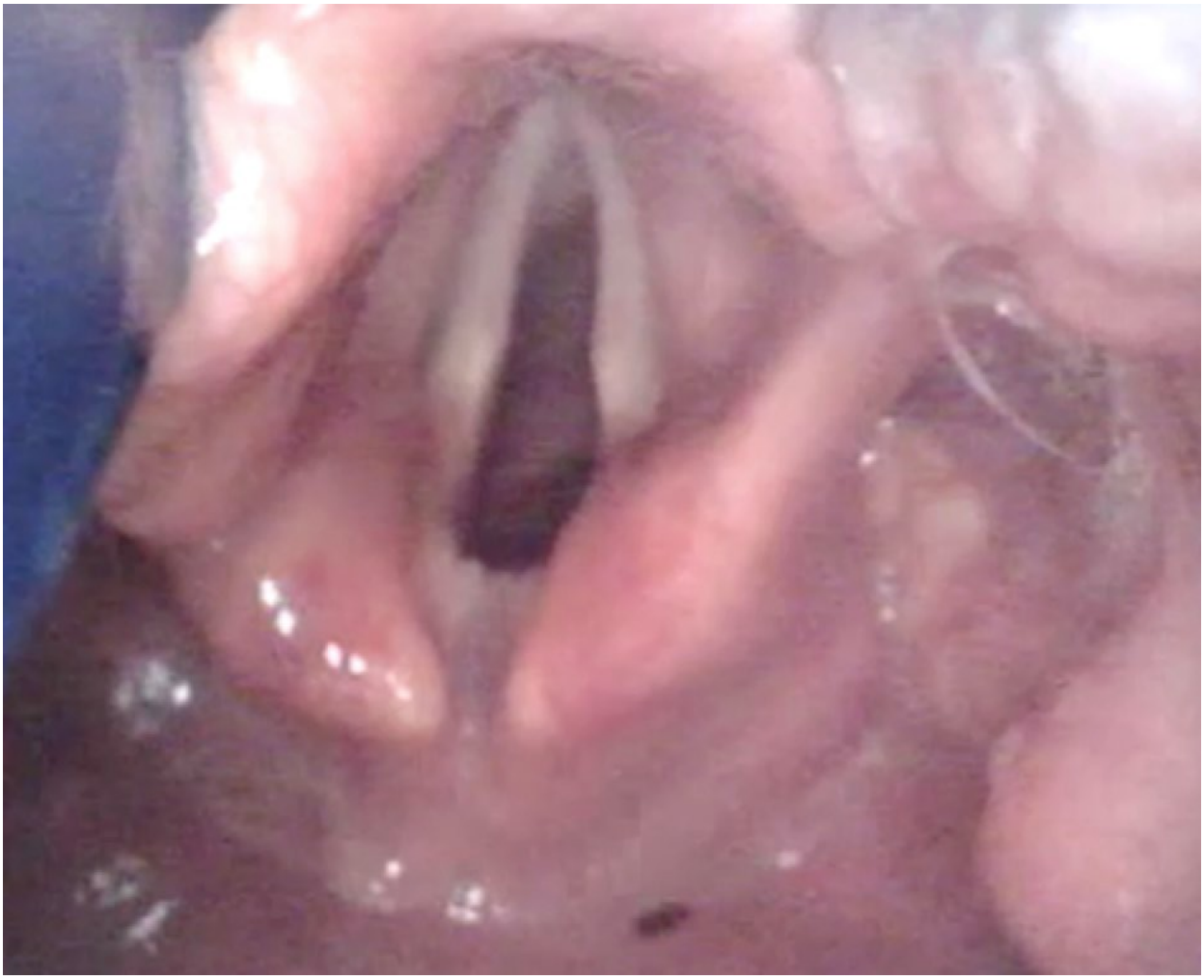
Intubation has traditionally been achieved by direct laryngoscopy. This demands a direct line-of-sight to the larynx. It is customary to speak of three anatomical axes: the mouth, the oropharynx and the trachea. We attempt to align these axes to achieve a line-of- sight, by positioning the head in the 'sniffing position' or flexion-extension. This involves lower cervical flexion and atlanto-axial extension.

> *Controversy 1: Such positioning may not be much better than the neutral position,[1] and in some cases, "flexion-flexion" actually improves the laryngeal view.[2] To the extent that positioning alone does not align the axes, direct laryngoscopy entails a complex set of maneuvers that include leftward tongue displacement*

and compression, mandibular and epiglottic elevation and occasionally the external application of posterior laryngeal displacement, referred to as BURP (backward, upward, rightward pressure). Thus, two simple maneuvers, HELP (head elevation laryngoscopy position) and BURP might quickly improve the laryngeal view.

The epiglottis resides just caudal to the tongue base. The space anterior to the epiglottis is the vallecula, the destination point for a curved laryngoscope blade, the most common of which is a Macintosh blade. By applying force along the axis of the laryngoscope handle, the epiglottis is raised revealing the larynx and its associated structures. These consist of the arytenoid cartilages (and the posterior commissure), the vocal folds and the vestibular folds. The vocal folds form a triangle with its apex, not always visible, at the anterior commissure and the base formed by the space between the corniculate cartilages of the arytenoids (see Figure 1). This is the most reliable landmark to differentiate the glottis from the esophagus.

FIGURE 1- LARYNGOSCOPIC VIEW. THE LARYNGOSCOPE HAS ELEVATED THE EPIGLOTTIS



Try to identify 1) epiglottis, 2) arytenoid cartilages, 3) posterior commissure 4) vestibular folds 5) vocal folds/cords and 6) esophageal inlet.

The trachea is immediately anterior to the esophagus and thus, in the recumbent position, gravity provides some protection against pulmonary aspiration. However, when the protective reflexes are abolished by decreased consciousness, neuromuscular blockade or diminished esophageal sphincter tone, gastric contents may migrate from the stomach to the oropharynx along the pressure gradient. If mask ventilation is attempted with a partial or completely obstructed airway, the oxygen will follow the path of least resistance, inflating the stomach and increasing the risk of passive regurgitation and pulmonary aspiration. To reduce this risk, we endeavor to relieve obstruction with a jaw thrust, oral or nasal airway. Bag to facemask ventilation is an important clinical skill but it is often poorly performed by non-experts. Factors that predict difficult face mask ventilation include are shown in Table 1.

TABLE 1. PREDICTORS OF DIFFICULT FACE MASK VENTILATION[3]

- Higher body mass index or weight
- Older age
- Male sex
- Limited mandibular protrusion
- Decreased thyromental distance
- Modified Mallampati class 3 or 4
- Beard
- Lack of teeth
- History of snoring or obstructive sleep apnea
- History of neck radiation

In high-risk settings, we employ a strategy referred to as a **Rapid Sequence Induction/**Intubation (RSI) which among other things includes the application of pressure against the cricoid cartilage, to reduce pulmonary aspiration (see below). Just above the cricoid cartilage is the cricothyroid membrane. This is an important landmark since it is the easiest surgical access point if other methods fail to establish an airway or provide adequate oxygenation. The cricothyroid membrane is superficial and relatively avascular, making it the site of choice for an emergency surgical airway when we can neither intubate nor oxygenate the patient.

Evaluation of the Airway

Airway history: The patient should be asked about previous anesthetics realizing that patients may not always be aware of previously encountered airway difficulties or how these were managed; they also may not appreciate the importance of conveying this information. Erroneous assumptions can be hazardous. When possible, previous anesthetic records should be reviewed. Determine whether there is a history of snoring, sleep apnea, recent food ingestion, nausea or gastroesophageal reflux (see Table 1).

Airway examination: should assess features that help predict the degree of difficulty for bag mask ventilation, (Table 1) direct laryngoscopy (Table 2), insertion of a supraglottic airway and emergency surgical access.[3]

TABLE 2: PREDICTORS OF DIFFICULT DIRECT LARYNGOSCOPY[3]

- Limited mouth opening
- Limited mandibular protrusion
- Narrow dental arch
- Decreased thyromental distance
- Modified Mallampati class 3 or 4
- Decreased submandibular compliance
- Decreased sternomental distance
- Limited head and upper neck extension
- Increased neck circumference

It is also important to identify the cricoid cartilage and cricothyroid space. The oropharyngeal view is commonly referred to as the Mallampati view though more commonly, a modification of this is used.[4] This assessment is made while facing a seated patient whose head is in a neutral position with the tongue maximally protruded, without phonation. Mobility of the temporomandibular joint can be assessed by asking the patient to bite his upper lip. The inability to prognath the mandible predicts greater difficulty for direct and video laryngoscopy.[5,6]

Modified Mallampati oropharyngeal views[4] (see Figure 3)

- Class I—reveals the entire palate, uvula and tonsillar pillars
- Class II—the tonsillar pillars cannot be seen
- Class III—the soft palate and the base of the uvula are seen
- Class IV—the soft palate is not visible.

Controversy 2: The Mallampati view focuses on the relative volume of the tongue within the mouth and the space available to accommodate a direct laryngoscope, ETT and the operator's line-of-sight. All of the airway tests, referred to above, individually and collectively at best have moderate sensitivity and specificity. In approximately 6% of adults, direct laryngoscopy will unexpectedly fail to reveal the larynx.[7] They also suffer from limited inter-observer agreement. Finally, they were all designed to predict difficulty with direct (Macintosh) laryngoscopy. Difficult direct laryngoscopy does not necessarily mean that intubation by other means will be difficult.

When we manage the airway, we are attempting to optimize oxygenation and ventilation, relieve obstruction, and protect the airway from soiling. The airway evaluation should be directed toward determining the ease of achieving these objectives.

1. **What airway intervention is required**? There are primarily four ways of providing oxygenation:

a. face mask

b. supraglottic airway

c. tracheal tube or rarely

d. a surgical approach (cricothyroidotomy or tracheotomy).

2. How can we best prevent oxygen desaturation? Is apnea during an airway intervention likely to lead to rapid desaturation? Is re-oxygenation likely to be feasible? Effective pre-oxygenation largely replaces the nitrogen in the lung with oxygen. Its effectiveness can be judged by end-tidal O_2 (rather than SpO_2). Some patients will desaturate more quickly or their airway intervention may be prolonged. Correction of hypoxemia (re-oxygenation) may also be more difficult in certain patients.

Factors associated with difficulties in mask ventilation (Table 1) include a poor face-to-mask fit, a beard, a patient lacking teeth, increased age, obesity, a history of snoring and a poor oropharyngeal view.[8] The mnemonic MOANS (Mask fit, Obesity, Advanced age, No teeth and Snoring, Stiff lungs) has been proposed.[9] It is important to quickly recognize and if possible correct inadequate bag-mask-ventilation (BMV) by repositioning the head, the jaw or the mask. If these fail, insertion of a nasal or oropharyngeal airway may be required. Sometimes, it will be necessary to apply the mask with two hands. Difficult BMV will be encountered in 1-5%; impossible BMV is much less common.[8] When these efforts fail, two approaches are possible: insertion of a supraglottic airway (e.g. laryngeal mask airway) or attempt tracheal intubation. Fortunately, the combination of failed ventilation and intubation is rare. It is referred to by various names, but CICO ("KY-KO": can't intubate, can't oxygenate) best describes the situation and to avert disaster, it requires prompt action.[10-12]

3. Anesthesia and neuromuscular blockers eliminate the patient's ability to protect their airway against soiling. Is the patient at increased risk of regurgitation, vomiting or aspiration? Patients falling into this category include those with recent food ingestion, gastro-esophageal reflux, decreased GI motility or obstruction, increased intra-abdominal pressure (ascites, pregnancy) or severe obesity. When such conditions are present, a "Rapid Sequence Induction" (RSI) is usually performed (see below).

4. Can the airway be secured? As mentioned above, the airway can be secured in a variety of ways. These can be categorized as supraglottic, transglottic and infraglottic. Our history and physical examination may reveal patients in whom one or more of these approaches may be predictably difficult or impossible. Most difficulties with intubation are encountered because of anatomic features that obstruct the view from the laryngoscopist's eye to the patient's larynx (see Figure 2). There are many possible approaches to such problem. The most important techniques include direct laryngoscopy, indirect laryngoscopy (e.g. videolaryngoscopy), use of a stylet or tracheal introducer ("bougie"), intubation through a conduit such as a supraglottic airway or flexible bronchoscopic intubation. If the problem relates to intrinsic obstruction or extrinsic compression, it may be necessary to use a smaller tube or to introduce the tube below the obstruction. This situation may result from anaphylaxis, angioneurotic edema, tumor, vascular, infectious or traumatic causes.

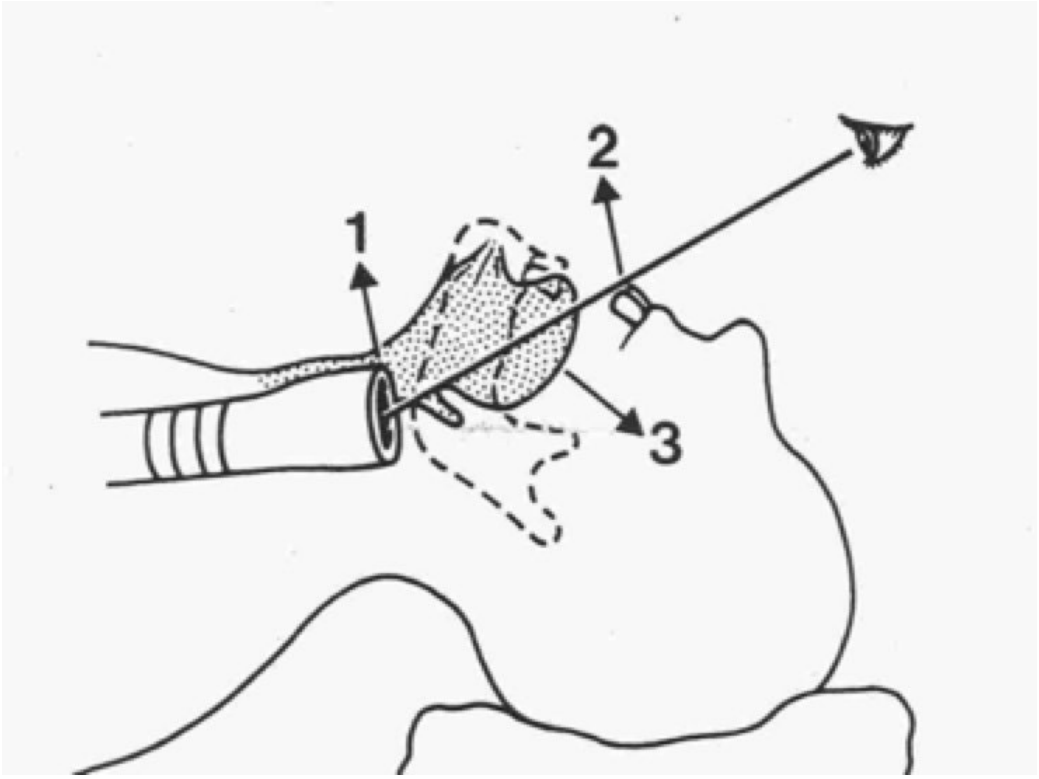
Pre-oxygenation[13]

We encounter some patients who present with diminished oxygen reserves or increased oxygen consumption. Furthermore, we know that our ability to predict a difficult airway lacks sensitivity and specificity. Attempting to maximize the patient's oxygen reserves will improve tolerance to apnea or inadequate ventilation. This can be achieved by the application of a tight face mask, continuous positive airway pressure (CPAP), bilevel positive pressure (BiPAP) or oxygen by high flow nasal cannulae (NODESAT [10 liters/min] or transnasal humidified rapid insufflation ventilator exchange ("THRIVE"™ [30-70 LPM]). We endeavor to achieve an end-tidal O_2 of 90%.

Direct Laryngoscopy (DL)

This is the traditional means of inserting an endotracheal tube (ETT) and a method you must become familiar with if not comfortable performing. Neither technique nor instrumentation has changed appreciably since first used by Miller (straight blade) and Macintosh (curved blade) in 1941 and 1942, respectively.

FIGURE 2-INEXPERIENCED USERS COMMONLY LEVER THE LARYNGOSCOPE HANDLE RISKING INJURY TO THE UPPER INCISORS. IN ADDITION TO DENTAL DAMAGE, THIS ACTUALLY WORSENS THE VIEW SINCE THE TIP OF THE BLADE ELEVATES THE LARYNGEAL AXIS, MAKING IT MORE DIFFICULT TO SEE. FROM CORMACK AND LEHANE.[14]



When performing DL, it is customary to position the patient in the sniffing position with the head elevated slightly and the neck extended. The laryngoscope is carefully introduced into the patient's mouth on the right side of the tongue. The curved Macintosh laryngoscope blade is advanced behind and around the tongue which is deflected leftward and compressed anteriorly. As the blade is advanced, the epiglottis should become visible. The blade is introduced into the space anterior to the epiglottis (vallecula) and the laryngoscope is lifted away from the operator in the plane of the laryngoscope handle. By applying pressure to the hypoepiglottic ligament, the epiglottis is elevated revealing the larynx. If an inadequate view is obtained, the patient and blade may be repositioned and/or "external laryngeal pressure" may be applied to manipulate the larynx backward, upward and rightward (BURP).[15] (N.B. BURP is NOT the same as cricoid pressure—see below).

The most commonly used classification of laryngeal views obtained during laryngoscopy is the Cormack-Lehane classification.[14] (see Figure 4)

- Grade 1: All the laryngeal structures are revealed.
- Grade 2: Only the posterior laryngeal structures are visible. This is sometimes sub-classified as 2A (posterior vocal folds) and 2B (arytenoids only).
- Grade 3: The larynx is concealed and only the epiglottis can be seen. This is sometimes sub-classified as 3A (epiglottis can be lifted) and 3B (epiglottis cannot be lifted).
- Grade 4: Neither the glottis nor epiglottis can be seen.

When a C/L 3 or 4 view is obtained, it may be possible to improve the view by applying BURP or switching blades. Some advocate the use of an adjuvant such as a bougie (also known as a tracheal introducer). This is a hockey stick-shaped device (coudé tip) which is inserted blindly under the epiglottis. An endotracheal tube is then advanced over the bougie. This technique was widely practiced and is reasonable when conditions do not permit an alternative technique that may provide a laryngeal

view.[11] If oxygenation is maintained and the equipment and expertise are available, it is preferable to use an alternative technique such as video laryngoscopy.[12] When the laryngeal view is blocked by the epiglottis, a straight blade (e.g. Miller, Henderson) can be introduced along the right side of the tongue and posterior to the epiglottis, lifting it up and out of the way. Whenever possible, blind advancement of the tracheal tube should be avoided. When a stylet has been used, it should be withdrawn after the tracheal tube is inserted a few centimeters beyond the larynx.

(NB. Inexperienced users commonly lever the laryngoscope handle risking injury to the upper incisors. Your mentors will be most impressed if you refrain from doing this.)

In addition to dental damage, such levering actually worsens the view since the tip of the blade elevates the laryngeal axis making it more difficult to see. The Mallampati ororpharyngeal view and Cormack-Lehane laryngeal views are depicted in Figures 3 and 4 respectively. The former is intended as predictive view; the latter is the outcome.

The intubation technique will be demonstrated through hands-on seminar in this rotation and you may also refer to the following video for a tutorial.

https://www.youtube.com/watch?v=ZJtFb7lGPic

Controversy 3: Failure to visualize the larynx using DL is usually referred to as "difficult" or "awkward" laryngoscopy; it's neither. If the larynx was not seen, it really is "failed laryngoscopy" even if intubation is successful.

FIGURE 3: THE MODIFIED MALLAMPATI CLASSIFICATION OF OROPHARYNGEAL VIEW AFTER SAMSOON AND YOUNG. IMAGES A THROUGH D SHOW CLASS I – IV RESPECTIVELY. FROM BARASH, CLINICAL ANESTHESIA 7TH ED. LIPPINCOTT WILLIAMS-WILKINS, 2013. (FIG 27-7)

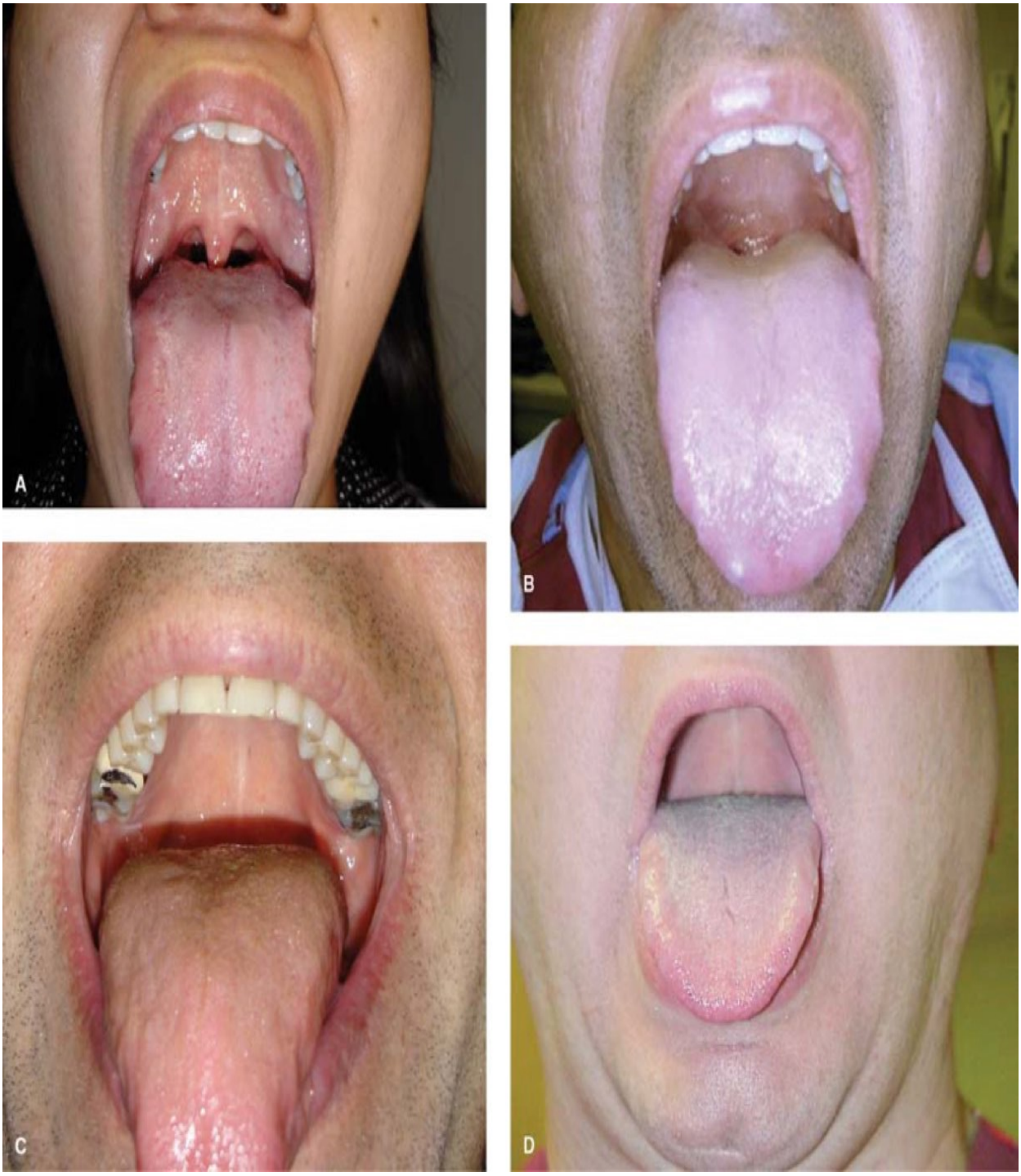
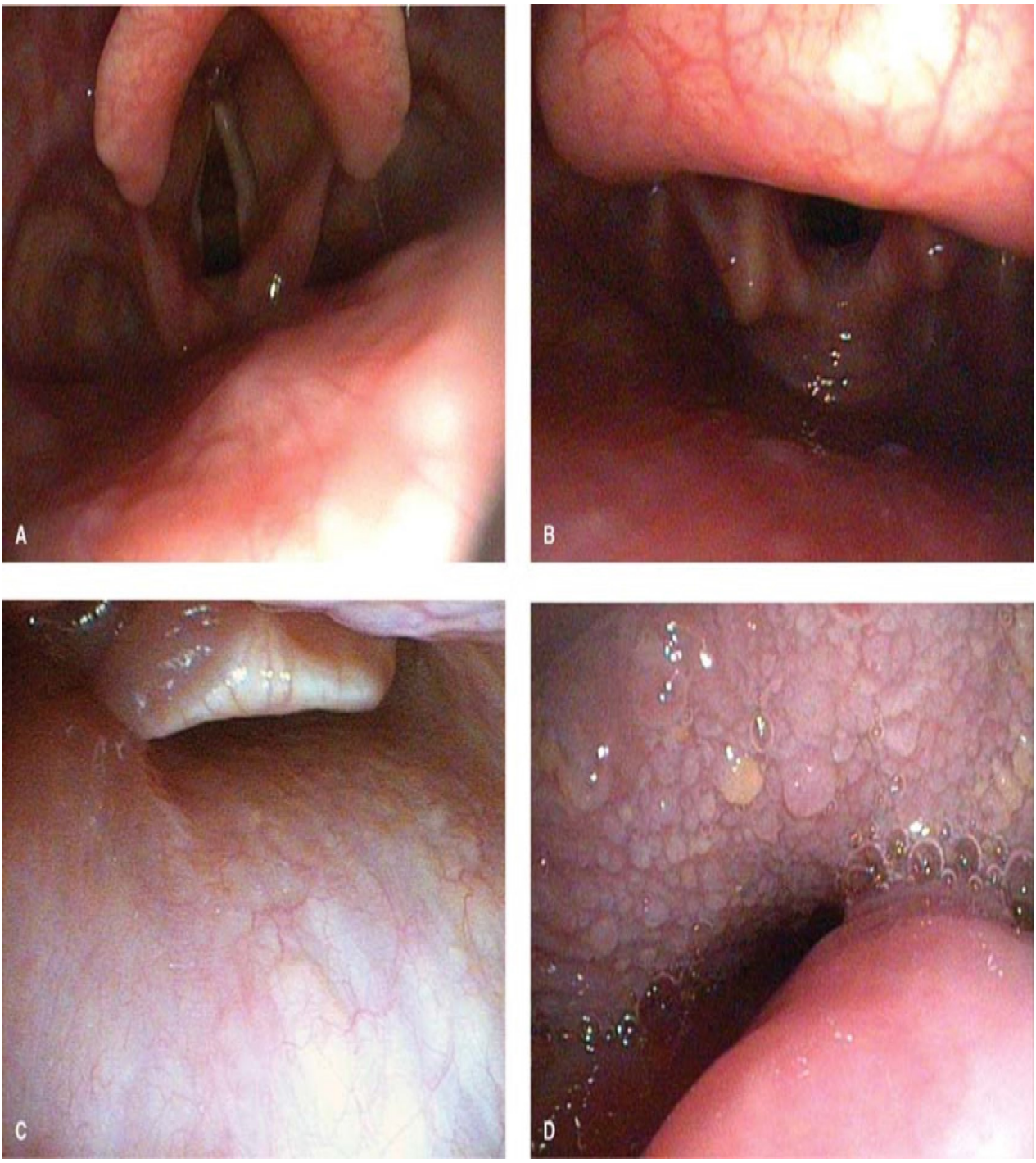


FIGURE 4: MODIFIED CORMACK-LEHANE LARYNGEAL VIEWS 1-4 (A-D) FROM BARASH, CLINICAL ANESTHESIA 7TH ED. LIPPINCOTT WILLIAMS-WILKINS, 2013 (FIG 27-10).



The following points require emphasizing: [11,12]

- the total number of attempts should be limited
- each subsequent attempt should be selected with the expectation that it is more likely to succeed; repeated attempts with the same technique squanders time risking additional injury and conversion to a "Can't intubate, can't oxygenate" or CICO (see below)
- call for help early

Difficult BMV *or* difficult DL is not uncommon, and does not constitute an emergency. Airway managers should be comfortable transitioning to alternative techniques. Such alternatives must be readily available (e.g., difficult airway cart) and familiar to the care provider or they are of no value and may put the

patient in further jeopardy. There are numerous algorithms pertaining to the management of the airway. Of particular relevance are those of the American Society of Anesthesiologists,[10] the Canadian Airway Focus Group[3,11] and the Difficult Airway Society.[12] The Vortex Airway Approach is a cognitive aid that complements these algorithms, emphasizing the importance of clear communication and situational awareness.[16] These are discussed below. A detailed discussion is beyond the scope of this chapter, but the reader is encouraged to seek out further information from references or clinicians.[17]

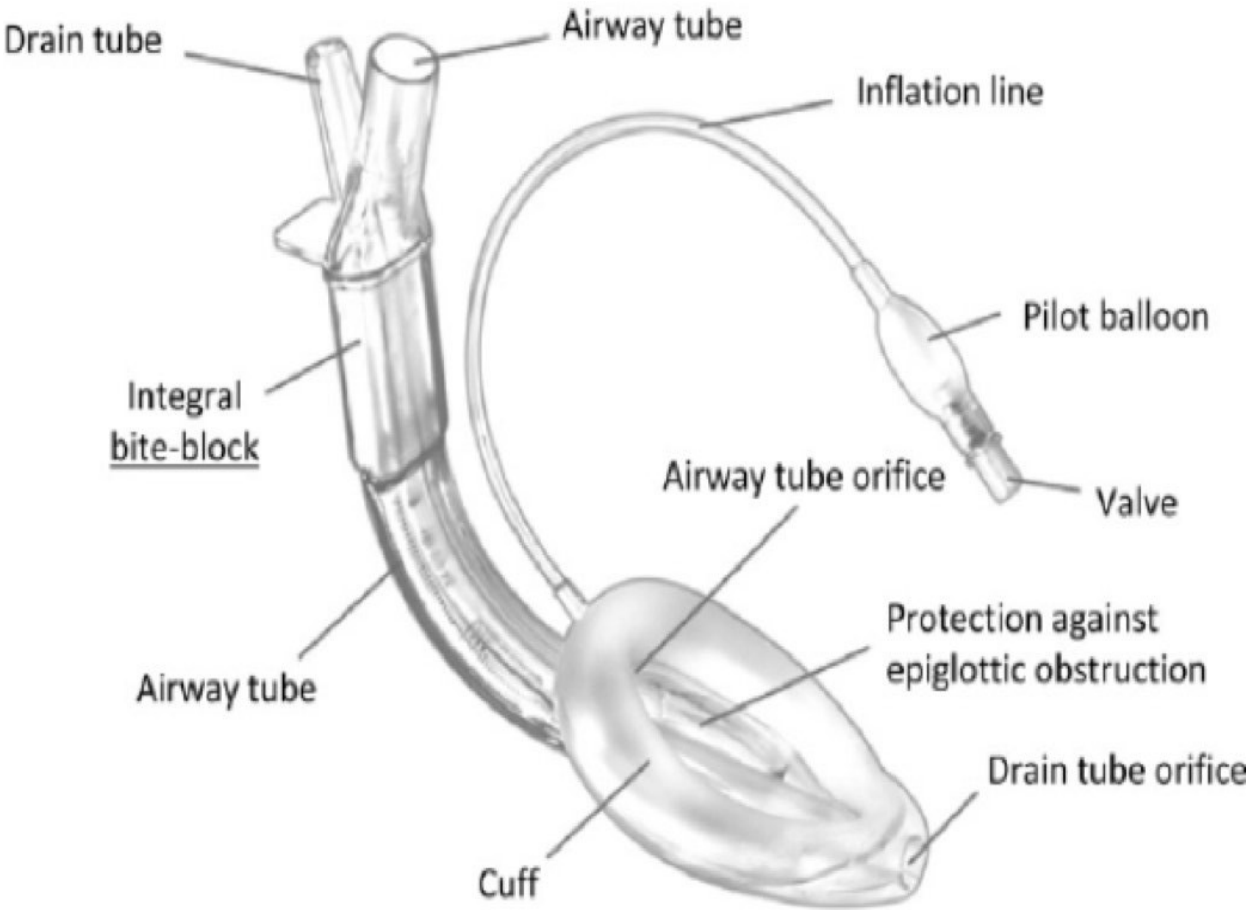
Supraglottic Airways (SGA)

The Laryngeal Mask Airway™ was originally introduced into clinical practice by Dr. Archie Brain in 1989 (slightly later in North America). Since that time, this device has profoundly changed airway management. In some places, this device has become the method of choice for spontaneously breathing and mechanically ventilated patients undergoing surgery. Newer generation SGAs provide a better airway seal permitting the ventilation of patients with reduced lung compliance. Some of these devices provide better separation of the respiratory and alimentary tracts.

The LMA (Figure 5) is so firmly entrenched into clinical practice that people mistakenly refer to all SGAs as LMAs. The LMA now consists of a family of related products and are available in single-use and reusable versions. These products have an excellent safety record and have spawned many related devices. The LMA products include the Unique,™ Supreme,™ Fastrach,™ Flexible LMA and LMA Protector™ (http://www.lmaco.com/products/). The range of these products can be seen at this website as well as videos depicting the insertion technique.

Examples of other SGAs include the iGel, Air-Q, Ambu AuraGain™ and TotalTrack™ among many others. Relative contraindications are controversial but for elective purposes, they should not be used in patients at increased risk of regurgitation. As a rescue device, when BMV fails and oxygenation is declining, the only contraindication is lack of familiarity. A detailed discussion of these devices and how they should be used is beyond the scope of this chapter. All but the iGel have inflatable cuffs and all are positioned in the hypopharynx, like a cork in a bottle, at the upper esophageal sphincter. Properly positioned, they provide a relatively good seal over the laryngeal inlet. However, if improperly placed, they may cause down-folding of the epiglottis or provide a direct conduit from the esophagus to the trachea. Some SGAs can serve as a conduit for bronchoscopic tracheal intubation.

FIGURE 5: LARYNGEAL MASK AIRWAY SUPREME™



This is a drawing of the LMA Supreme™, a single-use version of the LMA ProSeal™. There is a single inflating "pilot tube" that communicates with a two-compartment cuff: one that overlies the larynx and the other on its dorsal side, making contact with the posterior pharyngeal wall. The drain tube sits at the upper esophageal sphincter and provides access to the esophagus and stomach should decompression be required. The Supreme has a rigid shaft to facilitate insertion and there are multiple tests that can be performed to ensure that the device is well-seated.[18]

Controversy 4: The LMA has such a good safety record, some practitioners have extended the indications to include situations previously considered ill-advised if not frankly contraindicated, such as long cases (>4 hours), morbidly obese patients, compromised positions (e.g. prone), laparoscopic surgery with peritoneal insufflation and pregnant patients undergoing Caesarean section. Undoubtedly, the avoidance of complications has a great deal to do with familiarity with the devices and the skill of deployment. The greatest concern about the safety of SGAs relates to protection from aspiration. In this regard, the safety record of the LMA in experienced hands may be comparable to a cuffed ETT. SGAs are considered advanced airway techniques, comparable to endotracheal intubation for purposes of Advanced Cardiac Life Support.

Flexible Bronchoscopic Intubation[19-21]

Intubation over a flexible bronchoscope (FB) is a technically demanding but essential skill with considerable versatility. It is often referred to as the gold standard technique when managing difficult airways. This technique is often employed in the conscious, spontaneously breathing patient following the administration of mild sedation, an anti-sialagogue (e.g. atropine or glycopyrrolate) and the application of topical anesthesia or nerve blocks. A tracheal tube is preloaded over the bronchoscope, both of which are then introduced through the nose, mouth, tracheal stoma or a SGA conduit. The tracheal tube is then railroaded over the bronchoscope. When used orally, it is essential to displace the

tongue by grasping or elevating it. A bite block is used to ensure that a conscious patient cannot bite down on the bronchoscope. In capable hands, there are relatively few anatomical situations that a bronchoscope cannot circumvent. But the procedure takes some time and may not be suitable in the face of a low or falling SpO_2 or when the view is obscured by blood or secretions. In addition, ETT advancement over the bronchoscope is essentially blind; ETT advancement may be encumbered by a vocal cord or arytenoid cartilage.

Indirect Laryngoscopy (Video laryngoscopy and Optical Stylets)[22,23,24 25]

Indirect laryngoscopy essentially means that airway is viewed on a monitor. The view is obtained by fiberoptics or more commonly from a tiny video camera embedded in a laryngoscope blade, stylet or flexible endoscope. Because they do not rely on a direct line-of-sight (Figure 2) the laryngeal view may be far better than that seen by direct laryngoscopy. There are many devices that fall into this category. Essentially, these are stylet-type or retractor type devices.

Optical stylets: They can be divided into those that are essentially rigid stylets examples of which include the Bonfils, Shikani SOS, Levitan FPS and Clarus Video System.

Video laryngoscopes: laryngoscopes that retract the tongue can also incorporate video cameras (or prisms) and are often divided into channeled and non-channeled devices.

Channeled devices have a tube slot that accommodates the tracheal tube. The laryngoscope is positioned at the tongue base and depending upon the device, is introduced into the vallecula or beneath the epiglottis. Examples of channeled video laryngoscopes include the Airtraq, Pentax/Ambu AWS and the King Vision Scope.

Non-channeled video laryngoscopes require independent manipulation of the scope and the tracheal tube with the left and right hands respectively. These can be subdivided into two categories: Macintosh-style and acute angle video laryngoscopes. Macintosh-style blades can generally be used for direct and indirect viewing, the technique being much the same as that described for DL. The most popular examples of these devices include the C-MAC, GlideScope (Mac-T) and McGrath MAC. Acute-angled video laryngoscopes generally provide a more anterior view and are thus often used for airways that are assessed to be more difficult to visualize. The most common examples are the C-MAC D-blade, the GlideScope and the McGrath X-blade. They are intended for indirect viewing only and require a different technique. The blade is generally inserted in the midline (rather than on the right side of the tongue). The blade is essentially rotated around the tongue base (rather than displacing and compressing it). The blade should not be introduced too deeply into the vallecula. The laryngoscopist should endeav or to avoid rotating the handle back as this will tilt the larynx upward and despite a good view, intubation will be more difficult. A stylet should be employed since the larynx is not in the line-of-sight and the tracheal tube must therefore be directed around the tongue base and advanced toward and through the vocal cords.[22,26] To avoid soft tissue injuries, it is important to introduce the tracheal tube into the mouth and past the soft palate under direct vision, before turning your attention to the monitor. The tracheal tube should be positioned close to the blade, essentially mimicking the trajectory of the laryngoscope. The laryngoscope is lifted creating space in the pharynx; the tracheal tube is positioned in the midline between and below the arytenoids. Then a simple lift and slight tilt will generall y direct the tracheal tube through the vocal cords.

Direct laryngoscopy can be viewed only by the laryngoscopist; when using a video laryngoscope, others can share the view with the operator. This enables better supervision and more meaningful real-time feedback to a trainee.[27] Some of the video laryngoscopes permit video playback for subsequent review with a mentor. Video capture is also useful for clinical documentation, quality control, teaching and research.

> *Controversy 5: This author is of the opinion that VL represents the future of laryngoscopy much as ultrasound has become a point of care diagnostic tool. Collectively, these devices permit a much higher rate of visualized laryngoscopies, with less tissue distraction and compression, cervical manipulation and applied*

force enabling tracheal tube delivery and insertion but such outcomes are dependent upon operator technique. Video chips are becoming smaller, with higher resolution at a lower cost. Until these devices are universally available, we are obliged to teach DL though this can be achieved, perhaps more effectively with Macintosh-style VL.

Rapid Sequence Induction [28]

Glottic closure and a cough are two protective reflexes that guard against pulmonary aspiration. When unconsciousness and muscle relaxation are induced, these reflexes are surrendered. When patients have gastro-esophageal reflux or intragastric pressure that exceeds the lower esophageal sphincter tone, stomach contents may ascend into the esophagus leaving the patient at risk of pulmonary aspiration (Table 3). In such circumstances, we attempt to secure the airway as rapidly as possible. A routine, known as "rapid sequence induction" (RSI), is used to achieve this (Table 4). Before beginning this sequence, or any induction, it is important to ensure that all the required equipment will be immediately available. The mnemonic SLOPESSS (suction, laryngoscope, O2 source, positive pressure, endotracheal tube, stylet, syringe and stethoscope/CO2 detector) may provide a helpful reminder. Our efforts are aimed at minimizing the oxygen desaturation, preventing regurgitation, and securing the airway as expeditiously as possible.

TABLE 3 - PATIENTS AT INCREASED RISK OF REGURGITATION.

Diminished lower esophageal sphincter tone (GERD)
Increased intragastric pressure Bowel obstruction non-fasted stated
Increased extragastric pressure Pregnancy Ascites Morbid obesity
Altered GI motility
Altered esophageal anatomy Achalasia Zenker's Diverticulum
Neuropathy Diabetes Renal failure
Medications Narcotics

TABLE 4 - RAPID SEQUENCE INDUCTION (RSI).

1. Pre-oxygenation
2. Yankauer suction under the pillow
3. Spare laryngoscope/backup plans (discussed with team)
4. Predetermined dose of fast acting hypnotic/relaxant
5. Avoidance of positive pressure ventilation (PPV)
6. Cricoid pressure applied (2 kg/20N with drowsiness, 3 kg/30N with loss of consciousness)
7. Laryngoscopy performed when muscle relaxation achieved
8. Cricoid pressure maintained until ETT cuff inflated and placement confirmed

Controversy 6: Cricoid pressure was advocated by Sellick[29] to minimize the gastric insufflation during positive pressure ventilation and the risk of regurgitation. He stated that "firm" pressure applied to the cricoid cartilage forced the latter against a cervical vertebra thereby occluding the esophagus.

The scientific evidence is not very compelling but this became a standard of care in the management of patients at increased risk of regurgitation. Mysteriously, the proscription against positive pressure ventilation during a "rapid sequence induction" also became part of this regimen, though it was not recommended by Sellick. There are several flaws in the theory, including the recent recognition that the cricoid cartilage is compressible,[30] cricoid pressure may displace the esophagus, [31] the cricoid cartilage frequently does not align with the esophagus,[32] cricoid pressure may make laryngoscopy more difficult thus delaying intubation and it may actually promote airway obstruction. Though the scientific evidence may be lacking, cricoid pressure is still widely practiced, with various modifications, in patients at risk of pulmonary aspiration of gastric contents.

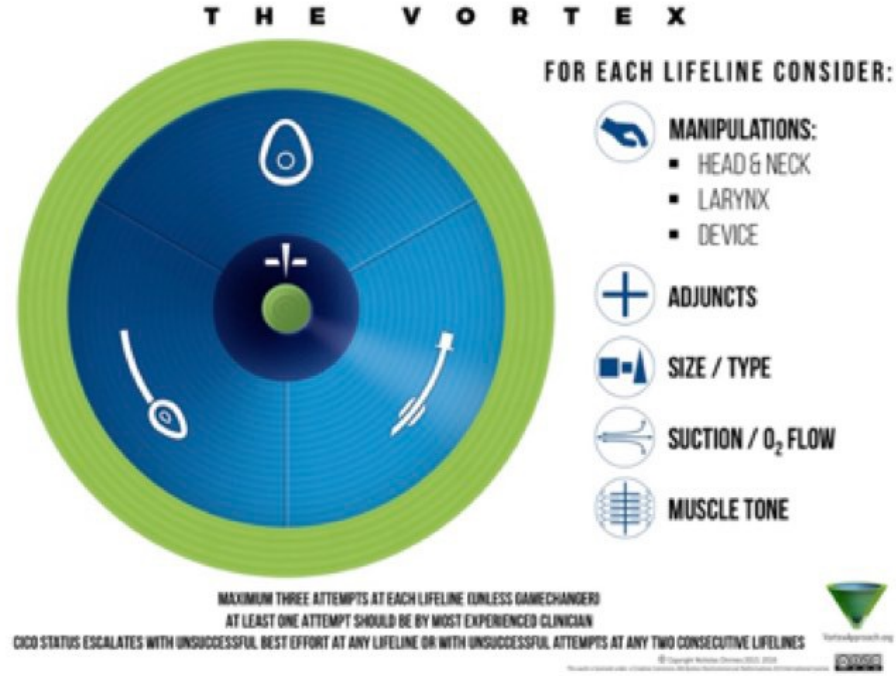
Surgical Airway

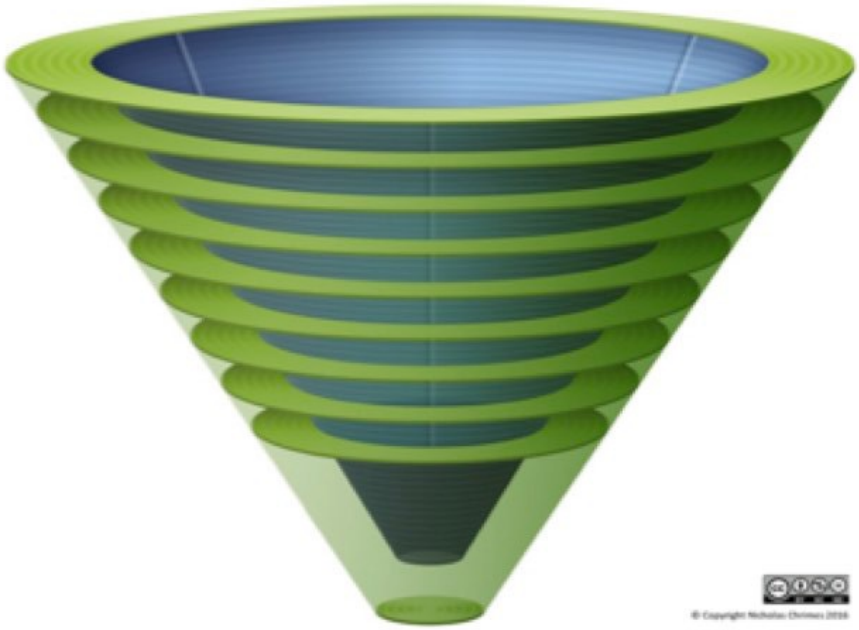
Rarely, all efforts to achieve ventilation fail: face mask, SGA and tracheal intubation. If spontaneous ventilation cannot be quickly reestablished, life-threatening hypoxemia may ensue. This situation, usually referred to as "can't intubate can't oxygenate" or CICO can be remedied in several ways: i) placement of a catheter through the cricothyroid membrane; ii) placement of a tracheal tube through the cricothyroid membrane or iii) performance of a tracheotomy. There is little debate about the site for rescue: the cricothyroid membrane. There has been very little research into the best method of performing "CICO rescue" but it is clear that this is poorly done. At least in cadavers, it appears that scalpel-bougie-tube technique was the easiest, fastest and safest approach after training.[33] This technique has been recommended as the preferred approach for an emergency surgical airway.[12]

Airway Algorithms

Respiratory complications remain the single greatest cause of serious adverse anesthetic events and these are often a consequence of poor planning, delays in recognition and denial of the difficulties and persistence with ineffective strategies. Airway algorithms have been developed to assist the clinician in critical decision making. Periodically revised, based upon evidence and expert opinion, these algorithms are intended as practice guidelines rather than standards of care.[3,10-12] The most widely-cited airway algorithm is depicted below (Figure 7) but it is complex and is difficult to recall in times of stress. The Vortex Approach is a cognitive aid (Figure 6), not a competing algorithm, intended to emphasize preparation for and a timely response to airway difficulties by an airway team. It conceptualizes airway management as three zones: a (safe) green zone where oxygenation is not threatened, and light and dark blue zones (where oxygenation is deteriorating with increasing rapidity). The blue intensifies as the vortex narrows with less time to achieve the objective of re-establishing oxygenation.[16]

FIGURE 16:





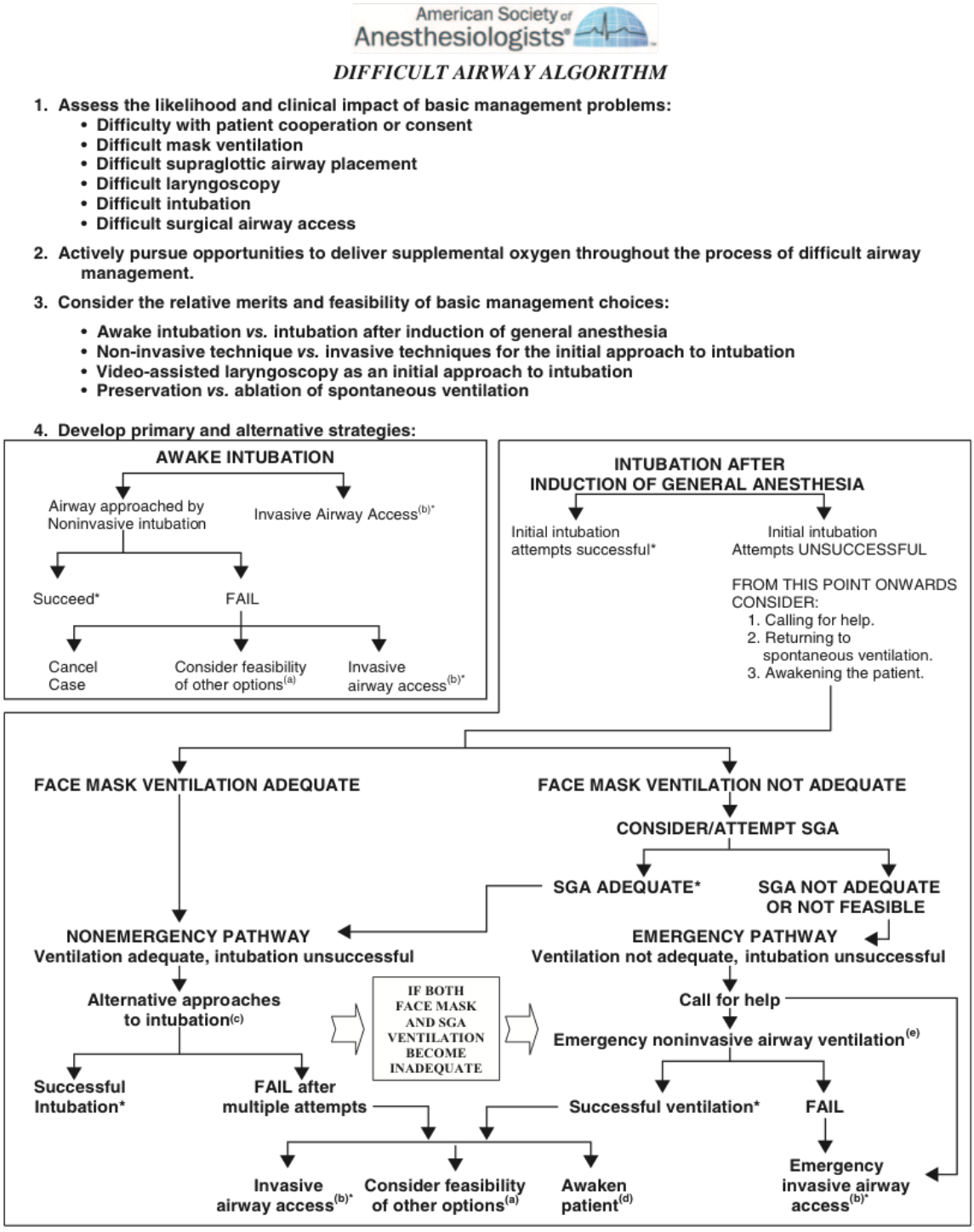
REPRINTED FROM HTTP://VORTEXAPPROACH.ORG/ WITH PERMISSION FROM NICHOLAS CHRIMES. WHILE VISITING THE WEBSITE, YOU ARE STRONGLY ENCOURAGED TO VIEW THE VIDEO OF "THE ELAINE BROMILEY CASE" ALSO AVAILABLE AT HTTPS://VIMEO.COM/103516601 REENACTING A TRUE AND TRAGIC CASE OF POOR PLANNING AND MANAGEMENT.

The most important take-away point of these documents is that the overall objective is the maintenance of oxygenation rather than the placement of plastic. If oxygenation by face mask cannot be achieved despite simple adjustments or adjuncts, placement of a SGA or intubation may correct the problem. It is important to call for help early. This should include additional personnel and equipment bundled on a "difficult airway cart". The latter ensures that all essential rescue devices are immediately available. The number of attempts is controversial: the ASA Practice Guidelines refers to this as "multiple" but virtually every other authority has set a limit. The Canadian Airway Focus Group proposes three but strongly advises that the same method should only be repeated if there is reasonable expectation that the subsequent effort is likely to succeed. Given that our ability to predict airway difficulty is only

moderately effective, the consequences of fixation errors and a limited skill set are high.

When patients with a difficult airway are encountered, it is important to explain to them the problems anticipated or encountered in a way that allows them to understand how this might impact upon their future care. Failure to do so may result in unnecessary risk. It is generally advised that such patients receive a letter and be advised to register with an agency such as the MedicAlert, accessible 24/7, much as they would if they had a life-threatening allergy.

FIGURE 7: THE ASA TASK FORCE IN THE MANAGEMENT OF THE DIFFICULT AIRWAY.[10]



***Confirm ventilation, tracheal intubation, or SGA placement with exhaled CO_2.**

a. Other options include (but are not limited to): surgery utilizing face mask or supraglottic airway (SGA) anesthesia (e.g., LMA, ILMA, laryngeal tube), local anesthesia infiltration or regional nerve blockade. Pursuit of these options usually implies that mask ventilation will not be problematic. Therefore, these options may be of limited value if this step in the algorithm has been reached via the Emergency Pathway.

b. Invasive airway access includes surgical or percutaneous airway, jet ventilation, and retrograde intubation.

c. Alternative difficult intubation approaches include (but are not limited to): video-assisted laryngoscopy, alternative laryngoscope blades, SGA (e.g., LMA or ILMA) as an intubation conduit (with or without fiberoptic guidance), fiberoptic intubation, intubating stylet or tube changer, light wand, and blind oral or nasal intubation.

d. Consider re-preparation of the patient for awake intubation or canceling surgery.

e. Emergency non-invasive airway ventilation consists of a SGA.

Extubation of the Airway

The timing of extubation is always elective and at a minimum the patient must fulfill the following criteria:

- Oxygenation: adequate SpO_2
- Ventilation: spontaneous, sustained, with minimal support able to maintain minute volume adequate to achieve acceptable ET CO_2
- Airway patency: this may be difficult to assess with a tracheal tube in situ
- Airway protection: sufficiently awake to safeguard against aspiration
- Hemodynamically stable
- Responsive to commands

Most surgical procedures are followed by extubation. Required reintubation is uncommon (0.1-0.2%). Certain patients are at an increased risk of requiring reintubation particularly those with reduced cardiorespiratory reserves or who have undergone airway interventions that may result in swelling or bleeding. Of even greater concern are those patients in whom reintubation would be difficult to achieve in a timely and safe manner. These include, among others, patients in whom laryngoscopy had been difficult, requiring multiple attempts or alternative devices, patients with reduced airway access and those whose airways may have become more difficult as a result of medical conditions or surgical interventions.[34] Furthermore, emergent reintubations are often more difficult than those performed under controlled conditions as a consequence of less time and information, hypoxemia, acidosis, hemodynamic instability and limited equipment and personnel. Numerous strategies have been described to manage such patients with the view to optimizing the timing and conduct of their extubation and increasing the likelihood of successful reintubation should this be required.[34,35]

Summary

Airway management is fundamental, challenging and evolving. Since airway and breathing are essential to survival, any physician, sooner or later, may be called upon to provide this service. The basic skills such as bag-mask ventilation and endotracheal intubation require practice to acquire and retain. A concerted effort should be made to learn these skills and opportunities to practice them should be sought out.

The good news is that airway management is improving and, at last, we are being presented with tools that are easier to learn. The bad news is that with the proliferation of equipment, the clinician must make choices. No longer is it a matter of doing your best with a face mask or a direct laryngoscope. We have choices of supraglottic airways, direct laryngoscopy, flexible and rigid fiberoptic scopes, video laryngoscopes and surgical approaches. Technical skill must be combined with clinical judgment. Hopefully, you will take advantage of this opportunity to expand both your skills and your judgment with respect to airway management. These may be called upon regardless of the direction your medical career takes.

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Chapter 3

PHARMACOLOGY

Sections:

1. The Autonomic Nervous System
2. General Pharmacology of Intravenous and Inhalational Anesthetics
3. Opioids
4. Neuromuscular Blocking Agents
5. Local Anesthetics

Section 3.1

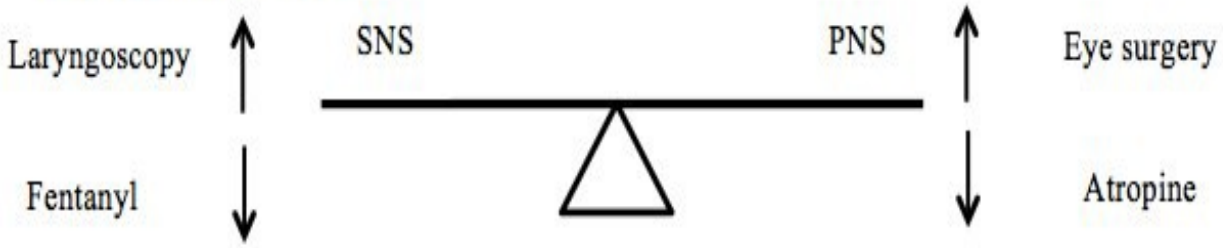
The Autonomic Nervous System

Mital Joshi and Eric You-Ten

Overview

Anesthesiologists constantly utilize and manipulate the autonomic nervous system (ANS). We constantly record and monitor patients' vital signs, a marker of their autonomic nervous system activity, in order to maintain intraoperative homeostasis. The importance of maintaining balance (ie. homeostasis) of the ANS is exemplified below in a clinical case scenario.

Figure 1. Balance of the ANS



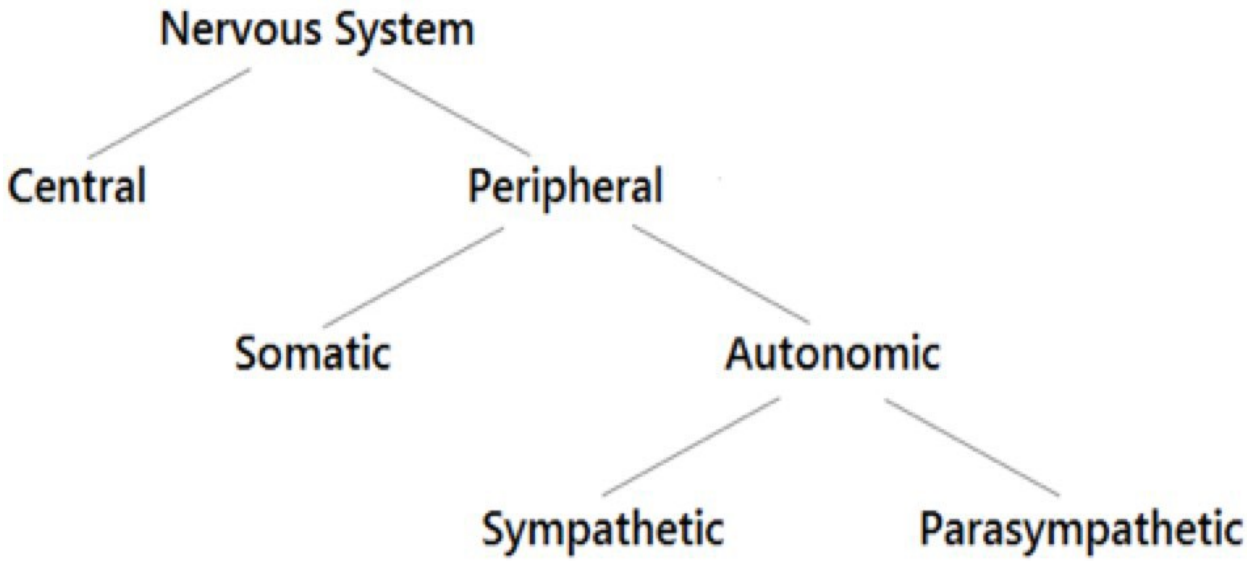
A patient undergoing a general anesthesia for eye surgery is intubated with direct laryngoscopy (Figure 1) which can stimulate the sympathetic nervous system (SNS) to cause significant increase in blood pressure. However, fentanyl is used prior to direct laryngoscopy to blunt the activation of the SNS, therefore maintaining ANS homeostasis. Conversely, traction on the eyeball during surgery can activate the parasympathetic nervous system (PNS) via the ocular-cardiac reflex to cause significant bradycardia. Atropine, an anti-muscarinic agent, is used to blunt the activation of the PNS, therefore preventing bradycardiac and maintaining ANS homeostasis.

Based on the above example, it is no surprise that anesthesia care providers need to have a mastery of the anatomy, physiology and pharmacology of the ANS.

Anatomy

The peripheral nervous system is divided into two major divisions: the somatic nervous system and the autonomic nervous system (Figure 2). The somatic nervous system is voluntary and under direct control, whereas the autonomic nervous system is comprised of intrinsic activity combined with reflexes to certain stimuli. The autonomic nervous system is further subdivided into two major branches: the sympathetic nervous system and the parasympathetic nervous system. Both sympathetic and parasympathetic systems arise from neurons in the spinal cord (preganglionic neurons) and synapse with neurons in the autonomic ganglia (postganglionic neurons) before reaching their effector organs. The SNS and PNS have a different anatomy, a different physiology, and sometimes can be thought of as oppositional systems. Normally, equilibrium exists between intrinsic sympathetic and intrinsic parasympathetic activity. It is in disease and with medications that this balance is altered.

FIGURE 2-ORGANIZATION OF THE NERVOUS SYSTEM.



Sympathetic Nervous System

The sympathetic nervous system is often referred to as the thoracolumbar outflow because the preganglionic neurons originate from the intermediolateral neurons of the spinal cord grey matter from levels T1 to L2 (Table 1). These preganglionic neurons synapse within the sympathetic ganglia, which are fused and lie in a chain formation relatively close to the spinal cord. The neurotransmitter responsible for sympathetic preganglionic transmission is acetylcholine via the nicotinic receptor on the postganglionic neuron. It is the postganglionic neurons that travel to the end organs and release norepinephrine, which produces the sympathetic effect. Therefore, the sympathetic preganglionic fibres are short, and postganglionic fibres tend to be longer. The adrenal medulla is an exception to the above stated paradigm of the SNS. There is only one neuron which originates in the spinal cord and releases acetylcholine at the adrenal medulla, which then causes the adrenal medulla to secrete norepinephrine and epinephrine. The sweat glands are innervated by the SNS, but the neurotransmitter released by the postganglionic cell is acetylcholine.

Parasympathetic Nervous System

The parasympathetic nervous system is referred to as the craniosacral outflow because the preganglionic neurons originate from the midbrain, medulla (the nuclei of cranial nerves III, VII, IX and X) and the sacral nerves (S2 – S4) (Table 1). The parasympathetic fibres run along the course of these nerv es and synapse in the parasympathetic ganglia which lie close to the end organs. In contrast to the sympathetic ganglia, the parasympathetic preganglionic fibres tend to be long, whereas the postganglionic fibres tend to be shorter. Similar to the sympathetic nervous system, acetylcholine is the main preganglionic neurotransmitter of the parasympathetic nervous system, activating nicotinic receptors in the ganglia. The postganglionic neurons also release acetylcholine but instead activate muscarinic receptors in the end organs.

TABLE 1. SUMMARY OF ANS

Organ System	Sympathetic	Parasympathetic
Preganglionic neurons	Thoracolumbar (short axon)	Craniosacral (long axon)
Preganglionic neurotransmitter	Acetylcholine	Acetylcholine
Postganglionic neurons	Long axon	Short axon
Postganglionic receptors	Nicotinic	Nicotinic
Postganglionic neurotransmitter(s)	Epinephrine Norepinephrine	Acetylcholine
End organ receptors	Alpha-1 and 2 Beta-1 and 2	Muscarinic 1-5

Physiology

The sympathetic nervous system can be thought of as the "overdrive mechanism" that prepares our body for a fight or flight response. Thus, activation of the sympathetic nervous system increases heart rate (chronotropy), increases heart conduction (dromotropy), increases heart contractility (inotropy), increases respiratory drive, mentally stimulates, and directs blood to muscle and away from the visceral organs. The parasympathetic nervous system can be thought of as the "rest and digest" mode. Activation of the parasympathetic nervous system decreases heart rate and cardiac output, decreases respiratory drive, and directs blood to the viscera. The following table 2 summarizes the major physiologic effects of the parasympathetic and sympathetic nervous systems.

TABLE 2 – MAJOR EFFECTS OF THE AUTONOMIC NERVOUS SYSTEM.

Organ System	Sympathetic	Parasympathetic
Eye	• pupillary dilation (α1)	• pupillary constriction
Cardiovascular System	• increased heart rate (β1) • increased conduction (β1) • increased contractility (β1) • coronary vasodilatation (β1) • vascular smooth muscle contraction (α1/α2) • vascular smooth muscle relaxation (β2)	• decreased heart rate • decreased conduction • decreased contractility
Respiratory System	• bronchial smooth muscle relaxation (β2) • increased bronchial secretion (α1, β2)	• bronchial smooth muscle contraction • increased bronchial secretion
Gastrointestinal System	• decreased wall motility and tone (β2) • sphincter contraction (α2) • increased salivary gland secretion (α1, β2)	• increased wall motility and tone • sphincter relaxation • increased salivary gland secretion
Genitourinary System	• bladder wall relaxation (β2) • sphincter contraction (α1) • uterine relaxation (β2) • uterine contraction (α)	• bladder wall contraction • sphincter relaxation • uterine contraction

Endocrine System	• gluconeogenesis (β2) • glycogenolysis (α1) • increased insulin secretion (β2) • decreased insulin secretion (α1) • stimulates lipolysis (β1) • inhibits lipolysis (α1) • stimulates renin release (β1) • inhibits renin release (α2)	• increased insulin secretion

Receptor Mediated System

The sympathetic and parasympathetic nervous systems exert their effects through neurotransmission via specific receptors: alpha (α1 and α2), beta (β1 and β2), nicotinic and muscarinic (M1-M5) classes. Numerous subtypes and a myriad of functions of these receptors exist, however the discussion in this chapter will focus on those which are directly applicable to the practice of anesthesia.

Sympathetic Nervous System

The α1 receptor is a G-protein coupled receptor and its activation leads to an increase in cytosolic calcium through an intracellular cell signaling cascade reaction. Their main actions are vasoconstriction, pupillary dilatation, bronchoconstriction, glycogenolysis in the liver, salivary secretion, insulin suppression and lipolysis suppression.

The α2 receptor is mainly known for its presynaptic activity. Activation of α2 receptors inhibits the adenylate cyclase cell signaling cascade to produce a decrease in intracellular calcium levels. Stimulation of the presynaptic α2 receptor produces inhibition of norepinephrine release. Post-synaptically, α2 receptors are responsible for the inhibition of lipolysis, inhibition of insulin release, inhibition of renin release and promoting platelet aggregation. Interestingly, post-synaptic activation of α2 receptors results in vasoconstriction, however, because of CNS inhibition and suppression of sympathetic outflow, α2 receptor activation leads to a net effect of vasodilation.

The β1 receptor stimulates adenylate cyclase to increase cAMP levels. In the heart β1 receptor activation increases heart rate, conduction, contractility and vasodilates the coronary artery. In addition, the β1 receptor mediates lipolysis in adipose tissue and mediates renin release to activate the renin-angiostensin system.

The β2 receptor also stimulates adenylate cyclase to increase cAMP levels. Their main actions are gluconeogenesis, insulin secretion, potassium uptake by smooth muscle, and relaxation of the blood vessels, bronchi, uterus, bladder, and gastrointestinal tract.

Parasympathetic Nervous System

The cholinergic receptors are subdivided into two classes: nicotinic and muscarinic. As discussed previously, the nicotinic receptors are found in the postganglionic neurons of the SNS and PNS, and are ligand-gated ion channels. There are also structurally distinct nicotinic receptors found at the motor end plate in skeletal muscle which produce muscle contraction. Muscarinic receptors are responsible for the

postganglionic actions of the parasympathetic nerve fibres. Five subclasses of muscarinic receptors are known (M1-M5). M1 receptors stimulate acid secretion in the stomach. Decreases in heart rate are produced by M2 receptor activation. M3 receptors promote smooth muscle contraction in the gut. Release of adrenaline is facilitated by the activation of M4 receptors in the adrenal medulla in response to sympathetic stimulation. Both M4 and M5 receptors are thought to be involved in the CNS.

Common Autonomic Agents In Anesthesia

Several drugs exist which interact with the sympathetic nervous system. This section will aim to highlight a few of the drugs commonly used in anesthetic practice.

Adrenergic Agonists:

1. **Ephedrine** is an indirectly acting agent that releases stores of endogenous catecholamines, activating α and ß receptors, with an end result of increased heart rate, blood pressure, and cardiac output. It is administered in small boluses (5-10 mg) to increase blood pressure in the operating room.

2. **Phenylephrine** is an α agonist, with greater α1 specificity, thereby producing vasoconstriction and increasing blood pressure. It is also an effective nasal decongestant and administered prior to nasal intubation to reduce the risk of epistaxis. A reflex bradycardia is often seen with phenylephrine administration. It also is a valuable vasopressor in the setting of coronary artery disease due to its ability to produce coronary vasodilatation.

3. **Norepinephrine** is an α1 and ß1 agonist. The major hemodynamic effect of norepinephrine is increased systemic vascular resistance. The main application of norepinephrine is to increase blood pressure in refractory, vasodilatory shock.

4. **Epinephrine** is a direct agonist of all adrenergic receptors (α1, α2, ß1 and ß2). The effects of epinephrine are to increase heart rate, contractility, cardiac output, overall vasoconstriction, blood pressure, and bronchial smooth muscle relaxation. It is an important drug in the treatment of anaphylaxis, cardiac arrest situations, and refractory shock.

5. **Dopamine** has both direct and indirect sympathomimetic effects. There is also a dose-dependent activity at dopaminergic and adrenergic receptors. At low doses, dopaminergic activity predominates, at moderate doses ß1 activity predominates and at high doses, α1 activity predominates. Depending on the concentration used, this agent works to increase blood pressure and heart rate. It is often used in the treatment of refractory shock.

6. **Clonidine** is an α2 agonist which has known analgesic, sedative, and hypotensive properties. It is utilized for the treatment of acute and chronic pain, as well as hypertension. This drug can be given orally, intravenously, epidurally, or intrathecally. Dexmedetomidine is much more specific for the α2 receptor and allows for greater hemodynamic stability than clonidine.

7. **Salbutamol** is an inhaled ß2 agonist which promotes bronchial smooth muscle relaxation and is, therefore, a cornerstone in the treatment of bronchospasm.

Adrenergic Antagonists:

1. **ß antagonists** (also referred as **ß blockers**) are a large class of antihypertensive, anti-arrhythmic, and heart rate-controlling drugs. Different agents have varying specificity of antagonism at ß1 and ß2 receptors.

2. **Labetolol** is a mixed α and ß antagonist. It blocks activity at α1, ß1, and ß2 receptors. This drug produces decreases in blood pressure with little or no change in heart rate or cardiac output.

3. **Phentolamine** is an α antagonist which produces a decrease in blood pressure with a reflex tachycardia. The reflex tachycardia is mediated through α2 receptor blockade, which results in the release of norepinephrine in cardiac cells.

Cholinomimetics:

Neostigmine acts indirectly to promote the activity of acetylcholine. It binds to cholinesterase, the enzyme responsible for breakdown of acetylcholine at the neuromuscular junction, thus accentuating the effects of acetylcholine. It is an important drug used in the practice of anesthesia because it allows for the reversal of non-depolarizing neuromuscular blockers, which will be discussed in a separate chapter.

Cholinoceptor antagonists:

1. **Atropine** is an anticholinergic agent that antagonizes muscarinic receptors. It has many physiologic effects, including pupillary dilatation, decreased GI motility, and reduction of bronchial secretions. Most importantly, it is used to treat bradyarrhythmias, as its action increases heart rate.

Glycopyrrolate is also an anticholinergic agent, however it has a slightly different structure compared to atropine, and thus does not cross the blood-brain barrier. It also increases heart rate, but to a lesser degree than atropine. Atropine inhibits bronchial and salivary secretions. It is often used during reversal of neuromuscular blockade, in order to prevent the cholinomimetic side effects of neostigmine.

Clinical Correlation: Spinal Anesthesia

Spinal anesthesia provides a good example to demonstrate the autonomic nervous system in action. Injection of intrathecal local anesthetic produces an ascending motor and sensory block at the level of the spinal cord. As outlined earlier in the chapter, the preganglionic neurons arise in the gray matter of the spinal cord. The addition of intrathecal local anesthetic into the lumbar region disrupts the neurotransmission of predominantly the sympathetic fibres (thoracolumbar outflow) and relatively spares the cranial outflow of the parasympathetic fibres. The net hemodynamic result is a loss of cardiac accelerator fibre activity (arising from T1-T4), which produces bradycardia and markedly decreased systemic vascular resistance, resulting in hypotension (in addition to the intended motor and sensory block). Hence, atropine and/or ephedrine may be given to counteract these hemodynamic consequences of a spinal anesthetic.

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Section 3.2

General Pharmacology of Intravenous and Inhalational Drugs

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Intravenous Anesthetics

A. Mechanism of Action

All intravenous agents such as **propofol** with the exception of Ketamine exert their sedative and hypnotic effects through increased activity at □-aminobutyric acid **(GABA)** synapses. The CNS effects of **ketamine** are related to antagonism at the N-methyl-D-aspartate **(NMDA)** receptor. Ketamine produces dissociation between the thalamocortical and limbic systems and this is termed "dissociative" anesthesia.

B. Onset and Duration of Effect

The **rapid onset** of the lipid soluble drugs after IV administration is due to their **rapid distribution** into highly perfused brain tissue (arm-brain circulation time). The central effect is terminated rapidly (and the patient regains consciousness) when CNS concentration decreases below a critical value as the drugs **redistribute** to the less well perfused areas like muscles and fat.

Drug **metabolism** plays a **very minor role** in determining the time of **awakening** after a **single dose.** However, differences in the rate of metabolism, elimination, and the presence of active metabolites do explain why propofol has short-lived residual effects. There is also variability (and thus unpredictability) amongst individual patients regarding time of awakening and the length of residual drug effects.

C. Effects on the Cardiovascular, Respiratory and Central Nervous Systems

The paragraph below should be read with Table 1.

TABLE 1 - MAJOR EFFECTS OF IV INDUCTION AGENTS.
BP = Blood Pressure; HR = Heart rate; RR = Respiratory rate; TV = Tidal volume; ICP = Intracranial pressure; CBF = Cerebral blood flow; CPP = Cerebral perfusion pressure.

Drug	CVS	Respiratory	CNS
Propofol	•□ BP •□Baroreceptor reflex •↔ HR	•□ TV •□ RR •□ Response to hypocarbia	•□ ICP •□ CBF •□ CPP
Ketamine	•□ BP •□ HR	•As propofol but milder •Bronchodilation	•?□ ICP •□ CBF
Etomidate	•↔ BP •↔ HR	•As propofol	•As propofol
Midazolam	•□ BP (mild) •↔ HR	•As propofol but milder	•As propofol •Anxiolysis •Amnesia
Midazolam	•□ BP (mild) •↔ HR	•As propofol but milder	•As propofol •Anxiolysis •Amnesia

CVS: The cardiovascular effects of IV anesthetic drugs are the combined result of direct myocardial depression (minimal with midazolam and etomidate), vasodilation (reduced preload and decreased systemic vascular resistance), and heart rate changes (variable).

The magnitude of CVS effects is strongly dependent on dose and speed of administration, but is also influenced by cardiac status, age and volume status. Central release of natural catecholamines after administration of ketamine overrides direct myocardial effects and the resultant increase in blood pressure and heart rate is clinically very useful in patients who are in shock.

Resp: Decreased (upper airway) muscle tone can result in airway obstruction, and obtunded laryngeal reflexes increase the risk of aspiration. In the case of ketamine, these effects are much less than the

other IV anesthetic agents, but apnea (after a large dose) and aspiration can still occur.

CNS: IV anesthetic agents (with the exception of ketamine) cause dose-related global suppression of consciousness, decreased intracranial pressure, reduced intracranial blood flow and energy requirements of the brain. Hypotension leading to decreased cerebral perfusion pressure will offset the effects, which are beneficial in the patient at risk for raised intracranial pressure.

D. Clinical Use: See Tables 2 and 3

These potent drugs should only be administered by health professionals competent in airway management and advanced resuscitation skills (with equipment available) as sedation can easily progress to hypnosis. This is especially true in children, elderly, and/or when combined with opioids and other IV anesthetic drugs like benzodiazepines.

The choice of agent is made on an individual basis after taking many factors into consideration (e.g., comorbidities, pregnancy status, age, and hemodynamic status). Propofol is the drug of first choice in the majority of patients for hypnosis and sedation in the hands of anesthetists and other physicians (with advanced training) for procedural sedation. Drugs with unique properties like ketamine (analgesia) and etomidate (minimal hemodynamic effects) are reserved for use in specific high-risk groups due to unwanted side effects. Thiopental (no longer available) was the drug of choice in pregnancy as it can protect against focal brain ischemia. Midazolam, although seldom used alone as an induction agent, is very useful as premedication (especially in children), during sedation (often used during local or regional anesthesia), or as an adjuvant during induction. Most IV anesthetic agents are anticonvulsants and midazolam is most often used to terminate convulsions.

TABLE 2 - COMMON USES OF IV INDUCTION AGENTS.

++ = Drug of choice; + = Used when another indication exists; - = Not used for this indication.

	Propofol	Ketamine	Midazolam	Etomidate
Sedative	++	+	++	-
Hypnosis	++	+	+	+
Analgesia	-	+	-	-

TABLE 3 - INDICATIONS AND CONTRAINDICATIONS OF IV INDUCTION AGENTS.
++ = Drug of Choice; + = Use acceptable, but better alternatives exist; - = Absolutely contraindicated.

	Propofol	**Ketamine**	**Midazolam**	**Etomidate**
Severe Asthma	++	++ (status)	+	+
Severe Hypovolemia	-	++	++	+
Poor cardiac function	+	+	++	++

E. Dosing of Common IV/IM Anesthetic Agents

TABLE 4 – DOSES OF IV ANESTHETIC AGENTS FOR INDUCTION AND SEDATION. (NOTE: REDUCE DOSE IN ELDERLY)

Drug	Induction Dose (mg/kg)	Onset (sec)	Duration (min)	Sedation dose (adults)
Propofol IV	1.5-2.5	15-45	5-10	25-75 mg
Ketamine IV	0.5-2	45-60	10-20	0.2 -0.8 mg/kg (same for analgesia)
Ketamine IM	4-6	5-15 (min)	20-30	2-4 mg/kg
Etomidate IV	0.2-0.4	15-45	5-10	N/A
Midazolam IV	0.05-0.15	30-90	10-30	0.5 -1 mg prn
Midazolam IM	N/A			0.07-0.1 mg/kg

F. Individual Agents

Propofol is prepared in a milky white emulsion ("milk of amnesia") to increase water solubility. Many different formulations exist – most also contain soybean oil, glycerin, and egg lecithin. Newer formulations contain antimicrobial agents like disodium edetate or metabisulfite. As the emulsion is an ideal culture medium for bacteria, opened propofol should be discarded after **six hours.** Hepatic and extrahepatic metabolism to inactive metabolites assures a quick recovery.

Other effects (not listed in Table 1)

1. Venous irritation (pain on injection)

a) IV administration causes pain in 50% to 75% of patients.

b) How to reduce pain 1) administer into a large vein, 2) premix with lidocaine, or 3) give lidocaine (0.5mg/kg) 1 to 2 min before propofol with a tourniquet proximal to the injection site.

2. **Reduced postoperative nausea and vomiting** (PONV) (compared to inhaled anesthetics)

a) Subhypnotic doses have short-lasting anti-emetic effects.

b) PONV occurs less frequently after a propofol-based anesthetic as opposed to maintenance with inhalational anesthesia.

3. Besides known **allergy** (extremely rare), there are no absolute contra-indications to the use of propofol. It is best avoided in extremely hypovolemic patients.

Ketamine is water-soluble and administered via IV, IM, or oral routes. Compared to the other IV induction agents, it has unique properties. As a grandchild of phencyclidine (PCP, Angel Dust, etc.) it has shed most (but not all) of the psychodelic effects of phencyclidine. The dissociative state (see mechanism of action above) is clinically reflected (at a low dose) by the eyes being wide open with a slow gaze, increased muscle tone, and/or myoclonic movements. Hepatic metabolism leads to active metabolites (e.g., norketamine) and prolongation of its effect. Tolerance to the analgesic effects due to enzyme induction is seen in chronic use, e.g. in burn patients, where it is often repeatedly used for dressing changes.

Other effects of Ketamine:

1. Even at subhypnotic doses it is a powerful **analgesic** (somatic > visceral)

2. **Bronchodilator** so may be useful in status asthmaticus.

3. **Oral and tracheobronchial secretions** are markedly **increased**. These can be effectively reduced by co-administration of an anti-sialagogue (e.g. glycopyrrolate).

4. **Restlessness** and **agitation** are common on emergence. **Nightmares** and **hallucinations** may last for weeks postoperatively. Risk factors for these events are 1) age >16 years, 2) dose > 2mg/kg, 3) female gender, and 4) those with pre-existing psychiatric disorders. These effects can be significantly reduced by co-administration of a benzodiazepine such as midazolam.

5. Relatively contra-indicated in patients with ischemic heart disease, certain valvular lesions, uncontrolled hypertension, and pre-eclampsia, as hypertension and tachycardia is commonly seen.

6. Its effect of increasing ICP and intra-ocular pressure (although controversial) 5,6 relatively contra-indicates its use in patients with these concerns.

Etomidate is an imidazole-containing hypnotic unrelated to other anesthetic agents. It is metabolized rapidly in the liver by esterases to inactive metabolites. It produces **minimal changes in blood pressure, cardiac output, and heart rate**. These are very attractive properties in the patients with poor cardiac function, severe cardiac valvular lesions, and severe uncontrolled hypertension and hypovolemia.

Other effects:

1. **Adrenal suppression** after a single bolus dose (for up to 24 h) is of little clinical significance. However, etomidate is not suited for use in repeated doses or as an infusion for this reason.

2. High incidence of **postoperative nausea and vomiting.**

3. **Venous irritation** and superficial thrombophlebitis due to the propylene glycol vehicle.

4. High incidence of **myoclonus** – which appear to be harmless.

Midazolam is a short-acting **benzodiazepine** that has (as opposed to diazepam and lorazepam) few active metabolites in healthy patients. It causes no pain on IV injection. Midazolam can also be given IM. It is rarely given orally for pre-operative sedation in anxious children. In adults with pre-operative anxiety, lorazepam sublingually is sometimes offered. Bendoziazepines are anticonvulsant and amnestic. Benzodiazepines may increase the risk of post operatiove delirium in elderly.

The hemodynamic effects are generally mild, but can be pronounced when administered to those with very poor cardiac reserve or when co-administered with opioids in a patient with hypovolemia. The respiratory depression effects, generally mild, can be pronounced when co- administered with opioids or in patients with COPD or obstructive sleep apnea.

The sedative effect of all benzodiazepines can be completely (and respiratory effect incompletely) reversed with flumazenil. Repeated administration of flumazenil may be necessary because of its short duration of action.

Inhalational Anesthesia

Introduction to Gaseous or Volatile Anesthetics

The introduction of ether as a general anesthetic during a public demonstration at Massachusetts General Hospital on October 16, 1846 served not only to revolutionize the practice of surgery but set in motion the establishment of Anesthesia as a specialty. Volatile agents induce a state of general anesthesia characterized by unconsciousness, analgesia, immobility, and amnesia. Older volatile agents such as ether and chloroform have been replaced by halogenated compounds, of which desflurane and sevoflurane are the most commonly used today.

Target Site of Action of Volatile Anesthetics

Volatile anesthetic potency is correlated with its lipid solubility as determined by its oil-water partition coefficient. This relationship prompted the proposal of the lipid solubility theory of anesthetic action by Meyer and Overton in the 1890s. Their hypothesis persisted almost a century and maintained that anesthetics disrupt the lipid bilayer of cellular membranes to bring about cellular dysfunction and neuronal depression, manifesting as a loss of consciousness. In 1994, Franks and Lieb challenged the Meyer Overton theory by showing that inhalational anesthetic potencies correlated even better with their ability to inhibit the activity of proteins. Further work in this area has revealed that **key receptors (GABAA, NMDA, glycine and two-pore-domain K+ channels)** are the most likely targets for actions of most anesthetics.

Minimum Alveolar Concentration

Volatile anesthetics, when administered through the inhalational route, partition into gas (alveolar), blood, brain and other tissue compartments determined by their physicochemical properties. Doses are in volume percent concentration. These compounds move along pressure gradients, usually quantified as a percentage measure of partial pressure in atmospheric pressure. As vapors exist in a gaseous state, volatile anesthetics are governed by the ideal gas law which defines the relationships between pressure (P), volume (V), and temperature (T) as P □ T/V. However, volatile anesthetic vaporizers are designed to deliver the gases at defined partial pressures irrespective of barometric pressures changes. Percent volatile anesthetic delivery varies only with marked temperature changes.

In 1963, Merkel and Eger made the observation that the anesthetic effects of volatile agents are directly correlated with their alveolar concentrations and coined the term **"minimal alveolar concentration" (MAC)** as a means of measuring anesthetic potency.

MAC is the minimum alveolar concentration of anesthetic required to prevent movement in 50% of patients in response to a painful stimulus (incision). Based on this definition, one may infer that anesthesiologists utilize at least one MAC to ensure that most patients do not respond to painful stimuli, however, this is frequently not the case. Primarily, the studies designed to determine MAC utilized only the volatile anesthetic agent in oxygen for both induction and maintenance of anesthesia. No premedication or other anesthetic agent was given.[1] In common practice, however, **IV agents such as benzodiazepines, opiates and muscle relaxants are used in combination with the inhaled agent and can reduce the MAC.**[2,3]

Patient specific factors also affect the MAC. **The MAC of the halogenated volatile anesthetics decreases with increasing age by approximately 6% per decade and is highest in the newborn.** Decreased MAC with age decreases the inspired concentration necessary for anesthesia. Chronic alcohol use, hyperthyroidism and hyperthermia increase MAC and requirements for inhaled anesthesia. Acute alcohol intoxication and hypothermia decrease MAC. Anesthetic potency of a volatile anesthetic, as measured by MAC, varies inversely with its lipid solubility (tissue-blood partition coefficient). The MAC values of the commonly used volatile anesthetics are listed in Table 1.

TABLE 1 - MINIMUM ALVEOLAR CONCENTRATION VALUES FOR COMMONLY USED VOLATILE AGENTS.

Agents (in order of increasing potency)	MAC (%) in adults (40 years old)	MAC (%) in neonates
Nitrous oxide	104	
Desflurane	6.3	9.2
Sevoflurane	2	3.3

The fraction of MAC for nitrous oxide and either sevoflurane or desflurane can be added to get a total MAC.

Variables that influence the alveolar concentrations of volatile anesthetics determine the pharmacokinetic properties of these agents. These pharmacokinetic properties govern the wash-in, maintenance, and washout of volatile agents from the alveoli. Sevoflurane and desflurane are less soluble and thus wash in and wash out faster.

Alveolar wash-in of volatile anesthetics is determined by the inspired concentration and alveolar ventilation (tidal volume and respiratory rate) over functional residual capacity (FRC). The greater the absolute FRC, the more time it takes to wash in the volatile agent at any given minute alveolar ventilation. Alveolar maintenance of a concentration of the volatile agent is influenced by pulmonary blood uptake, which is influenced by cardiac output, the alveolar-venous gradient, and the solubility of the volatile agent in blood. In general, decreased cardiac output, decreased alveolar-venous gradient, and increased solubility (blood-gas partition coefficients) of the gas will slow the equilibration of inspired to alveolar concentrations of volatile anesthetics, and hence, prolong inhalational induction of anesthesia. However, in the pediatric patient, a higher cardiac output, greater distribution of blood to vessel rich areas, and a reduced blood solubility of all the volatile anesthetics actually results in faster induction of inhalational anesthesia. Similarly, the solubility of volatile anesthetics also determines the wash-out of the anesthetic whereby less soluble agents equilibrate faster, are easier to titrate for anesthetic depth, and are eliminated more rapidly. Elimination of a volatile anesthetic is largely by exhalation or wash-out from the alveoli, as liver metabolism is minimal.

Malignant Hyperthermia and halogenated inhaled anesthetics

Any of the potent halogenated volatile anesthetics like desflurane and sevoflurane can trigger a life threatening malignant hyperthermia reaction in susceptible patients. Nitrous oxide does not cause malignant hyperthermia. Details of malignant hyperthermia are in another chapter.

Nitrous Oxide

Nitrous oxide (N2O) is a colourless, odourless, and tasteless gas and is non-flammable but supports combustion. Therefore, its use is limited during laser surgery or procedures requiring cautery near the airway. Its use can be associated with **postoperative nausea and vomiting**. Nitrous oxide easily

diffuses into airspaces due to its greater solubility in blood compared to Nitrogen and **can expand gas filled compartments** e.g. pneumothorax, dilated bowel and middle ear cavity.

Nitrous oxide is an "inert" gas in that it is not significantly metabolized in the body. It is distinguished from other volatile anesthetics by its **low potency (MAC 104%)**. Its MAC is too high for it to be a sole anesthetic. Unlike other volatile anesthetics for which MAC decreases with decreasing temperature, the MAC of nitrous oxide does not change appreciably with temperature. Nitrous oxide has a low solubility in blood (low blood-gas coefficient), therefore, onset and offset of effect is rapid. When nitrous oxide is co-administered with another potent volatile anesthetic, there is a second gas effect, whereby the alveolar concentration of the other anesthetic is increased by the more rapid diffusion of nitrous oxide from the alveoli to the blood. This second gas effect is age-dependent.

Nitrous oxide has been used for **labor analgesia** in the form of nitronox (50% nitrous oxide in 50% oxygen) and there is no effect on uterine contractility.

Although nitrous oxide has minimal cardiovascular effects in normal patients, it can cause myocardial depression in patients with existing heart disease or underlying hemodynamic compromise, especially when concomitantly administered with an opioid.

The respiratory effects of nitrous oxide are minimal and it is not known to cause any neuromuscular junction blocking effects. More importantly, patients with pre-existing pulmonary hypertension may develop dangerous levels of pulmonary vascular resistance when receiving nitrous oxide. For this reason, nitrous oxide is **contraindicated in patients with pulmonary hypertension.**

The potential for hypoxic mixtures with nitrous oxide was a problem in the past, but with the implementation of fail-safe devices in modern anesthetic machines preventing the delivery of undesirably high concentrations of nitrous oxide and oxygen detectors, this risk has been essentially eliminated.

Sevoflurane

Sevoflurane (2,2,2-trifluoro-1-[trifluoromethyl]ethyl fluoromethyl ether, $(CF_3)_2$-CH-O- CH_2F) is a non-flammable, halogenated methyl ethyl ether that has a relatively pleasant odour. It is the volatile anesthetic of choice in **inhaled induction** of general anesthesia. It has a rapid onset and offset of action due to its low solubility in blood and tissue (low blood-gas and tissue-blood partition coefficients, respectively). Furthermore, it is non-irritating to airway mucosa.

Sevoflurane causes respiratory depression and bronchodilation. As well, sevoflurane causes a dose-dependent reduction in arterial blood pressure due to peripheral vasodilation (but not of the coronary vessels) and can cause direct myocardial contractility impairment.

Sevoflurane increases cerebral blood flow by the vasodilation of cerebral blood vessels. However, sevoflurane preserves CO_2 reactivity of the cerebral vessels and hyperventilation may be used to reduce cerebral blood flow and intracranial pressure. Consistent with the other halogenated volatile anesthetics, decreases in amplitude and increases in latency of cortical somatosensory evoked potentials as well as brainstem auditory evoked potentials are seen with sevoflurane.

Effects on uterine contractility (can contribute to atony), uterine arterial vasodilation and blood flow, direct muscle relaxation, and potentiation of neuromuscular blockers are also similar to the other halogenated volatile anesthetics.

Due to a relative higher rate of liver metabolism (5%), sevoflurane has been associated with transient hepatic dysfunction in some patients. Sevoflurane also undergoes temperature-dependent biodegradation in baralyme or soda lime, which are found in anesthetic machine breathing circuits. This produces compounds A (fluoromethyl-2,2-difluoro-1-(trifluoromethyl)vinyl ether) and B. Of these, **compound A** has been shown to cause renal necrosis in rats but there has been no histological evidence to date of human nephrotoxicity, although dose-dependent proteinuria and glycosuria have been documented.

Desflurane

The newest of the commonly used volatile anesthetics(2-(difluoromethoxy)-

1,1,1,2-tetrafluoro-ethane, CF_3-CHF-O-CHF_2). Desflurane is **pungent and an airway irritant** that can provoke breath holding, laryngospasm and salivation so it is not used for inhalational induction, Desflurane is less potent than sevoflurance and has a **lower blood and tissue solubility** (decreased blood-gas and tissue-blood partition coefficients, respectively). Therefore, it washes in and out of the lungs and brain tissue **more rapidly**, thereby allowing an easily **titratable depth** of anesthesia and **faster wake up.** Desflurane has a low boiling point (23.5 °C) approximating room temperature compared with the other volatile agents (48.5 to 58.6 °C) and must be stored in heated vaporizers for administration.

With light levels of desflurane anesthesia there is minimal effect on heart rate; however, deeper levels of desflurane may cause an increase in plasma catecholamines resulting in **higher heart rate and blood pressure.** Desflurane causes mimimal direct decreases in myocardial contractility and coronary artery vasodilation. Desflurane vasodilates and attenuates baroreceptor and vasomotor reflex responses to hypovolemia.

Desflurane increases cerebral blood flow by vasodilation of cerebral blood vessels. However, desflurane preserves CO_2 reactivity of the cerebral vessels and hyperventilation may be used to reduce cerebral blood flow and intracranial pressure. Desflurane causes a decrease in amplitude and increase in latency of cortical somatosensory evoked potentials as well as brainstem auditory evoked potentials.

Desflurane has similar effects as other volatile anesthetics on uterine physiology, causes direct muscle relaxation and potentiates the effect of neuromuscular blockers.

Desflurane is minimally biotransformed by the liver. However, it is known to produce significant levels of carbon monoxide (CO) in reaction with desiccated soda lime and baralyme (CO_2 absorbers).

Summary

1. IV anesthetic agents are used for induction and maintenance of general anesthesia and sedation.

2. Some IV anesthetic agents also have other properties, including analgesia (ketamine), anticonvulsant (midazolam, and propofol), anti-emetic (propofol), and anxiolysis (midazolam), for which they are sometimes primarily used.

3. Propofol is often the agent of choice for hypnosis as recovery is rapid with little residual effects. It can cause apnea and hypotension. It is used as an induction agent. It can be used as an infusion for maintenance as a total intravenous anesthetic (TIVA) or sedation. Dosage is decreased in the elderly.

4. Midazolam is a benzodiazepine and is mostly used as premedication or for intra-operative sedation. Benzodiazepines are used as anxiolytics, amnestics and anticonvulsants.

5. Ketamine may be useful for induction in severely hypovolemic patients. It is also a bronchodilator and an analgesic. Side effects include tachycardia, hypertension, emergence reactions (agitation and hallucinations) and increased secretions.

6. Etomidate is an induction agent that may not affect heart rate, blood pressure and intracranial pressure but it can cause adrenal suppression.

7. Nitrous oxide can be part of the maintenance of general anesthesia in combination with either a more potent inhaled anesthetic or a propofol infusion. Its use is a risk factor for post operative nausea and vomiting and can expand air filled spaces. Nitrous oxide may be an option for labor analgesia.

8. Halogenated inhaled anesthetics in use today include desflurane and sevoflurane. They are often used for maintenance of general anesthesia. Sevoflurane can be used for inhalation induction. They are contraindicated in patients with a personal or family history of malignant hyperthermia.

9. Define Minimum Alveolar Concentration (MAC) and know that the MAC of the inhaled anesthetic helps anesthesiologists decide how much inspired concentration to use, which is a determinant of alveolar concentration, and thus brain concentration and anesthetic depth. MAC can be

affected by factors such as age.

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Section 3.3

Opioids

Dr. Josh Gleicher and Dr. Mabel Choi

Introduction

The term *opioid* is used to designate a class of natural or synthetic agents with morphine- like properties. It can refer to agonists, partial agonists, mixed agonist-antagonists and competitive antagonists. Opioids produce analgesia without loss of touch, proprioception or consciousness. All opioids can produce serious side effects. Physicians who prescribe opioids for acute or chronic pain need to know how to use these drugs safely.

Clinical effects of a particular opioid depend on which specific receptor type that it binds. An ideal opioid should have high specificity for receptors, therefore, producing desirable effects (analgesia) and little or no specificity for receptors associated with side effects (nausea, respiratory depression).

TABLE 1 - CLASSIFICATION OF OPIOID RECEPTORS AND THEIR KEY ACTIONS.

	Receptor			
	Mu1	**Mu2**	**Kappa**	**Delta**
Effects	• Analgesia (spinal) • □ GI transit • □ HR	• Analgesia (spinal) • Respiratory Depression • □ GI transit • Physical dependence	• Analgesia (spinal & supraspinal) • Sedation • Miosis	• Analgesia (spinal & supraspinal • Respiratory Depression • □ GI transit • Physical dependence

Basic Pharmacology

Opioids can be administered via different routes (transdermal, oral, nasal, subcutaneous, intramuscular, intraarticular, intravenous, epidural, and intrathecal). In clinical anesthesia practice, the intravenous route is the most common and will be the focus of discussion. In order for an opioid to reach its effector sites in the central nervous system, it must cross the blood-brain barrier. Important factors determining rate of penetration to the CNS include lipid solubility (greater penetration with higher lipid solubility), ionization (non- ionized molecules are more lipid soluble), and protein binding (unbound fraction is free to diffuse across membranes but least important of the three). Termination of action is associated with redistribution of the drug away from the CNS to inactive tissue sites such as fat and skeletal muscle, followed by a slow elimination phase determined by many factors including age, disease state, renal, and hepatic function. To illustrate this, think about the use of fentanyl in comparison to morphine. The same clinical effect can be achieved using a smaller dose of fentanyl. Its onset is faster but the duration of action is also shorter. The greater potency and more rapid onset of action reflect the greater lipid solubility and less ionization at physiologic pH compared to that of morphine, which facilitates its passage across the blood-brain barrier. The short duration of action reflects its rapid redistribution away from the CNS.

CNS Effects

Opioids produce analgesic and sedative effects but not amnesia. Secondly, opioid administration can lead to nausea and vomiting because of stimulation of the chemoreceptor trigger zone in the brain stem.

Respiratory Effects

Opioids have a direct effect on the respiratory centers in the medulla. The apneic threshold, which is the $PaCO_2$ at which one starts to breathe, is increased. Opioids also blunt the hypoxemic response and reduce the minute ventilation by decreasing the respiratory rate. As a result, administration of opioids can lead to life-threatening respiratory depression. Respiratory problems from opioids are more common in special patient populations including patients with obstructive sleep apnea (OSA), premature neonates, and very old or very ill patients.

Musculoskeletal Effects

Rapid opioid administration can lead to generalized skeletal muscle rigidity. This is mediated by the mu-receptor. Chest wall compliance and laryngeal muscles can be affected, leading to difficulties in ventilation. This can be prevented by slower administration of the drug or giving a muscle relaxant.

Cardiovascular Effects

Most opioids exert their cardiovascular effects by blunting the sympathetic response. They tend not to cause much myocardial depression. Morphine is also associated with histamine release, which contributes to hypotension. Opioids can also cause bradycardia at higher doses.

Gastrointestinal Effects

Opioids cause an increase in bowel transit time. They also increase common bile duct pressure and delay gallbladder emptying.

Opioid Induced Hyperalgesia and Tolerance

Following administration of high intraoperative doses of opioids such as remifentanil, patients can develop opioid-induced hyperalgesia. This is a paradoxical opioid effect whereby pain sensitivity increases following opioid administration. Similarly, opioid tolerance is seen after chronic use of opioids resulting in tachyphylaxis. This leads to decreased analgesic effect and increased doses of opioid.

Commonly Used Opioids

Agonists:

Morphine

Morphine is the prototype opioid agonist. Its duration of action is about 4 hours. The principle pathway of metabolism of morphine is conjugation with glucuronic acid in hepatic and extrahepatic sites, most notably the kidneys. Morphine-3-glucuronide is inactive, whereas morphine-6-glucuronide produces analgesia and respiratory depression and has potency and duration of action greater than morphine. Elimination of this active metabolite can be impaired in patients with renal failure.

Fentanyl

Fentanyl is about 100 times more potent than morphine. It is metabolized by the liver and the major metabolite, norfentanyl, is excreted by kidneys. Norfentanyl is less potent than fentanyl as an analgesic. Fentanyl has a rapid onset (peak clinical effect can be seen 5-7 minutes after IV administration). It also has a short duration of action because of its rapid redistribution to inactive tissue sites. However, its elimination half-life is 4 to 5 hours. Therefore, if given as an infusion for a long time, its effects can become prolonged.

Administration of fentanyl is associated with more stable hemodynamics than morphine. There is no histamine release. Decrease in blood pressure and heart rate is a result of blunting of sympathetic tone rather than myocardial depression.

Hydromorphone

Hydromorphone is a derivative of morphine and is about 5 times more potent than morphine. It has a gentler side effect profile (nausea, pruritis, euphoria) than morphine, especially in elderly patients.

Remifentanil

Remifentanil is a short acting synthetic opioid commonly used in the operating room. Its half-life is approximately 1.5 minutes and is usually fully metabolized by plasma estrases within 8 minutes. It is not metabolized by the liver or cleared by the kidneys, making it safer to use in patients with compromised hepatorenal systems. Given its very short half-life, it is usually administered as an infusion with typical doses ranging from 0.02 to 0.2 mcg/kg/min. Remifentanil is approximately 200 times more potent than morphine. Given its potency and brief duration of action, it is useful for short stimulating surgical

procedures that result in little postoperative pain. Common uses for remifentanil outside the operating room include for patient controlled analgesia (PCA) for obstetric labour pain in the presence of a contraindication to labour analgesia.

Methadone

Methadone is a synthetic opioid that is a mu receptor agonist but is also a NMDA antagonist and inhibitor of monoamine transmitter uptake. These properties make it useful for patients with opioid tolerance and neuropathic pain. It is also often used as maintenance therapy to treat opioid dependence and opioid detoxification. Conversion from morphine to methadone is variable and caution must be taken. The morphine-to-methadone conversion ratio is 3:1 at morphine doses of <100 mg/day, but the ratio of 20:1 used at higher morphine doses of >1,000 mg/day.

Mixed Agonists:

Buprenorphine

Buprenorphine is a mixed agonist-antagonist synthetic opioid with analgesic potency 25 to 50 times greater than morphine. It is less prone to abuse because it causes less euphoria and is associated with less drug-seeking behavior and physical dependence. Another advantage of buprenorphine is that it has a ceiling effect for respiratory depression but not for analgesia. Therefore, when compared to other opioids such as hydromorphone, increasing the dose of buprenorphine for added analgesia effect has a lesser chance of causing inadvertent respiratory depression.

Antagonists:

Naloxone

Naloxone is an opioid antagonist used commonly in the treatment of opioid-induced depression of ventilation in the perioperative period. It has a short duration of action, lasting 30-45 minutes. It is metabolized in the liver.

Reversal of respiratory depression is accompanied by reversal of analgesia. Increased perception of pain can lead to significant sympathetic stimulation leading to tachycardia, hypertension, arrhythmias, cardiac ischemia, and pulmonary edema. If administered to a patient with chronic opioid use, it can precipitate acute withdrawal seizures. Because of this, naloxone should always be administered in small, titrated doses. Due to its short duration of action, effects of naloxone often wear off prior to those of the opioids and therefore the patient is again at risk of respiratory depression.

Oral Opioids:

Some of the more common opioids prescribed in the oral form include codeine, oxycodone, morphine, and hydromorphone. They are available in immediate release formulations (IR) or long-acting formulations ('-contin' for continuous release). When using morphine in the acute pain setting, a conversion ratio from intravenous to oral of 1:3 is commonly used.

Oral codeine has roughly one-quarter the potency of oral morphine. It is commonly used in the treatment of mild to moderate pain. Tylenol #3 contains acetaminophen, caffeine and 30mg of codeine.

Oral oxycodone is 1.5-2 times more potent than oral morphine. Percocet contains acetaminophen and 5mg of oxycodone.

Opioid Equianalgesic Dosing

Drug	IV/IM/SQ	Oral
Morphine	10 mg	30 mg

Hydromorphone	1.5 – 2.0 mg	6 – 8 mg
Oxycodone		20 mg
Fentanyl	100 mcg	N/A
Codeine	100 mg	200 mg
Methadone	The conversion rate for methadone is variable	

*Adapted from Clinical Anesthesia, 7th Edition

Further Readings:

1. Clinical Anesthesia, 7th Edition, Barash, Cullen and Stoelting, 2013
2. Pharmacology and Physiology in Anesthetic Practice, 5th Edition, Stoelting, 2014.
3. Anesthesia, 8th Edition, Miller, 2014.

Section 3.4

Neuromuscular Blocking Agents

Melissa Ho, MD FRCPC

Neuromuscular blocking agents (NMB) are drugs that cause interruption of transmission at the neuromuscular junction. They can be given as part of **balanced general anesthesia**. They have **no analgesic, amnestic, or anxiolytic properties**.

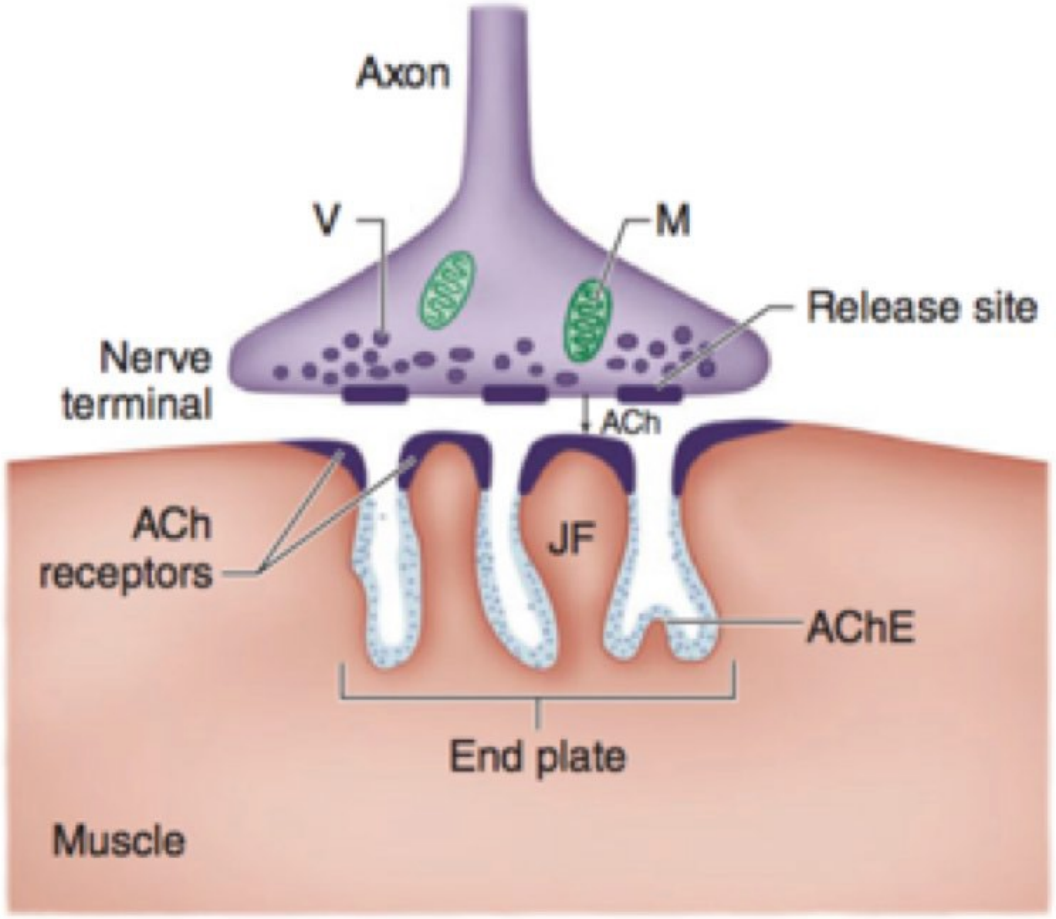
Clinical Indications:

- Provide skeletal muscle relaxation
    - Facilitate tracheal intubation
    - Relieve laryngospasm
    - Improve surgical working conditions during general anesthesia
- Provide muscle relaxation for some ventilated patients in critical care units
- Prevent trauma in ECT

Normal Physiology

At the synaptic cleft of the neuromuscular junction, acetylcholine (Ach) is released from the presynaptic axon and binds to the nicotinic acetylcholine receptors (nAchR) on the muscle endplate. Two Ach molecules binding to the nAchR results in a conformational change, causing sodium and calcium influx into the muscle, potassium efflux, and subsequent depolarization. The resultant action potential propagates along the muscle membrane and T-tubule system within the muscle, causing the release of calcium from the sarcoplasmic reticulum into the muscle cytoplasm, and leading to muscle contraction. After Ach is hydrolyzed by acetylcholinesterase embedded in the motor endplate membrane, the ion channels close with Ach unbinding. The muscle endplate repolarizes, and calcium is sequestered back into the SR for muscle relaxation.

FIGURE 1: NEUROMUSCULAR JUNCTION: V, TRANSMITTER VESICLE; ACH, ACETYLCHOLINE; ACHE, ACETYLCHOLINESTERASE; JF, JUNCTIONAL FOLDS (REPRODUCED FROM LANGE, 2013).



Mechanism of Action

Two commonly used drugs are succinylcholine and rocuronium. These drugs belong to the two classes of NMB - **depolarizing** and **non-depolarizing,** respectively. The drugs interfere with native ACh binding and stimulation of the nicotinic receptor at the muscle endplate in the NMJ. Binding of the drug ultimately results in flaccid paralysis.

Depolarizing NMB: Succinylcholine

Succinylcholine is the only **depolarizing** NMB agent, and consists of two acetylcholine molecules held together by an ester bond. When one molecule of succinylcholine binds to the NMJ receptor, the channel opens and the action potential is reached, causing depolarization. Fasciculations and increased tone are seen clinically as contracture of skeletal muscles. The flaccid paralysis that follows occurs because the channel remains open in the presence of succinylcholine, preventing repolarization. This is termed Phase I block.

Succinylcholine has rapid onset of action with flaccid paralysis occurring 30-60 seconds after a 1mg/kg dose, and recovers rapidly (90% of muscle strength regained in 9-13 minutes). Succinylcholine is often chosen for rapid sequence intubation (RSI) or where the duration of muscle relaxation required is brief.

Termination of the block occurs when succinylcholine diffuses away from the NMJ back into the circulation and rapidly hydrolyzed by plasma cholinesterase (pseudocholinesterase). Patients who are deficient of this enzyme (pseudocholinesterase deficiency) will clinically present with prolonged muscle paralysis, up to 8 hours for those who have zero enzymatic activity. Neostigmine should not be given as it prolongs the duration of succinylcholine due to inhibition of pseudocholinesterase.

Phase II blockade may occur with repeated and large doses of succinylcholine. Recovery in the expected time does not occur with phase II blockade. The muscle actually does repolarize but will remain blocked to stimulation by ACh. The blockade clinically looks and acts like a non-depolarizing muscle relaxant (NDMR).

Unique risks to succinylcholine are due to the stimulation and then blockade of cholinergic receptors.

- **Hyperkalemia:** Patients' K^+ levels increase by 0.5 mEq/L with the generalized fasciculations. However, patients with denervation injury (i.e. stroke, burns) or patients who have an abnormal number and location of end-plate nAchR (i.e., myasthenia gravis) can actually increase their K^+ by 4 mEq/L. Drug induced hyperkalemia can put the patient at risk for cardiac arrest and CNS abnormalities. Exaggerated potassium release can occur in patients with previous stroke, burns and neuromuscular disorders such as Duchenne muscular dystrophy and myasthenia gravis – all which are contraindications to the use of succinylcholine.

- **Myoglobinuria** and resultant acute kidney injury: Release of myoglobin can also occur with succinylcholine. Dark coloured urine is the clinical marker of myoglobinuria which can precipitate an acute kidney injury. Patients noticing dark coloured urine postoperatively should be counseled to seek medical attention immediately as haemodialysis may be required.

- **Cardiac dysrhythmias:** Cholinergic receptors are also found in the parasympathetic and sympathetic system and at the sinus node of the heart. Administration of succinylcholine can bind muscarinic Ach receptors. Dysrhythmias such as sinus bradycardia, junctional rhythm, and ventricular dysrhythmias can be seen. These are especially seen after a second dose of succinylcholine.

- Increases in intraocular, intragastric, and intracranial pressure can be seen. The exact mechanism of these increases is unknown, but these relatively contraindicate the use of succinylcholine.

- Post-operative myalgias: thought to be due to the fasciculations, may not be completely attenuated with a small dose of NDMR.

- **Malignant hyperthermia:** Autosominal dominant mutation in ryanodine receptor in sarcoplasmic reticulum leading to uncontrolled calcium release into muscle cytoplasms and a hypermetabolic state, triggered by succinylcholine and volatile anesthetics. This does not occur with non-depolarizing NMB agents. Patients with a known family or personal history of MH require a "trigger-free" anesthetic.

TABLE I

Complications and side effects of succinylcholine.

1. Myalgias (due to muscle fasciculations)
2. Hyperkalemia
   a) Burns
   b) Denervation (e.g., CVA, paraplegia)
   c) Neurological disorders (e.g., Duchenne muscular dystrophy)
3. Cardiac dysrhythmias
   a) Bradycardia (especially with second dose)
   b) Junctional
   c) Ventricular
4. Increased intracranial pressure
5. Increased intraocular pressure
6. Increased intragastric pressure
7. Trigger for malignant hyperthermia (MH)
8. Prolonged paralysis with cholinesterase deficiency
9. Salivation
10. Masseter muscle rigidity (MMR)

Non-depolarizing agents

Rocuronium is a member of the **non-depolarizing** muscle relaxant (NDMR) group. Other medications in this class include cisatracurium, atracurium, vecuronium and pancuronium. As given by the name, this class of drugs does not cause depolarization of the NMJ endplate. Rather, competitively binds and inhibits the nAchR (competitive antagonist). The different members of this group are differentiated by their onset times and offset times depending on their potency, affinity for the receptor, redistribution, and their speed of metabolism and elimination.

Rocuronium is an intermediate acting NDMR. At 2*ED95 (0.6 mg/kg), the usual dose used for intubation, its onset is 1.5 min and lasts approximately 35 min. Its onset can be sped up by increasing the initial dose, 4*ED95 (1.2 mg/kg), and is used clinically in a rapid sequence intubation (RSI) when succinylcholine is being avoided.

Termination of effect occurs when the molecule diffuses away from the receptor. Non-depolarizing NMBs are not metabolized by acetylcholinesterase or pseudocholinesterase.

- Passive termination of effect: via diffusion away from the nAchR along concentration gradients as the drug is progressively metabolized or eliminated either centrally in the plasma or metabolized through the kidney or liver.

- Alternatively, the drug will diffuse away from the receptor if the concentration of ACh increases in the NMJ. Administering neostigmine, an anticholinesterase inhibitor, will do just that. Reversal agents can only be given when there has been some recovery of blockade.

Duration of blockade may be prolonged in some disease states that delay NMB metabolism

(liver/kidney failure, hypothermia), electrolyte abnormalities, and use of certain drugs (aminoglycosides, volatile anesthetic agents) which have a synergistic effect on muscle relaxation.

Side effects of NDMRs may be due to interactions with nicotinic and muscarinic cholinergic receptors in the sympathetic and parasympathetic nervous systems. Similar to succinylcholine, there can be dysrhythmias, with their prevalence based on the drug and dose chosen. Additional interaction in the bronchioles can cause dilation or constriction with administration of NDMR. Rocuronium is clinically stable in this regard.

Allergic reactions, both immune mediated and anaphylactoid, can occur with NDMR administration. Where studied, it was the most common cause of anaphylaxis under anesthesia, ahead of latex.

Neostigmine, when given to antagonize an NDMR blockade, will also cause bradycardia and salivation due to the increase in Ach in the parasympathetic system and binding to muscarinic Ach receptors. For reversal of NMB agents, an anticholinergic is always given (i.e., atropine or glycopyrrolate) along with neostigmine.

Suggamadex is a cyclodextrin selective muscle relaxant binding agent. It forms a 1:1 complex with steroidal non-depolarizing NMB (rocuronium, vecuronium) and is gradually being made available in Canadian hospitals for emergency reversal of deep neuromuscular blockade (eg. cannot intubate, cannot ventilate situations; residual neuromuscular blockade despite conventional reversal).

Risks and Side Effects

Important risks of NMB agents include given they have no analgesic, amnestic, or anxiolytic properties. Patients can experience a spectrum of awareness, from vague memories of being in the operating room during the surgery to being able to describe exact events in the operating room and having experienced these as well as the pain of surgery.

Because NMBs prevent movement, patients who are aware under anesthesia do not exhibit the normal movement responses to pain. Patients who are unfortunate enough to experience awareness are at high risk of post-traumatic stress disorder (PTSD). Those that express awareness require consultation and follow-up with psychiatry for management. Students who encounter such patients in other services or ultimately in their medical practice should inform the anesthesiologist who gave the anesthetic so that proper follow-up can be instituted.

Due to weakness of the muscles of respiration, these drugs should only be used by medical staff that are able to mechanically support ventilation and in settings where patients' respiratory parameters can be monitored. **Residual postoperative neuromuscular blockade** causes decreased chemoreceptor sensitivity to hypoxia, functional impairment of the pharyngeal and upper esophageal muscles, impaired ability to maintain the airway, and an increased risk for the development of postoperative pulmonary complications, such as aspiration[2].

Use of NMB in the ICU may contribute to Critical Illness Polyneuropathy, a condition characterized by limb weakness, failure to wean from a ventilator and electrophysiologic testing abnormalities due to motor axonal dysfunction[2].

Monitoring of Blockade

It is important to monitor the depth of neuromuscular blockade; too much NMB can result in either not being able to reverse or antagonize the block at the end of surgery, or post-operative residual blockade. Assessment of neuromuscular block is usually performed with a peripheral nerve stimulator (e.g. placed at ulnar or facial nerve). Responses to repetitive (train of four, TOF) or tetanic stimuli are most useful for evaluation of blockade of transmission. With ulnar nerve stimulation, the adduction of the policis longus is observed and depending on the twitch response characteristics, the clinician can determine the depth of blockade and whether antagonism of the blockade is possible or complete. Antagonism of an NDMR with neostigmine should not be initiated before at least two responses to TOF stimulation are present or before obvious clinical signs of returning neuromuscular function are seen.

References

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2. Miller, R. D. (2010). Miller's anesthesia (7th ed.). Philadelphia, PA: Churchill Livingstone/Elsevier

Section 3.5

Local anesthetics

Dr. Stephen Halpern and Dr. Jose CA Carvalho

Introduction

Local anesthetics are a useful class of drugs that can be used in a number of circumstances. They can be used in the operating room to "numb" specific areas of the body so that the surgeon can perform an operation. They can also be used effectively for post-operative pain relief. In addition, they can be used as diagnostic tests in certain pain syndromes. In this chapter, we will outline what local anesthetics are and how they are used. We will then discuss nerve anatomy and pharmacology. We will then show how the unique chemistry interacts with the nerves to produce the desired effect. Finally, we will discuss side effects, toxicity and some practical applications.

Definition

Local anesthetics are drugs that:

1) Interrupt nerve conduction
2) Are reversible
3) Act on a localized part of the body
4) Do not, in clinically relevant doses, affect consciousness

Clinical uses

Local anesthetics have a wide range of uses in the operating room, the obstetrics suite, the emergency department and in the pain clinic. Some examples can be found in Table 1:

TABLE 1

Type of anesthesia	Example of clinical use	Comments
Local infiltration	Subcutaneous use of local anesthetic	Stitching in the emergency department, line placement.
Nerve block	Digital nerve block	Finger lacerations in the emergency department

Nerve block	Intercostal nerve block	Post trauma in the intensive care unit
Nerve block	Pudendal block	Obstetrics for delivery
Field block	Abdominal block	Hernia operation, post-operative analgesia
Plexus block	Brachial plexus block	Operations on the arm
Intravenous block	Upper limb	Hand surgery of 15-60 min duration (“Bier Block”).
Mucus membrane block	Nebulized local anesthetic	Bronchoscopy, awake endotracheal intubation
Neuro-axial block	Spinal anesthesia	Operations below the umbilicus. Cesarean section

Neuro-axial block	Epidural anesthesia	Same as spinal anesthesia with the possibility of increasing the duration and providing postoperative analgesia
Special uses	Hematoma block	Colle's fracture
Special uses	Instillation/injection for eye surgery	

History

Cocaine was first used as a local anesthetic in 1884. Carl Koller, an ophthalmologist, used cocaine topically for eye surgery primarily to provide an immobile field, free of blinking. In addition, he noted the analgesia.

The first nerve block was performed using cocaine at about the same time. By 1885, numerous single nerve and plexus blocks had been performed. In the 1890's, Bier performed operations under spinal anesthesia.

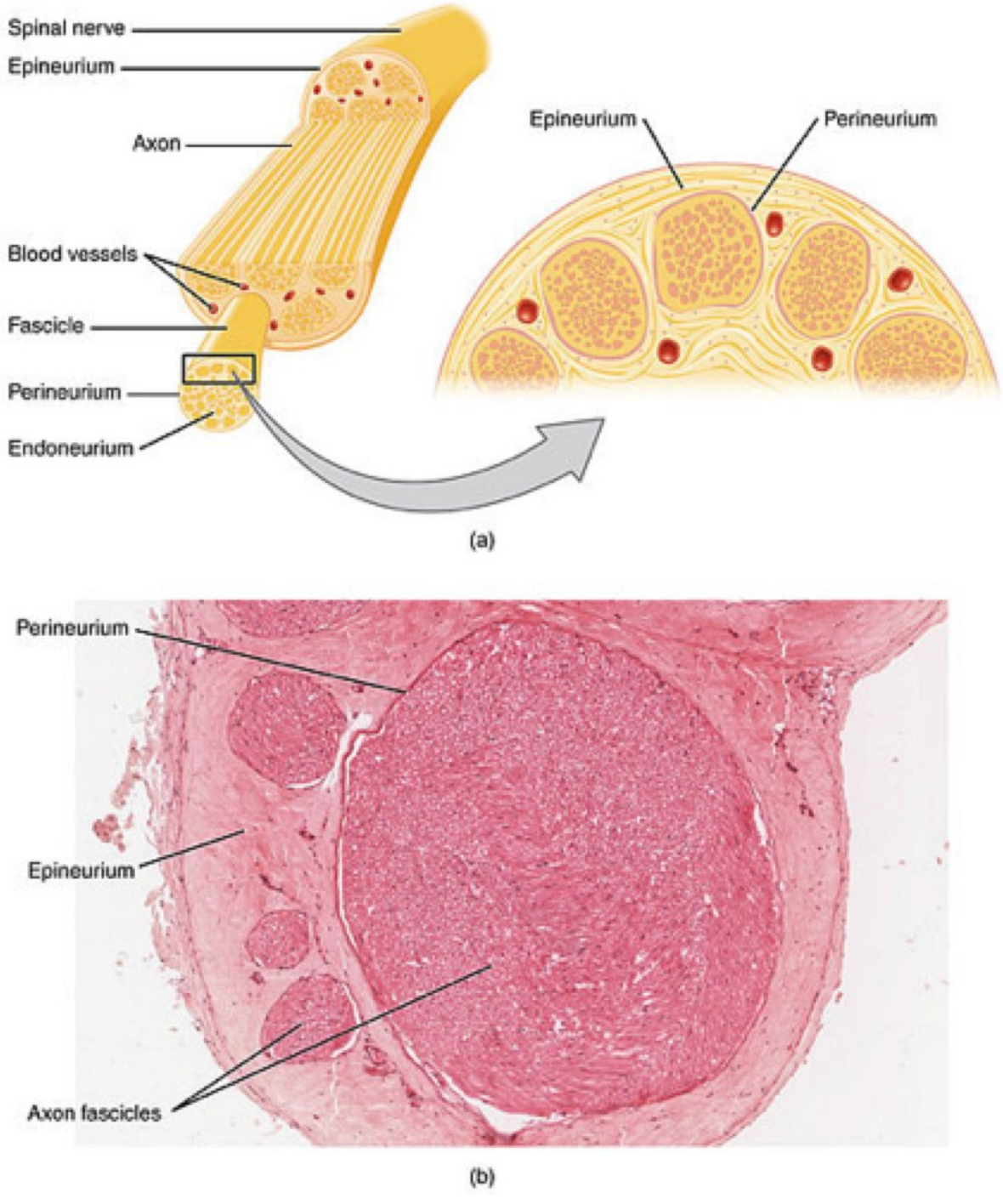
Since that time, several local anesthetic compounds have been discovered or manufactured. The goal was to increase duration of action and reduce toxicity. These agents included some of the commonly used drugs at present such as Lidocaine (discovered in 1948), Bupivicaine (discovered in 1963) and Ropivicaine (discovered in 1997).

Fun fact:

> *Meperidine, a potent opioid, was discovered in 1939 while chemists were searching for an anticholinergic drug. It turns out that meperidine is also a potent local anesthetic that, when given intrathecally performs well as a spinal anesthetic. This was first reported in 1985 (Can Anaesth Soc J 1985;32:533).*

Nerve Anatomy and Physiology

FIGURE 1: ANATOMY OF A PERIPHERAL NERVE. ILLUSTRATION FROM ANATOMY & PHYSIOLOGY, CONNEXIONS WEB SITE. HTTP://CNX.ORG/CONTENT/COL11496/1.6/, JUN 19, 2013



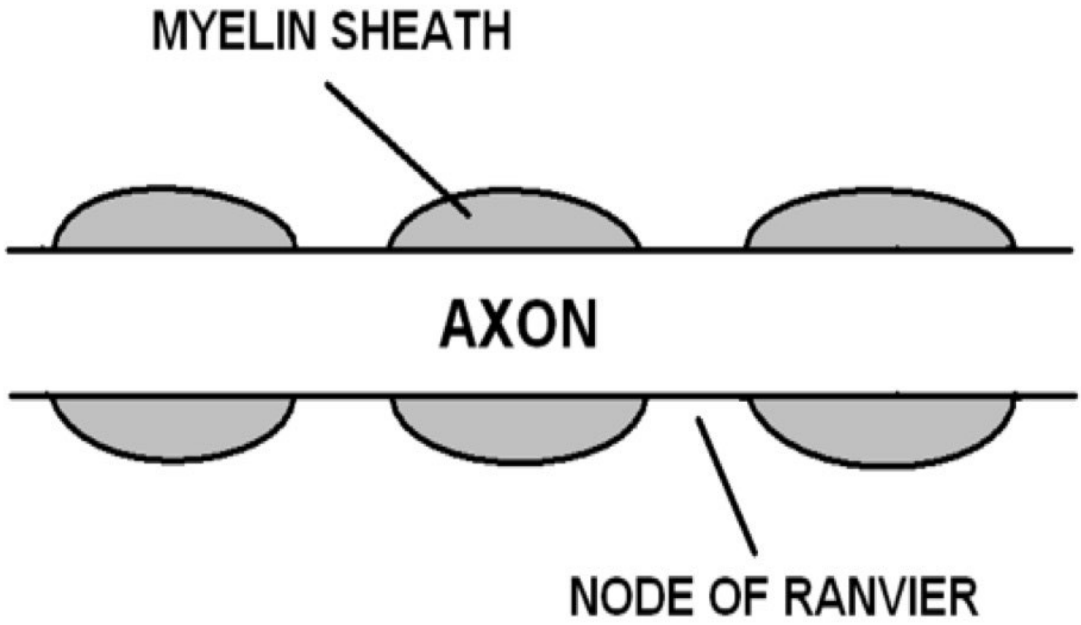
Nerve Anatomy

The microscopic anatomy of nervous tissue determines how it conducts electrical impulses (Figure 1). The outer covering of a peripheral nerve is composed of a connective tissue layer called the epineurium. The structures inside the nerve are separated into segments called fascicles, each of which is covered by a layer of connective tissue called perineurium. Each fascicle contains axons and nerve fibers, which are separated from each other by the endoneurium. The endoneurium is composed of non-neuronal glial cells. See Figure 1.

Nerve fibers can be classified as either myelinated or unmyelinated. The axons of myelinated nerve

fibers are encased several hundred times by a lipid layer formed by dedicated Schwann cells. Multiple Schwann cells span the length of the axon. Along the axon exist areas devoid of myelin called Nodes of Ranvier (Figure 2). Unmyelinated nerve fibers do not contain this myelin sheath. Instead, the body of a Schwann cell surrounds the axon. In this scenario, the body of one Schwann cell may encase many axons along its length.

FIGURE 2- SCHEMATIC OF A MYELINATED NERVE FIBRE. THE NERVE CELL AXON IS ENROBED WITH THE MYELIN SHEATH FROM SCHWANN CELLS (GRAY AREAS). THE MYELIN SHEATH IS SEPARATED BY UNCOVERED AREAS OF AXON REFERRED TO AS NODES OF RANVIER



The size and the degree of myelination determine the specific characteristics of individual nerve fibers, such as conduction velocity, and allow for their classification. Different nerve fibers thus serve different purposes.

Neuronal Electrophysiology and Nerve Impulse Conduction

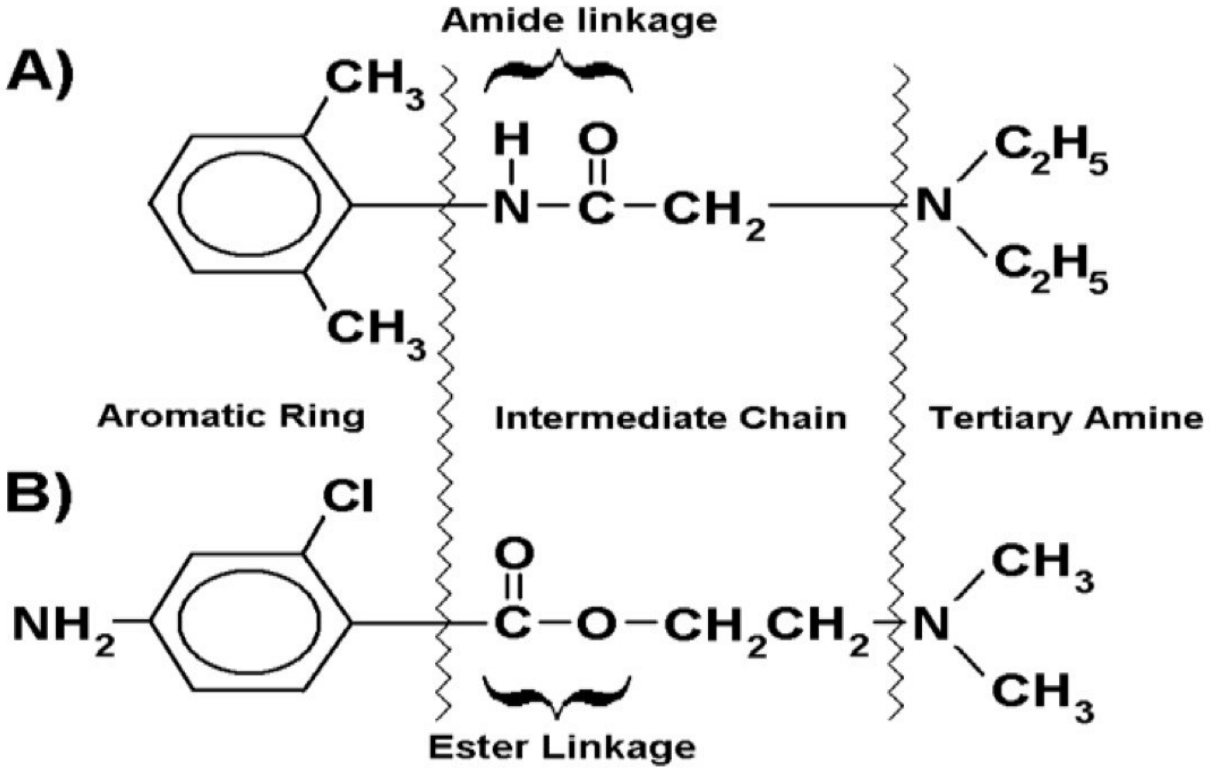
Active transport of potassium into cells and sodium out of cells against their concentration gradients results in a negative electrical gradient across the cell membrane (resting potential -60 to -70mV, negative intracellular). For an action potential to be generated, the opening (activation) of resting (inactive) sodium channels must depolarize the cell past a threshold potential. Once this occurs, a massive influx of sodium ions through activated channels generates an action potential, depolarizing the trans- membrane potential to a peak of +35 mV. The action potential will be propagated if adjacent nervous tissue also reaches the threshold potential and develops an action potential. In unmyelinated nerve fibers, the nervous tissue directly adjacent must reach the threshold potential to continue the impulse propagation. Impulses in myelinated nerves must reach threshold potential at the next Node of Ranvier (termed "saltatory conduction"). This difference partially accounts for the high conduction velocity of myelinated (via saltatory conduction) vs. unmyelinated nerve fibers.

Mechanism of Action of Local Anesthetics

Chemical Structure and Related Clinical Properties

Local anesthetics are composed of three important components: i) an aromatic ring, ii) an intermediate alkyl chain, and iii) a tertiary amine (Figure 3).

FIGURE 3- CHEMICAL STRUCTURE OF A) THE AMIDE LOCAL ANESTHETIC LIDOCAINE AND B) THE ESTER LOCAL ANESTHETIC CHLOROPROCAINE. LOCAL ANESTHETICS ARE COMPOSED OF 3 MAIN PARTS: THE AROMATIC RING, THE INTERMEDIATE ALKYL CHAIN AND THE TERTIARY AMINE. THE BOND BETWEEN THE AROMATIC RING AND THE REST OF THE MOLECULE CAN BE EITHER AN AMIDE OR AN ESTER LINKAGE.



The **aromatic ring** is the lipophilic component of the drug and helps determine the drug's **potency**. As potency is **directly related to toxicity,** local anesthetics with higher potency also have greater toxicity. The aromatic ring and the tertiary amine are linked by the **intermediate alkyl chain**. This intermediate chain contains either an ester or amide linkage, which binds the aromatic ring to the rest of the molecule. The type of linkage allows one to classify the local anesthetics as either amino-esters or amino-amides. This distinction is crucial, as drug **metabolism** is very different depending on whether an ester or amide linkage exists in the molecule.

> ***Fun fact.*** *The generic name of the local anesthetic is the key to determining whether or not the drug is an ester or amide. Apart from the "-caine" part of the name, there is no other "i" in the name of an ester anesthetic. There is always an extra "i" in amide anesthetics. For example: procaine is an ester, lidocaine is an amide.*

The **tertiary amine** is the hydrophilic component of the molecule, and classifies local anesthetics as weak bases (proton acceptors). As defined by the Henderson- Hasselbalch equation, weak bases accept protons in acidic environments and become positively charged (ionized). They are unionized in basic environments (Figure 4).

FIGURE 4 - THE HENDERSON-HASSELBALCH EQUATION. WHEN BASES ARE PLACED IN AN ENVIRONMENT CONTAINING HYDROGEN IONS, THEY READILY BIND, PRODUCING AN IONIZED MOLECULE.

The ratio of ionized to un-ionized local anesthetic in a solution is determined by the solution's pH as well as the drug's pKa. The pKa is the pH at which 50% of the drug exists in the ionized form and 50% in the unionized form. Local anesthetics are weak bases that are insoluble in water. To make them soluble, commercially prepared solutions tend to be acidic compared to physiologic pH. This results in a large proportion of the drug being in the ionized form and, therefore, soluble. **Yet it is the un-ionized (non-soluble) form which readily enters cells to have effect**. The extent of the difference between a given drug's pKa and plasma's pH will determine the ratio of ionized to un-ionized drug in plasma. The closer the drug's pKa is to the pH of the blood, the more it is found in the unionized form, while in plasma. For this reason, drugs with a **lower pKa** have a **faster onset**, in general. Accordingly, if a patient were to develop acidosis, then blood pH drops, the gap between pH and pKa widens, more of the drug becomes ionized, and the speed of onset is reduced.
Note 1: Chloroprocaine is an exception to the above trend; it has a high pKa but fast onset.
Note 2: Administering a larger dose or concentration of local anesthetic will also hasten onset.

Although potency, toxicity, and speed of onset are all clinical properties of local anesthetics that are related to their chemical structure, one must also consider their duration of action when using these drugs. The degree of protein binding of local anesthetics will affect their duration of action. Local anesthetics with high protein binding (e.g., bupivacaine and ropivacaine), as compared to those with lower protein binding (e.g., lidocaine), exhibit prolonged duration of action. In addition to **protein binding**, the local anesthetic's ability to alter regional blood flow to the area of infiltration will affect its **duration of action**. Intrinsic vasodilation properties of local anesthetics (lidocaine, bupivacaine, chlorprocaine) will result in increased systemic absorption due to increased regional blood flow. This will decrease the duration of action. Similarly, local anesthetics possessing intrinsic vasoconstricting properties (cocaine, ropivacaine) or those containing epinephrine will decrease regional blood flow, slow systemic absorption, and prolong the duration of action. It must be noted, however, that the effect of epinephrine prolongs duration of block in some local anesthetics (i.e., lidocaine) greater than others (i.e., bupivacaine).

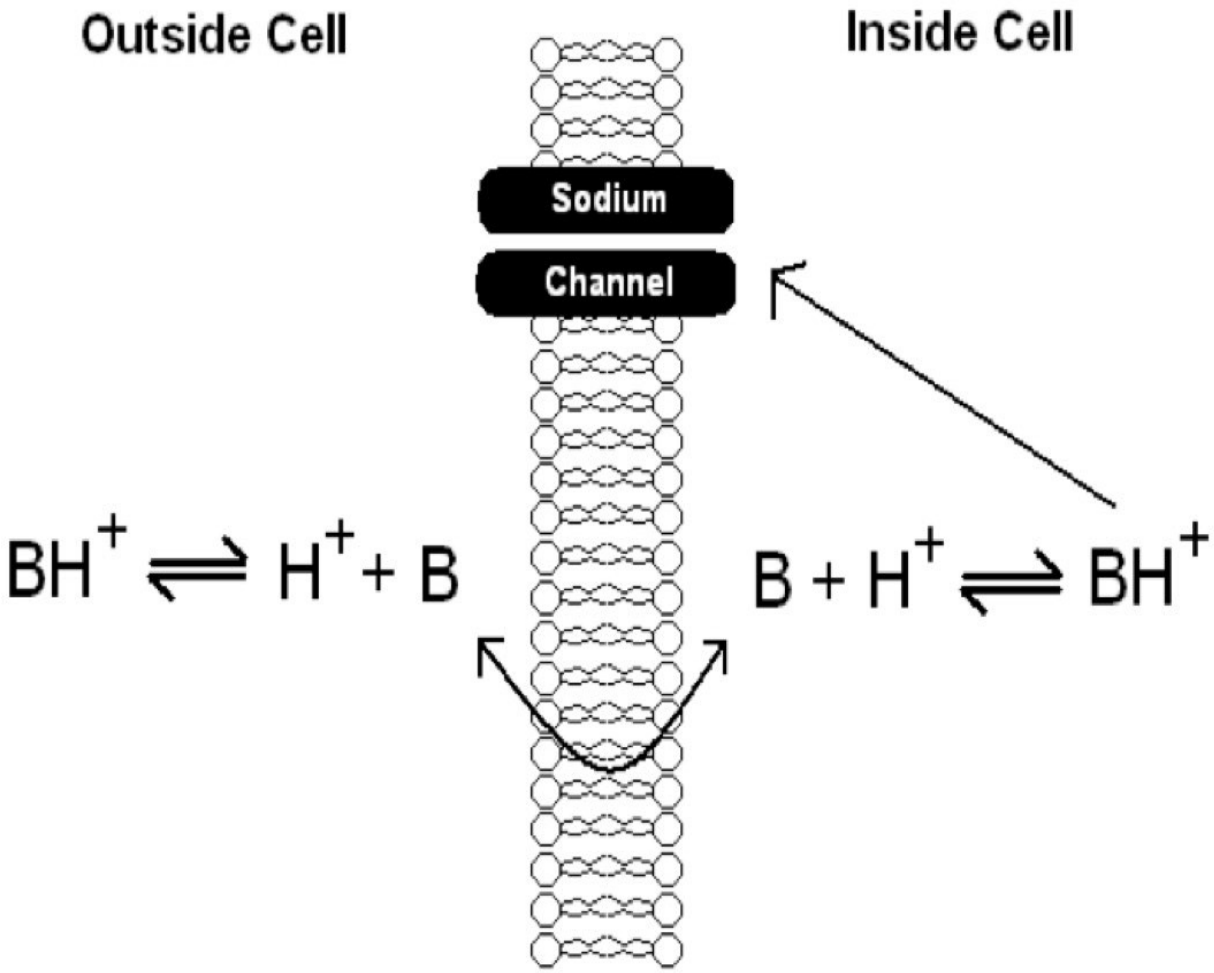
> ***Fun fact:*** *Tetrodotoxin, a natural neurotoxin produced by the puffer fish, has a similar structure to local anesthetics. However, the binding to the sodium receptor is not specific to neural tissue and it is not reversible.*

Mechanism of Action

The sodium channel involved in the action potential generation, located on the cell membrane of the axon, is the primary site of action of the local anesthetics. The drug must first penetrate the different layers of the nerve (i.e. epineurium, perineurium, endoneurium) and enter the interior of the cell. Only the un-ionized form of the local anesthetic can cross these layers and the axon cell membrane. Once inside the cell, the un-ionized form equilibrates with its ionized counterpart due to the acidic intracellular environment (Figure 5). Only the ionized form which adheres to the binding site on inactive sodium channels has an effect. Binding prevents channel opening, thereby slowing depolarization of the

cell membrane, preventing it from reaching the threshold potential, and preventing the achievement of an action potential.

FIGURE 5 - ACTION OF LOCAL ANESTHETICS. ONLY THE UN-IONIZED FORM OF THE DRUG CAN CROSS THE BI-LIPID MEMBRANE TO ENTER THE NERVE CELL. ONCE INSIDE, THE ACIDIC ENVIRONMENT PERMITS THE BASE TO BECOME IONIZED. IT IS THIS IONIZED FORM THAT BINDS TO THE SODIUM CHANNEL EMBEDDED IN THE LIPID MEMBRANE.



New research: The sodium channel comes in many phenotypes. Current research has found over 15 different types. There may be specific phenotypes for sensory nerves that do not affect motor nerves. Long acting compounds such as neosatitoxin may be clinically useful as it is very long acting and does not cause motor block.

Pharmacokinetics of Local Anesthetics

Absorption

Multiple factors affect a local anesthetic's ability to be absorbed from the injected site into the systemic circulation.

i. Site of injection: High vascularity at the area of infiltration will increase systemic absorption. In decreasing order of highest uptake to lowest uptake, these sites include:

tracheal→intercostal→caudal→paracervical→epidural→brachial plexus→sciatic /femoral→subcutaneous

(mnemonic T-ICPEBSS).

*Caution must be exerted when injecting local anesthetic in an area of high vascularity to avoid systemic toxicity.

ii. Regional blood flow: local anesthetics with intrinsic vasoconstricting properties, or those containing epinephrine, will decrease regional blood flow and slow systemic absorption. Drugs with intrinsic vasodilating properties will increase regional blood flow and enhance systemic absorption.

iii. Lipophilicity: Local anesthetics with high lipophilicity will remain bound to tissues and slow systemic absorption. The opposite is true for drugs with low lipophilicity.

iv. Balance of lipophilicity and blood flow: The balance between the drug's ability to alter regional blood flow (ii) and the drug's lipophilicity (iii), both intrinsic properties of local anesthetics, will affect absorption.

v. Dose and concentration: Administering larger doses or concentrations increases systemic absorption and increases the risk of toxicity.

Distribution

Distribution of local anesthetic is affected by:

i. Regional blood flow: local anesthetics are more rapidly distributed to vessel rich organs.

ii. Plasma protein binding: Highly bound molecules will have a smaller volume of distribution because less drug can leave plasma to enter tissues.

Metabolism

Amide local anesthetics are metabolized in the liver by microsomal enzymes. Metabolites are subsequently eliminated by the kidney.

Ester local anesthetics are metabolized by plasma cholinesterase (pseudocholinesterase), the same enzyme responsible for the metabolism of other anesthetic drugs, including succinylcholine. Metabolism of amino-esters is **extremely rapid, decreasing risk of systemic toxicity.** (The exception is tetracaine). Decreases in pseudocholinesterase quantity (e.g. liver failure) or activity (the genetic disorder —pseudocholinesterase deficiency) may slow elimination of these drugs.

Systemic Toxicity

Local anesthetics given in large doses may produce significant end-organ effects on most excitable membranes in the body, but particularly of the central nervous and cardiovascular systems. Preparedness when administering a large volume of drug is therefore mandatory. A sample checklist of items necessary prior to using local anesthetics in large quantities is found in Table 1.

Table 1 - Checklist prior to using local anesthetics in large volumes.
• Appropriate patient history and physical exam (including allergies)
• Intravenous access
• Oxygen
• Resuscitation and airway equipment
• Personnel skilled in airway management
• Resuscitation drugs (for BOTH cardiovascular and CNS toxicity)
• Availability of lipid infusion

CNS Toxicity

The CNS is affected in a dose-dependent manner. Early signs of high blood levels of local anesthetic include **circumoral numbness and a metallic taste in the mouth.** These are not CNS manifestations, but are rather local effects of the drug in the oral cavity and lips. As the concentration increases, early excitatory signs of CNS toxicity manifest, including **light-headedness and agitation**. This is followed by **seizure activity**. As mentioned earlier, local anesthetics are membrane depressants. The mechanism explaining these initial excitatory phenomena with membrane depressant drugs is the preferential blockade of the inhibitory neurons of the CNS. Depressing these inhibitory neurons results in unopposed global excitation (Figure 6). Excitatory CNS symptoms are therefore a result of CNS depression by local anesthetics. The excitatory symptoms are followed by CNS depression and coma. In general, more potent local anesthetics are more likely to cause CNS effects.

As seizures induced by short-acting local anesthetics (i.e. lidocaine) are usually self-limiting, **treatment involves support of the airway, breathing, and circulation, as well as hyperventilation. The dose of bupivacaine that causes seizures is very close to the dose that causes cardiovascular collapse. In the case of sustained seizures caused by long-acting local anesthetics (i.e. bupivacaine, ropivacaine), anti-convulsants (e.g. benzodiazepines) and potent general anesthetics (i.e. propofol) may be required. Intralipid should be started as soon as possible.**

Cardiovascular toxicity

The pathogenesis of cardiovascular toxicity with high plasma concentrations of local anesthetics is multi-factorial:

i. Direct effects on the myocardial cells and vasculature: the blockade of cardiac myocyte sodium channels can result in both profound myocardial depression (contractile myocytes) and conduction abnormalities (conduction pathway myocytes). **Ventricular dysrrhythmias,** particularly with bupivacaine, may occur. Direct vasodilating effects on the vasculature may also contribute to the **cardiovascular collapse.**

ii. Effects on the central nervous system and autonomic nervous system: High doses of local anesthetic may block autonomic and central nervous system nerve fibers producing profound hypotension.

More potent agents, such as bupivacaine, are more cardiotoxic when compared to less potent agents. Bupivacaine, which is lipophilic and highly protein bound, appears to have a greater affinity for the

cardiac sodium channels and also dissociates from them much slower. This can lead to accumulation of the drug in the heart, resulting in major toxicity. This is the so called "fast-in, slow-out" phenomenon.

Significant cardiovascular collapse and arrhythmias are very difficult to treat. As hypoxia and acidosis greatly potentiate cardiovascular toxicity, prompt resuscitation, including support of airway, breathing, and circulation, is key to management. Although often used, traditional anti-arrhythmics have limited success in this setting. **The use of intravenous lipid infusion is a useful tool to treat cardiovascular toxicity.** Availability of intravenous lipid is thus important when performing nerve blockade with large volumes of potent local anesthetics.

Commonly Used Local Anesthetics

Lidocaine

Lidocaine is very commonly used in clinical practice. It is used extensively in spinal and epidural anesthesia, peripheral nerve blockade (e.g., brachial plexus block), sub-cutaneous infiltration, and topical anesthesia (e.g., anesthesia of the airway during intubation). In addition, it is used intravenously to blunt the increase in blood pressure during laryngoscopy, as the local anesthetic of choice for intravenous regional anesthesia (IVRA), as an anti-arrhythmic, and to treat certain chronic pain conditions. More recently intravenous infusions of lidocaine are used *intraoperatively* to treat *postoperative* pain.

Lidocaine is selected for major peripheral nerve blockade because of its rapid onset of action and intermediate duration (approximately 1-3 hours). It is ideally suited for short procedures where there is no significant post-operative pain once anesthesia has resolved. Similarly, lidocaine for spinal anesthesia is ideal for very short procedures as its duration of action is approximately 45-60 minutes. The popularity of lidocaine for spinal anesthesia has decreased slightly due to the possibility of a side effect called "transient radicular irritation" in certain high-risk patients. This phenomenon results in pain in the buttocks and thighs, which may last up to one week after spinal anesthesia with lidocaine. It is completely transient.

The maximum recommended dose of lidocaine is approximately 5mg/kg plain and 7mg/kg with epinephrine. Maximum dose depends on site of administration, but generally should not exceed 300 mg plain or 500 mg with epinephrine. By reducing absorption from the site of injection, the addition of epinephrine may significantly prolong blockade and reduce toxicity.

Bupivacaine

Bupivacaine is very often used primarily because of its long duration of action. It is the most commonly used agent in spinal anesthesia as well as epidural infusions for both labour analgesia and post-operative pain control.

For spinal anesthesia, both a hyperbaric (density greater than CSF) and an isobaric (density similar to CSF) form are used. Duration of the spinal block is dependent on the dose and type of solution used, but can range from 1.5 to 3 hours.

Bupivacaine is used for epidural analgesia via infusion because it is devoid of tachyphylaxis and produces good sensory analgesia with preserved motor function when dilute concentrations are used. Bupivacaine is ideal for major peripheral nerve blockade where the surgical procedure is of a long duration or is associated with significant post-operative pain. Effective analgesia can be achieved for many hours (up to 20 hours). Onset, however, is slower compared to lidocaine.

The maximum dose of bupivacaine is 3mg/kg. Again, the maximum dose depends on the site of administration, but generally should not exceed 175 mg plain or 225 mg with epinephrine. The addition of epinephrine reduces toxicity but does not significantly prolong blockade. Care must be taken to avoid intra-vascular injection as significant cardiovascular collapse and arrhythmias can occur, which are difficult to treat.

Ropivacaine

Ropivacaine is structurally similar to bupivacaine. It may be somewhat less potent but the duration of action is similar. Because of this, it is commonly used for epidural anesthesia as well as for major

peripheral nerve blockade where prolonged analgesia is required. Like bupivacaine, the speed of onset is slower than lidocaine.

The main advantage ropivacaine exhibits over bupivacaine was thought to be the lower potential for cardiovascular toxicity and the drug was designed with this in mind. For practical purposes, the cardiovascular toxicity of ropivacaine, in equipotent doses, is the same as bupivacaine. The recommended maximum dose is the same as bupivacaine. Toxicity, however, is greater than lidocaine.

> ***Fun Fact:*** *to determine the number of mg/ml of local anesthetic just multiply the percent concentration with 10, e.g. Lidocaine 1% (1 X 10=10) contains 10mg/ml of Lidocaine, Bupivicaine 0.5% (0.5 X 10 = 5) contains 5mg/ml.*

Chapter 4

RESUSCITATION

Sections:

1. **Cardiopulmonary Resuscitation**
2. **Blood Component Replacement Therapy and Perioperative Blood Conservation**

Section 4.1

Cardiopulmonary Resuscitation

Viren N. Naik MD MEd FRCPC, Susan DeSousa B.Sc, RRT, CTDP

Introduction

Cardiac arrest is cessation of the circulation of blood from heart pump failure, presenting clinically as a pulseless loss of consciousness. The aim of Basic Life Support (BLS) is to provide oxygenated blood to the heart and brain. BLS involves the oxygenation and artificial pumping of blood to the vital organs by use of simple airway techniques and cardiac massage. Advanced Cardiac Life Support (ACLS) is based on BLS and includes more advanced airway techniques, delivery of drugs and electric shock. Its overall aim is to return spontaneous circulation for patient survival.

There are many causes of cardiac arrest. However, out-of-hospital cardiac arrest is often sudden and caused by an acute coronary event, whereas in-hospital cardiac arrest is often preceded by warning signs such as hypotension, tachycardia and a reduced level of consciousness (when patients are said to be "pre-arrest").

The outcome from cardiac arrest is poor. Survival to go home is 22.3% to 25.5% for in-hospital sudden cardiac arrests (SCA) [1]. Outcome depends on the initial presenting cardiac rhythm. Ventricular fibrillation (VF) and ventricular tachycardia (VT) have far more favourable outcomes than asystole and pulseless electrical activity (PEA). Cardiopulmonary resuscitation (CPR) prolongs the time that VF is present following SCA, and also increases the chance of a shock being successful.

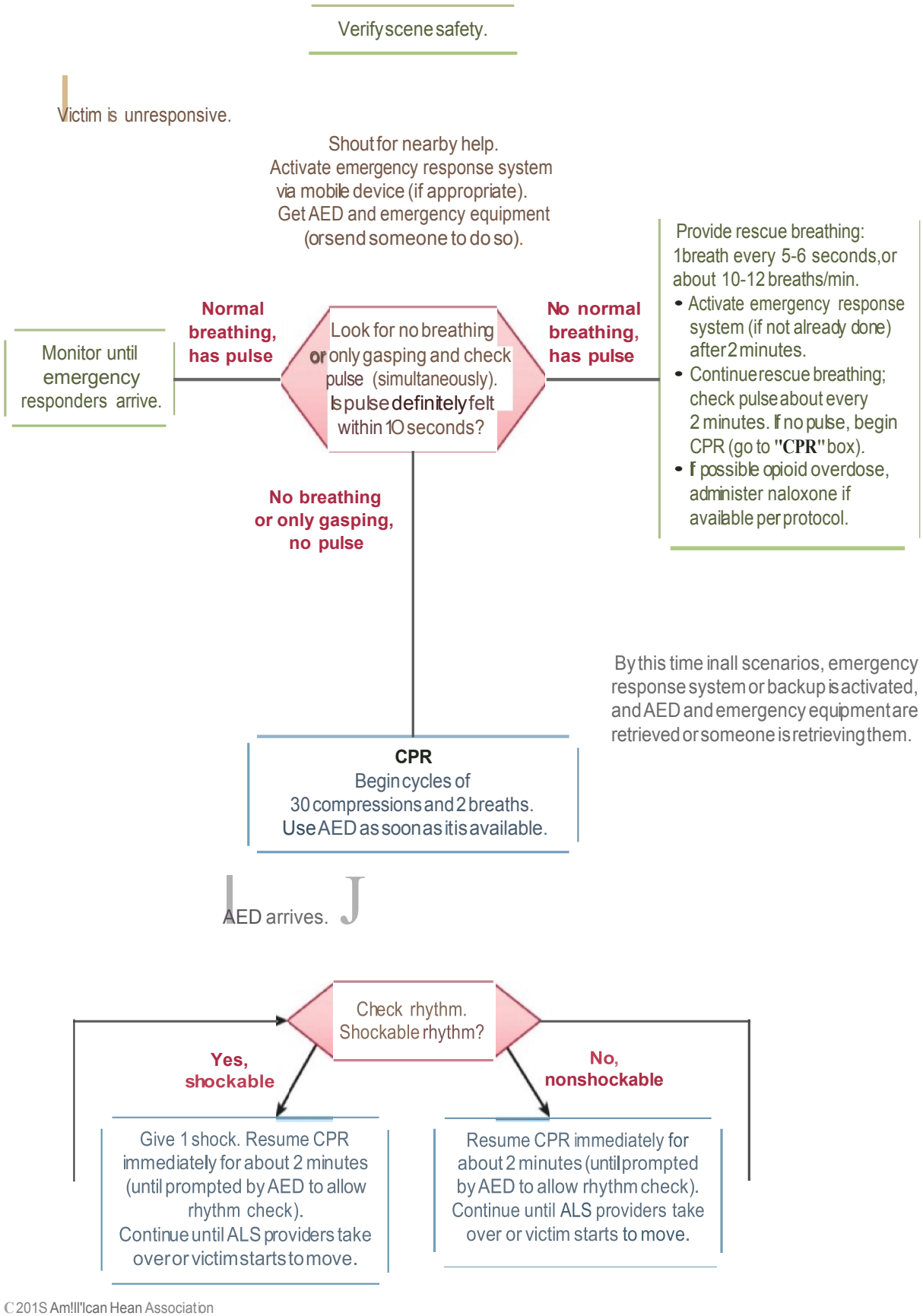
ACLS is a multidisciplinary team effort undertaken following a standardized, internationally agreed upon and evidence-based approach. Algorithms are regularly reviewed and updated, most recently in 2015. North American algorithms are published by the American Heart Association[2].

Basic Life Support (BLS)

Before starting BLS providers must always ensure that it is safe to approach the patient first. Response is assessed by gently shaking the patient and asking "Are you alright?" No response ensures further progress down the algorithm. A positive response means the patient should be placed in the recovery position and further help should be sought.

Before starting BLS you must "call for help." In the hospital, this means calling a "code blue." Out of the hospital setting this means dialing 911, even if this means going to find a phone first. The exception to this rule is drowned and asphyxiated victims where 5 cycles of CPR should be provided before going for help.

FIGURE I - ADULT BASIC LIFE SUPPORT (AMERICAN HEART ASSOCIATION 2015)



Chest Compressions are a Priority Over Airway and Breathing

Assess the adult victim for absence of breathing or no normal breathing (gasping). If there is no effective breathing, then the rescuer immediately begins chest compressions (CPR). Lay rescuers should not check for a pulse. Healthcare providers should take no longer than 10 seconds to check for a pulse. If a pulse is absent or if you are unsure, immediately start CPR. Pulse is best assessed at the carotid artery. After 30 compressions, 2 breaths (1sec each) are given (30:2) via bag-valve-mask and the cycle repeated. The rate of chest compressions should be 100-120 per minute. Effective chest compressions are vital. The heel of one hand is placed over the lower sternum with the other hand placed on top. Arms are kept straight and the rescuer should lean over the patient using body weight to push directly down to a depth of 5 cm or 2 inches. The chest must be allowed to recoil. Minimize interruptions in chest compressions and alternate rescuers every 2 minutes.

If a pulse is present, the rescuer should continue to provide 1 breath every 6 seconds. (10 breaths per min) Recheck the pulse every 2 minutes. If no pulse is present, then CPR is started immediately. Head tilt and chin lift to open the airway. This is contraindicated in victims with suspected spinal injury. If a spinal injury is suspected, a jaw thrust without head extension is utilized. Occasional gasping or intermittent breathing is not effective and rescue breaths should be given. Rescue breaths are delivered commonly in-hospital by bag-mask ventilation.

Automatic external defibrillators (AEDs) have been shown to increase survival significantly in the out-of-hospital setting. These machines analyze if a patient's rhythm is amenable to defibrillation (i.e. shockable). If shockable, the defibrillator will instruct the rescuer to stand clear and deliver a current. Regardless of whether a shock is delivered, 5 CPR cycles (approximately 2 mins) should follow before further automated analysis.

Physiology of Cardiopulmonary Resuscitation (CPR)

After 3 minutes, the brain's oxygen reserves are depleted and ischemic injury is inevitable. In the myocardium, the high oxygen extraction ratio places the heart at early risk of ischemic injury. The aim of CPR is to provide oxygenated blood to the myocardium and brain to prevent or minimize ischemic injury.

Aortic diastolic pressure (AoDP) is critical to coronary artery perfusion. Chest compressions raise AoDP in a gradual manner, thereby increasing flow of oxygenated blood to the myocardium and via the carotids to the cerebrum. It is critical that AoDP is not allowed to fall during CPR. Clinically, this means chest compressions should continue uninterrupted as any break results in a fall in AoDP.

Chest compressions work by a two-fold mechanism. First, there is direct massage of the heart in an attempt to pump blood through the heart. Second, the repeated increase and decrease of intrathoracic pressure acts as a mechanical pump. During effective CPR, cardiac output is 25-33% of normal.

Adult Advanced Cardiopulmonary Life Support (ACLS)

The algorithm for ACLS pulseless arrest is shown in Figure 2. Pulseless arrest occurs due to 4 cardiac rhythms. The algorithm is divided into shockable rhythms, Ventricular Fibrillation (VF) and pulseless Ventricular Tachycardia (pVT) and non-shockable rhythms, asystole and pulseless electrical activity (PEA). High quality BLS should be provided, 100% oxygen given, and monitors/defibrillator attached.

Shockable Rhythms – Ventricular Fibrillation / pulseless Ventricular Tachycardia

The Key to survival from VF/VT is good, early CPR and early defibrillation

In witnessed SCA, CPR should begin immediately followed by administration of a shock. In unwitnessed SCA, 5 cycles of CPR should be provided before administering a shock. (Note: evidence remains unclear if delaying defibrillation to perform CPR is beneficial in unwitnessed arrests)

If monitors confirm VF or pulseless VT, then a single shock is delivered. Compressions must continue as the defibrillator is charging. Monophasic defibrillators are set at 360J and biphasic defibrillators are set according to manufacturer's recommendation (120 to 200J). After the shock, cardiac compressions are resumed immediately without checking pulse or rhythm. Instead, 5 cycles of CPR (or 2 minutes if an advanced airway is placed) should be provided before reassessing rhythm and pulse.

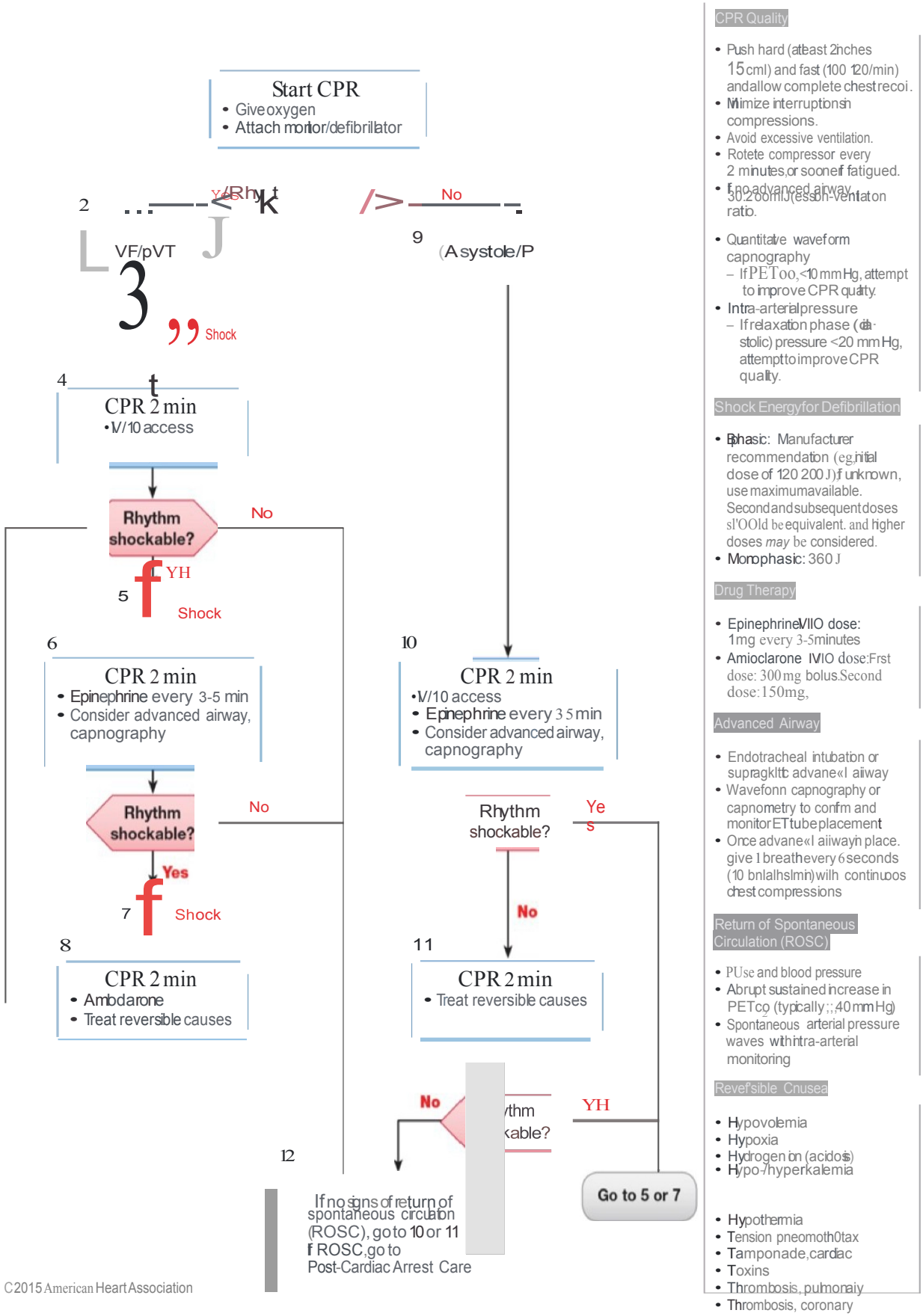
When an advanced airway (endotracheal tube, laryngeal mask airway or combitube) is placed, compressions should continue uninterrupted at a rate of 100-120/minute. Ventilation is provided at a rate of 8-10 breaths/minute.

Intravenous (IV) access is of secondary importance to CPR and delivery of shocks. Peripheral IV access is usually sufficient. Epinephrine 1 mg IV is given during CPR after the second shock and repeated at 3-5 minute intervals.

If VF or pulseless VT persists after CPR, 3 shocks and epinephrine then amiodarone 300 mg IV should be given. Administration of amiodarone has been shown to increase the chances of shocking VF/VT back to sinus rhythm.

If there is doubt about a pulse being present, then continue CPR. Compressions should only be interrupted for shock delivery, rhythm check, and ventilation (without advanced airway).

FIGURE 2 - ADULT CARDIAC ARREST ALGORITHM (AMERICAN HEART ASSOCIATION 2015).



Non-shockable rhythms – Asystole / Pulseless Electrical Activity (PEA)

The Key to survival from PEA/Asystole is good, early CPR and excluding all reversible causes

During PEA, the heart produces mechanical contractions insufficient to maintain a cardiac output and blood pressure. In asystole there are no cardiac contractions, and outcome is poor. The reversible causes of PEA are the "5 H's and 5 T's" shown in Table 1.

TABLE 1 - REVERSIBLE CAUSES OF PULSELESS ELECTRICAL ACTIVITY.

5 H's	5 T's
1. Hypoxia 2. Hypovolemia 3. Hydrogen ion (acidosis) 4. Hypo/Hyperkalemia 5. Hypothermia	1. Tamponade, cardiac 2. Tension pneumothorax 3. Thrombosis, coronary 4. Thrombosis, pulmonary 5. Toxins (overdose/poisoning)

If monitors confirm a non-shockable rhythm, then 5 cycles (2mins) of CPR are started before reassessing the rhythm. Epinephrine is given every 3-5 minutes. Discuss reversible causes throughout. (5 H's and 5 T's)

To exclude hypoxia, an advanced airway is recommended early.

If the rhythm converts to VF/pulseless VT, a shock should be delivered as per the shockable rhythms algorithm.

Pharmacology and Defibrillation

No drug given during ACLS has been shown to increase survival. Drugs are given on a physiological basis.

Drug Administration

ACLS drugs can be administered via different routes. The IV route is commonest with drugs given as a bolus reaching the central circulation in 1-2 minutes. Drugs are given immediately following the rhythm check. Central venous access is not necessary. The intraosseous (IO) route provides access in all ages to a non-collapsible venous bed and absorption is similar to central access. When all other access fails, drugs can be administered via the endotracheal tube (ETT) at 2-2.5 times the IV dose. Drugs should be diluted in 5-10mls water and injected directly down the ETT. The following drugs can be administered

via the ETT: epinephrine, atropine, lidocaine and naloxone.

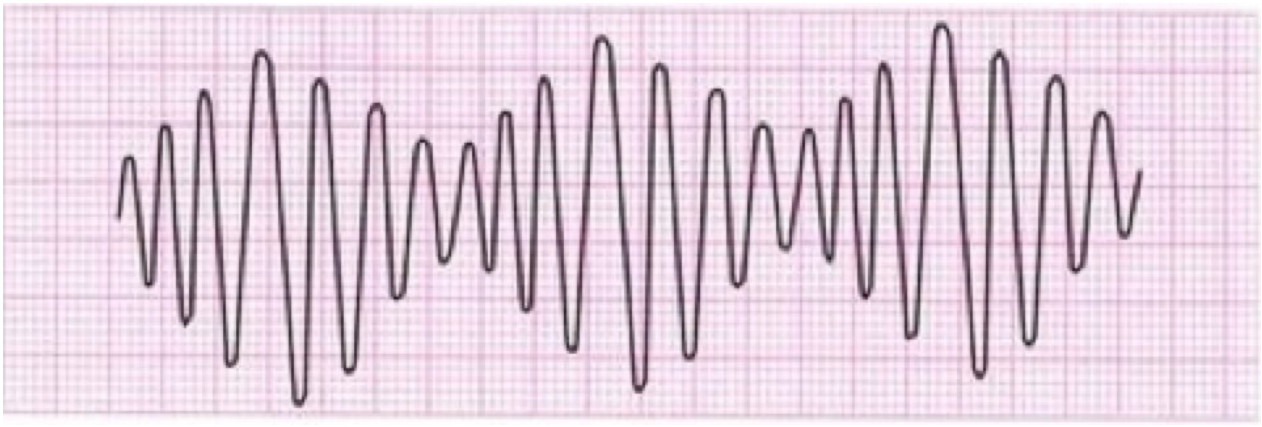
Vasopressors

High dose epinephrine has predominantly alpha adrenergic effects, resulting in peripheral vasoconstriction, increased aortic diastolic pressure, and an increased coronary and cerebral perfusion. However, it also increases cardiac work and myocardial oxygen consumption.

Antiarrhythmics

Antiarrhythmics are used in refractory VF and pulseless VT after 3 shocks have failed to convert to sinus rhythm. First line therapy is amiodarone 300 mg IV/IO bolus and is followed by 150 mg IV/IO bolus if required. Amiodarone acts on cardiac potassium channels and alpha- and beta-adrenergic receptors. It has mild negative inotropic effects. Lidocaine (1-1.5 mg/kg) acts on sodium channels. It can be used as an alternative to amiodarone only if amiodarone is not available. Lidocaine has less success in achieving a return to spontaneous circulation, and more conversion to asystole than amiodarone. Magnesium (1-2 g bolus over 10-20 mins) is used as an anti-arrhythmic for torsade de pointes, a form of VT (see Figure 3).

FIGURE 3 - TORSADE DE POINTES VENTRICULAR TACHYCARDIA.



Defibrillators and Safe Defibrillation

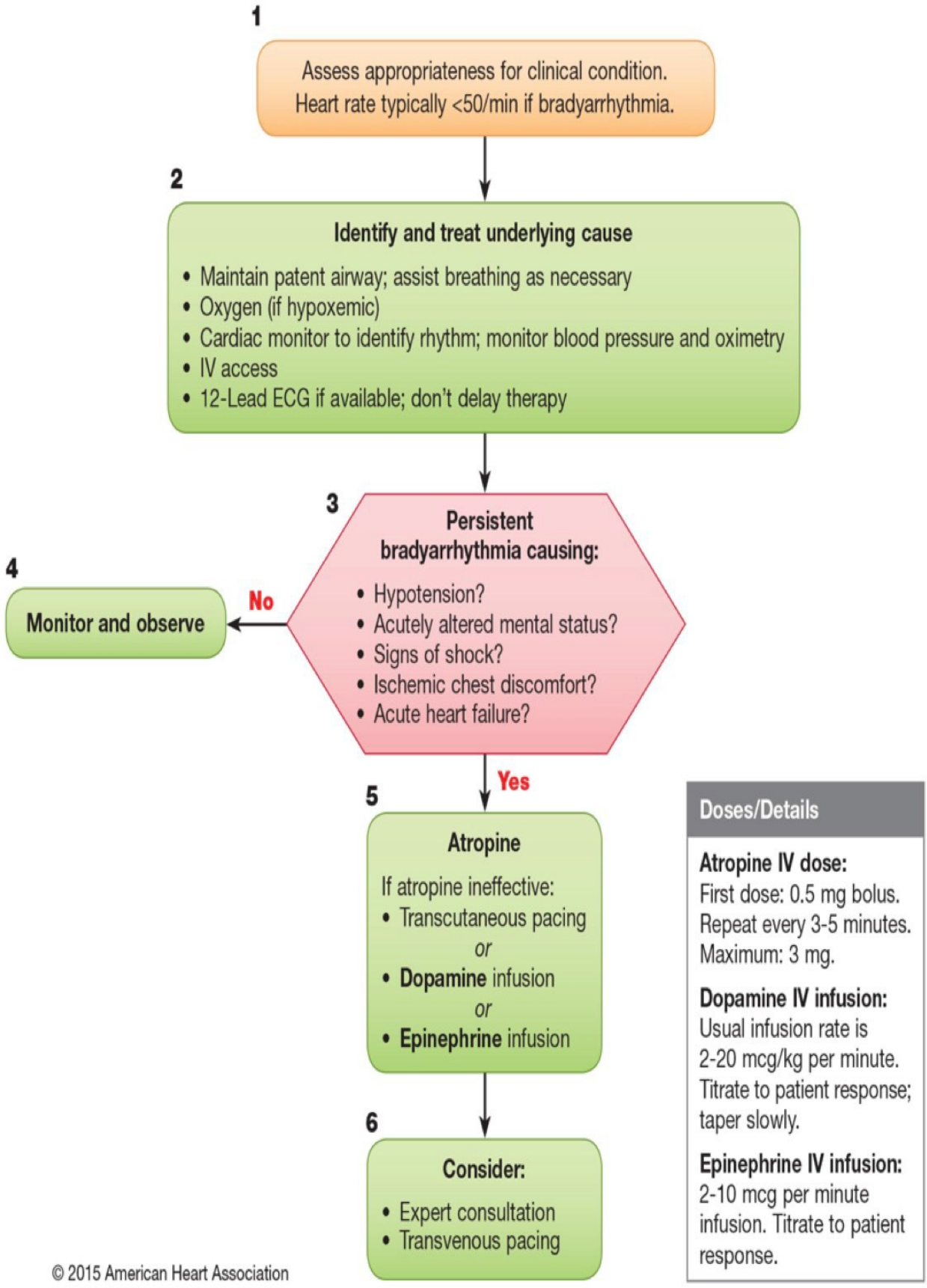
Defibrillation involves delivery of electric current through the heart to depolarize myocardial cells and "reset" the myocardium. Resistance to current is called transthoracic impedance. Chest wall impedance is high, but is reduced by the application of gel pads and by applying paddles firmly. Lower impedance means that more current can be delivered to the myocardium and defibrillation is more likely to be successful. Defibrillators can be monophasic or biphasic. Biphasic defibrillators have been shown to be more effective at terminating VF.

Safe defibrillation is essential for ACLS providers. Pads are placed to the left side of the sternum and at the apex of the heart. Oxygen should be disconnected from the patient and withdrawn to a safe distance, as fires can occur. Manual paddles should always be placed back on the defibrillator when not in use, and should never be discharged into air. Before defibrillating, an audible instruction for all rescuers to "stand clear" and a visual confirmation of rescuer safety should always occur.

Adult Bradycardia Algorithm

Figure 4 shows the adult bradycardia algorithm. Bradycardia is defined as a heart rate < 50. Treatment with drugs and/or pacing is required for all bradyarhythmias causing poor perfusion. Bradyarhythmias of most concern are second degree (type 2 Mobitz) and third degree heart block, which can both degenerate to asystole.

FIGURE 4 - ADULT BRADYCARDIA ALGORITHM (AMERICAN HEART ASSOCIATION 2015).



Treatment

Airway and breathing must be maintained at all times. Give 100% oxygen, gain IV access, and attach

monitoring.

It is important to recognize the signs of poor perfusion: a reduced level of consciousness, chest pain, acute heart failure, and signs of shock. If any of these signs exist, then atropine (0.5 mg IV up to a max. of 3 mg IV) should be given as first line drug therapy. Atropine administration should not delay transcutaneous pacing (TCP) for patients with poor perfusion. Atropine is a temporizing measure while awaiting trans-cutaneous/venous pacing for patients with symptomatic sinus bradycardia. If the heart rate fails to respond to atropine, give epinephrine (2-10 mcg/min) whilst preparing for transcutaneous pacing. Immediate pacing should be given to all patients with second degree (Mobitz type 2) and third degree heart block, as atropine will not treat these rhythms.

Transcutaneous pacing pads are placed anteriorly and posteriorly, at the sternal and interscapular positions. Defibrillators are set to the pacing mode. Electrical capture on the EKG is achieved by slowly increasing the current. Verify mechanical capture of the myocardium by assessing the pulse. Pacing is painful so analgesia and sedation should be considered. Transvenous pacing is undertaken by specialists.

Adult Tachycardia Algorithm

Figure 5 shows the adult tachycardia algorithm. Tachycardias are defined as a HR greater than 150 beats/min. Tachycardias are classified into narrow complex supraventricular tachycardias (SVT) or wide complex tachycardias. SVTs include sinus tachycardia, atrial fibrillation (AF), atrial flutter and accessory pathway-mediated tachycardia. An irregular SVT is usually AF. Wide complex tachycardias include VT and SVT with aberrant conduction.

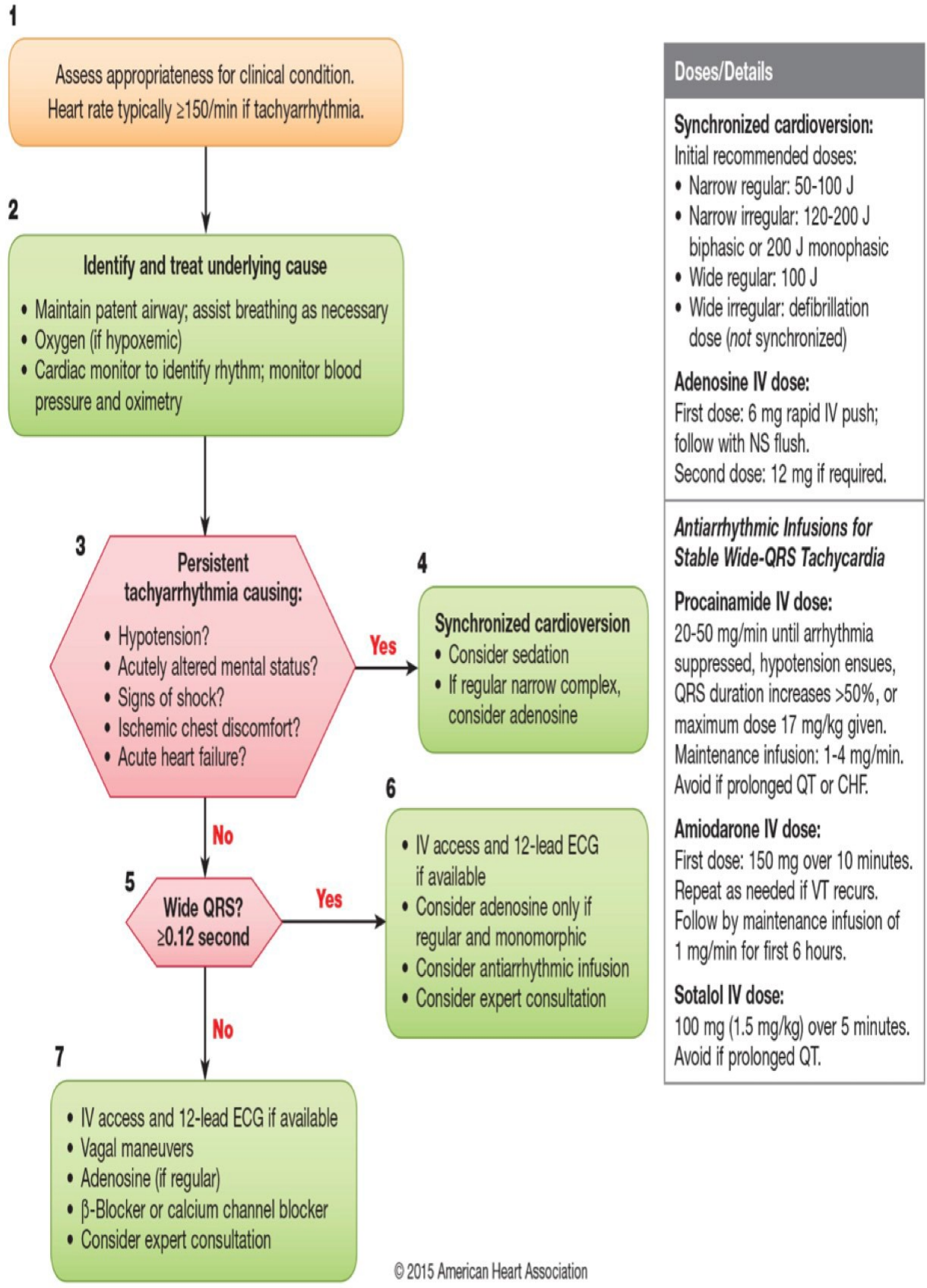
Treatment

Ensure a patent airway, supply 100% oxygen and ensure adequate breathing; gain IV access and attach monitors. A 12-lead EKG is required for interpreting these cardiac arrhythmias. Recognize poor perfusion by reduced level of consciousness, chest pain, signs of shock, acute heart failure or hypotension. If any are present, then the patient is unstable and immediate cardioversion should be considered. A stable patient allows time for antiarrhythmic drugs.

Emergency cardioversion requires IV access and sedation if the patient is conscious. Defibrillators should be set to the synchronized cardioversion mode. It is important to ensure that delivered shocks are synchronized, to avoid current delivered during the cardiac relative refractory period, which can result in VF.

If the patient is stable, then determine whether tachycardia is narrow complex (QRS <0.12 seconds) or wide complex (QRS >0.12seconds). Conversion of narrow complex tachycardias can be undertaken by vagal maneuvers and adenosine 6-12 mg IV bolus. If this fails, consider beta blockers, calcium channel blockers, and/or expert consultation. Wide complex tachycardias can be treated by amiodarone 150 mg IV bolus and/or expert consultation.

FIGURE 5 - ADULT TACHYCARDIA ALGORITHM (AMERICAN HEART ASSOCIATION 2015).



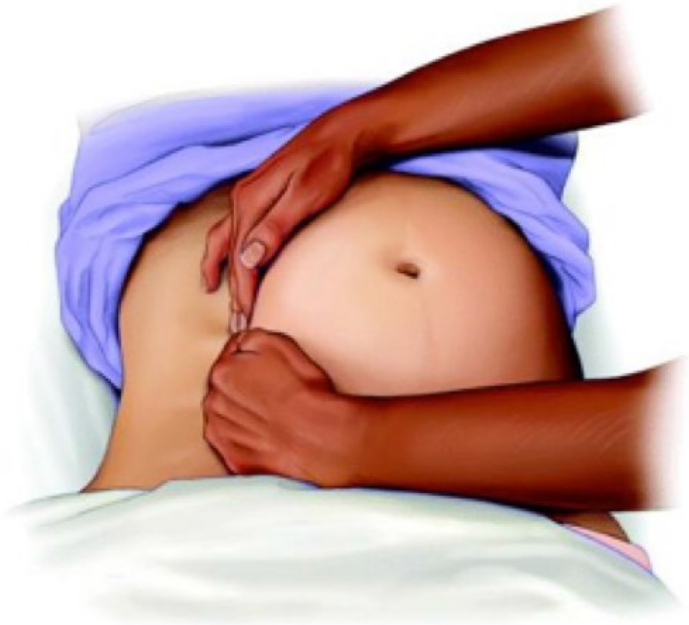
Special Circumstances

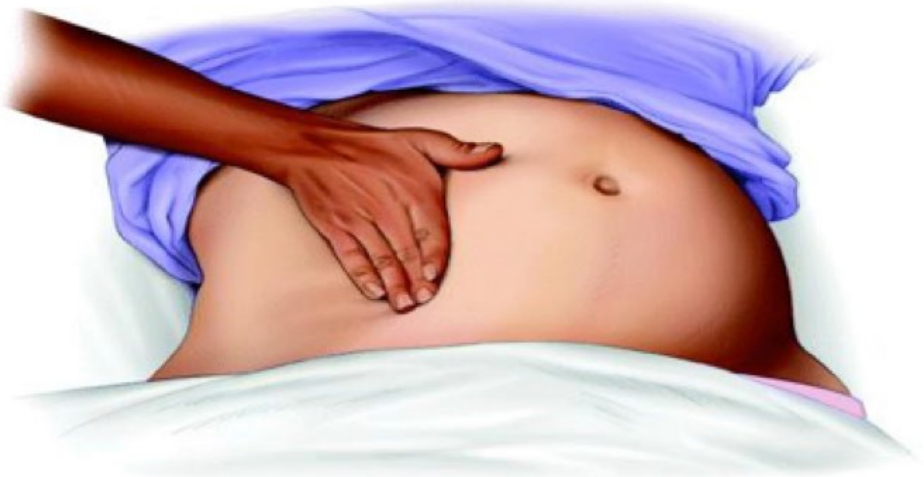
Pregnancy

During pregnancy, the airway is prone to regurgitation due to relaxation of the lower esophageal sphincter and gravid uterus. Cricoid pressure should be applied until the airway is secured by an endotracheal tube. Intubation may be difficult because of airway edema or large breasts. Increased oxygen consumption and reduced oxygen reserve make the mother at early risk of hypoxia, so ensure effective oxygenation early. It is important to place the patient in a left lateral tilt to relieve aortocaval compression; this can be maintained by a kneeling rescuer or wedge.

In maternal cardiac arrest, high-quality CPR and relief of aortocaval compression are the priorities. Emergency caesarean section is indicated for an arrest not reversed by ACLS. It should be considered immediately, as both maternal and fetal outcome are greatly improved if delivery happens within 5 minutes. Evacuation of the uterus significantly increases the chances of maternal survival by relieving aortocaval compression, and should therefore be considered within 4 minutes of cardiac arrest even if the fetus is not viable.

CPR on a patient in left lateral tilt is ineffective. CPR should be performed on a patient in the supine position. To relieve aortocaval compression during CPR, a manual left uterine displacement in the supine position may be performed. This can be performed from the patient's left side with the 2-handed technique or the patient's right side with the 1-handed technique (see diagrams below).





Hypothermia/Drowning

Drowning and hypothermia can often be associated with alcohol, drug overdose and trauma. Hypothermia can have a protective effect on the brain and other vital organs, and in view of this, resuscitation attempts are prolonged. Hypothermic patients tend towards bradycardia and VF.

Drowning is respiratory failure leading to hypoxia and the priority is early rescue breaths and securing an airway. CPR for drowning victims should follow the traditional ABC approach due to the hypoxic nature of the arrest. Cervical spine trauma can occur (e.g., a diving accident) but routine immobilization of the C-spine is not recommended.

Poisoning / Overdose

Poisoning is a leading cause of cardiac arrest in young adults. ACLS follows standard algorithms but management is tailored towards the suspected drug. Often the drug taken is unknown and management is supportive. Table 2 lists common drug overdoses and their specific therapy.

TABLE 2 - ANTIDOTES FOR COMMON POISONS.

DRUG POISONING	ANTIDOTE
Paracetamol	N-Acetylcysteine
Opioid (including heroin)	Naloxone
Cocaine	Nitroglycerin/phentolamine Propranolol contraindicated
Benzodiazepine	Flumazenil
Tricyclic antidepressants	Sodium bicarbonate
Anticholinergics (including central anticholinergic syndrome)	Physostigmine
Digoxin	Digoxin-specific antibodies
Beta Blockers	Isoproterenol

Calcium channel blockers	Glucagon/epinephrine
Organophosphate, Nerve agents	Atropine

Role of Intravenous lipid emulsion (ILE) therapy in management of cardiac arrest due to poisoning:

The 2015 guidelines brings a new recommendation that ILE may be used to treat other drug toxicities besides local anesthetic systemic toxicity (LAST) not responding to standard ACLS care.

Anaphylaxis

Introduction

Anaphylaxis is a systemic immune reaction to an allergen that the body has previously been exposed to. During anesthesia, the patient receives a "cocktail" of IV drugs and exposure to many allergens from the health care environment. Any of these exposures can cause an anaphylactic reaction, but the most commonly implicated are neuromuscular blockers (>60%), followed by latex, antibiotics, induction agents and colloids[3].

Incidence of anaphylaxis during anesthesia is thought to be 1:10,000 to 1:20,000. Less than 50% of patients with an anaphylactic reaction under anesthesia have a history of previous exposure to the allergen, which makes most reactions sudden and unexpected. Females are more likely to have anaphylaxis.

Physiology

Anaphylaxis is an IgE-mediated immune reaction resulting in the release of vasoactive substances from mast cells and basophils. These degranulate, releasing histamine, serotonin (5-HT), and a protein called tryptase. These vasoactive substances can affect any body system, but most concerning are the effects on the cardiovascular and respiratory systems.

Anaphylaxis is a type I hypersensitivity reaction. An anaphylactoid reaction is clinically indistinguishable from anaphylaxis, but the underlying mechanism is different. Anaphylaxis is IgE-mediated, whereas an anaphylactoid reaction causes release of vasoactive substances from the mast cell by direct action.

Clinical Recognition

More than 90% of anaphylactic reactions occur at or soon after induction of anesthesia. Latex anaphylaxis is the exception and commonly occurs 30-60 minutes after induction. Anaphylaxis under anesthesia can present in a variety of different ways, but the commonest presenting features are cardiovascular collapse with bronchospasm.

Immediate Management

If anaphylaxis is suspected, it must be dealt with as an emergency using an A, B, C approach. If the patient is pulseless, follow the ACLS algorithm.

Early treatment of anaphylaxis with epinephrine is associated with a successful outcome. The immediate management is outlined below.

1. Stop administration of all agents that could cause anaphylaxis.
2. Call for help.
3. Maintain the airway and give 100% oxygen.
4. Give epinephrine. Epinephrine can be given IM 0.5-1 mg (0.5-1 ml 1:1000 epinephrine) or IV 50-

100mcg (0.5-1ml 1:10,000 epinephrine). Continue to titrate epinephrine boluses at intervals of 1 min until a response occurs.

REMEMBER: Anaphylaxis Treatment = Epinephrine

Secondary therapy includes antihistamines (e.g. diphenhydramine 25-50 mg slow IV) and corticosteroids (e.g., hydrocortisone 100-400 mg slow IV). Consider the use of bronchodilators for bronchospasm.

Intensive care management is required for ongoing vasopressor and supportive therapy. Monitoring in a critical care setting is also important because following initial presentation, patients can have a second delayed reaction hours to days later.

Immediate Investigations

Degranulation in anaphylactic and anaphylactoid reactions releases a protein called tryptase. Serum tryptase levels rise transiently and reach a peak 1 hour following the reaction. They are used to confirm that an anaphylactic or anaphylactoid reaction has occurred, but give no indication as to the causative agent.

Later Investigation

A referral should be made to an allergist. Allergists perform skin prick tests using diluted allergens to elicit a cutaneous reaction.

Special thanks to Dr. Nicholas Crabtree and Dr. Viren N. Naik for their contribution to the previous edition of this chapter.

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Section 4.2

Blood Component Replacement Therapy and Perioperative Blood Conservation

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Introduction

The indication for perioperative blood transfusion is an area of on-going debate and requires careful patient evaluation and re-evaluation.[1] In this chapter we will review the basic information on the available blood components, their indication for transfusion, and risk of known complications.

Patients undergoing surgery are asked to sign an informed consent to receive blood products. This implies that the patient is aware of the risks of receiving a blood product (Table 1) and alternatives to allogeneic blood transfusions (see Blood Conservation). The signing of an informed consent for blood products holds the physician ordering the blood product to clearly stipulate the reason for administering it and to administer the minimum amount possible.

TABLE 1 - RISK OF COMPLICATIONS WITH BLOOD TRANSFUSION. DATA FROM MULTIPLE SOURCES INCLUDING THE CANADIAN BLOOD SERVICES (HTTP://WWW.BLOODSERVICES.CA), ONTARIO REGIONAL BLOOD COORDINATING NETWORK (HTTP://WWW.TRANSFUSIONONTARIO.ORG) AND BLOODY EASY.2

Infectious Complications	Average Estimated Risk per Unit
HIV	1 in 21 million
Hepatitis C	1 in 13 million
Human T-Cell Lymphotropic virus (HTLV)	1 in 7.6 million
Hepatitis B	1 in 7.5 million
Chagas disease	1 in 4 million
Symptomatic bacterial sepsis	1 in 200,000 per pool of platelets 1 in 250,000 per RBCunit

Non-Infectious Complications	Average Estimated Risk per Unit
Acute Hemolytic Reaction	1 in 40,000
Delayed Hemolytic	1 in 7,000
Minor Allergic	1 in 100
Transfusion Associated Circulatory Overload	1 in 100
Red cell sensitization (increasing risk of hemolytic transfusion reaction and hemolytic disease of the fetus and newborn)	1 in 13
Hyperkalemia	Associated with massive transfusion
Hypocalcemia/Hypomagnesemia/Citrate toxicity	Associated with massive transfusion
Hypothermia	Associated with massive transfusion

All blood products should be transfused using blood tubing containing a filter of at least 170 – 260 microns to capture fibrin debris. The blood filter should be changed after 4 units of blood, 12 hours after a blood transfusion or earlier if flow becomes compromised.[2] Platelets should be transfused using a blood filter that has not been used to transfuse red blood cells to avoid being trapped by debris in the filter from a previous blood unit.

Red Blood Cells (RBCs)

Indications: A transfusion guideline for RBCs is given in Table 2. The specific transfusion triggers should not be used without considering:

- The rate of on-going blood loss
- Hemodynamic stability
- Timing of available blood work
- Evidence of tissue ischemia e.g. tachycardia, myocardial ischemia, patient co-morbidities e.g. coronary artery disease

TABLE 2 - A GUIDELINE FOR RBC TRANSFUSION BASED ON HEMOGLOBIN CONCENTRATION.

Bleeding Patient

Clinical Setting	Recommendation	Dose
Low risk patient	Maintain hemoglobin over 70 g per L during active bleeding.	As per rate of blood loss
• Cardiovascular disease • Acute coronary syndrome	Maintain hemoglobin over 80 g per L during active bleeding.	As per rate of blood loss

Non-bleeding Patient

Hemoglobin Level	Recommendation	Dose*
Less than 60 g per L	Transfusion recommended. Asymptomatic young patients with chronic iron deficiency anemia can often be managed with iron supplementation alone.	1 to 2 units
Less than 70g per L	Transfusion likely appropriate.	1 unit
Less than 80 g per L	Transfusion likely appropriate if there is known cardiovascular disease.	1 unit
Less than 90 g per L	Transfusion likely appropriate with clear signs of inadequate tissue oxygen deliver.	1 unit
Greater than 90g per L	Transfusion likely inappropriate.	None

Allowable Blood Loss (ABL) can be estimated from the initial hemoglobin (Hbi), a final hemoglobin value considered safe for a given patient (Hbf), and a conservative estimate of the Blood Volume (EBV) of 60 mL/kg for adult females and 70 mL/kg for adult males.

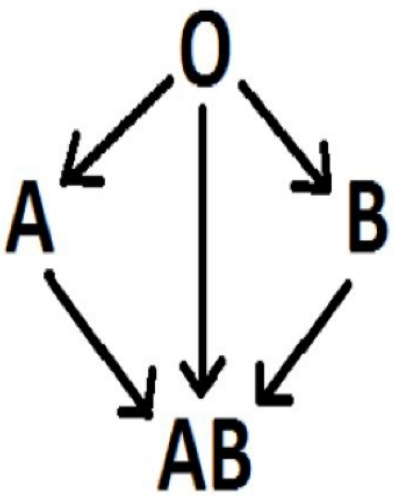
$$ABL = \frac{(Hbi - Hbf)}{Hbi} \times EBV$$

However, the indication for transfusion should never rely on this calculation, but should be established from laboratory measurement and the clinical circumstance (Table 2).

RBC Compatibility and Cross Matching

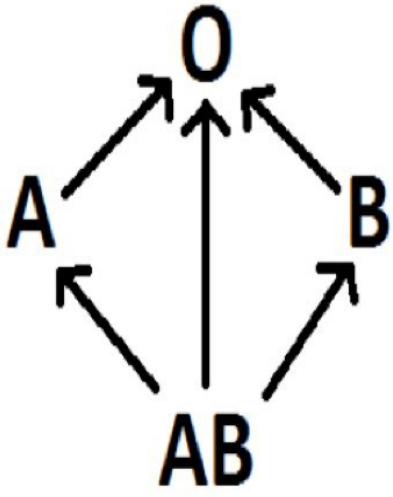
The most important part of compatibility testing is to ensure that the ABO type is correct (FIGURE 1). The third leading cause of death due to transfusion is an ABO hemolytic transfusion reaction, and the majority of these reactions are ultimately due to clerical error. This is the reason for the strict application of the Canadian Standards Association standards and standard operating procedures for unequivocal identification of the patient in the collection of blood samples for compatibility testing and the administration of blood products.

Figure 1: RBC and Plasma Compatibility Guide. The arrows indicate the transfusion from the donor to the recipient.



RBC COMPATIBILITY

Group O blood is referred to as the universal donor as it can be given to a patient with any ABO type. In contrast, type AB donor blood can only be given safely to patients with type AB blood.



PLASMA COMPATIBILITY

Compatible plasma transfusion is the opposite to RBC transfusion. Serum from patients with type AB blood will not contain either anti-A or anti-B antibodies and is therefore the universal plasma donor.

When a Group & Screen is processed in the lab, both the RBC antigen and the plasma antibodies are tested separately. The Group tests for the ABO blood type which is based on the antigen expressed on the surface of the RBC and leads to the production of predictable, antithetical antibodies. ABO antibodies are primarily IgM antibodies capable of causing life-threatening hemolysis. The Screen (or antibody screen) tests the patient's plasma for alloantibodies against minor non-ABO antigens on the surface of the RBC.

Once ABO typing and tests for alloantibodies (i.e., Group and Screen), are complete, cross-matching of blood is performed to ensure ABO compatibility. Cross-matching is done by adding a sample of the patient's plasma to a sample of the donor RBC. When agglutination or hemolysis of the mixture occurs, this is evidence of an incompatible cross-match. For patients with no detected antibodies, and no history of previous alloantibody, an electronic cross-match can be performed using the laboratory computer information system. To perform an electronic cross-match, there must be at least 2 group samples on file for the patient.

Patient blood types are also designated as Rh positive or negative. The Rh antigen system is made of 50 different antigens, but the RhD-antigen is the most important. After ABO, the RhD antigen is the next most important antigen for selecting blood components. Unlike the naturally occurring anti-A and anti-B antibodies, anti-D is formed only after a RhD-negative person is exposed to RhD-positive blood. This is of particular concern to women of childbearing age, as RhD immunization may put future pregnancies at risk for hemolytic disease of the fetus.

Complications: RBC transfusion risk can be divided broadly into infectious and non- infectious complications (Table 1). In addition, there are several biochemical changes associated with massive transfusion, including citrate toxicity, hypocalcemia, hyperkalemia and hypothermia.

Frozen Plasma (FP)

Plasma can be frozen and stored for up to 1 year. It is referred to as frozen plasma (FP) when frozen within 24 hours of collection (most of our plasma) and fresh frozen plasma (FFP) if it is frozen within 8 hours of collection. FP contains all of the coagulation factors found in whole blood. The quantity of each factor is dependent on the biological half-life of the protein, i.e. 3-6 hours for factor VII, 8 – 12 hours of factor VIII and 2- 3 days of factors II (prothrombin) and factor XI.

Indications:

To determine if FP is indicated for abnormal coagulation test results in the setting of bleeding or pre-procedure treatment, the cause of the elevation must be determined to ensure that the correct replacement option (i.e., FP vs. prothrombin complex concentrates vs. single factor concentrate) is selected.

A single dose of plasma is 10 – 15 mL/kg, enough to replace approximately 20% of a patient's coagulation factors. FP is indicated for:

- Bleeding or prior to a significant operative procedure in patients with INR, PT or PTT more than 1.8 times normal due to multiple factor deficiency (e.g. liver disease, DIC) when no coagulation factor concentrates or other alternative therapy are available
- Microvascular or massive transfusion AND patient's clinical status precludes waiting for 30-45 minutes for the INR/PT/PTT results.

FP is NOT indicated for:

- Elevated INR where the patient is not actively bleeding or awaiting a significant operative procedure
- Elective reversal of warfarin where time allows for warfarin cessation and/or use of vitamin K
- Urgent reversal of warfarin in a bleeding patient or a patient requiring an emergency invasive procedure (within 6 hours) where prothrombin complex concentrates are available
- Reversal of other anticoagulants (e.g. heparin, low molecular weight heparin, dabigatran, rivaroxaban,

apixaban).

Platelets

Platelets for perioperative transfusions come in 2 forms: Pooled random donor units derived from whole blood (4 donor units per pool) and single donor units collected by apheresis. Platelets are stored at room temperature with constant mixing to preserve platelet function. Unlike other blood products, platelets are not cooled; thus platelet transfusions carry the highest risk of bacterial contamination and bacterial sepsis (1 in 200,000 per pool of platelets).

Indications: While platelet transfusions have been associated with poor patient outcome in cardiac surgery and liver transplantation, they are essential in the management of post- operative bleeding. As with any blood product the benefit of transfusion must be balanced with the potential risk. The indications for platelet transfusion are given in Table 4.

TABLE 4 - PERIOPERATIVE INDICATIONS FOR PLATELET TRANSFUSION. PLATELETS SHOULD BE TRANSFUSED AS ONE ADULT DOSE OF PLATELETS (1 POOL OF 4 UNITS OR A SINGLE DONOR APHERESIS UNIT). MULTIPLE PLATELET TRANSFUSIONS ARE NOT RECOMMENDED UNTIL THE PATIENT HAS BEEN REASSESSED.

Platelet Count (x 10^9/L)	Procedural Indication
Less than 20	Procedures not associated with significant blood loss
20-50	Procedure not associated with significant blood loss Transfusion only if significant blood loss occurs
Less than 50	Procedures associated with blood loss, major surgery
50-100	Neuraxial blockade
Less than 100	Transfuse prior to neurosurgery or head trauma

Any	Platelet dysfunction and active blood loss (e.g. post- cardiopulmonary bypass, or anti-platelet agents*)

*There is new evidence (PATCH trial) suggesting that in the setting of antiplatelet agents (e.g. aspirin, clopidogrel) AND CNS bleeding with no surgery planned AND platelet count greater than 100 x 10^9/L that transfusion of platelets may lead to increased morbidity and disability[3]. Thus in this specific situation, platelet transfusion is NOT recommended.

Cryoprecipitate

Cryoprecipitate contains factor VIII, fibrinogen and von Willebrand factor. Each unit contains a minimum of 150 mg of fibrinogen and 10 units of cryoprecipitate contains on average 4 g of fibrinogen. The dose of cryoprecipitate is 1 unit per 10 kg. The standard dose for an adult is 10 units of cryoprecipitate. Each dose should raise the fibrinogen concentration by 0.5 g/L.

Indications: The indications for cryoprecipitate include microvascular bleeding or massive blood loss in patients with a fibrinogen concentration of less than 1 g/L or suspected low fibrinogen levels. For life-threatening hemorrhage, cryoprecipitate is indicated when the fibrinogen is less than 2 g/L.

ONLY when factor concentrates are not available, cryoprecipitate may be used to treat von Willebrand disease or Hemophilia A.

Peri-operative Blood Management

The aim of perioperative blood management is to reduce or eliminate the need for allogeneic blood transfusions with surgery. The blood-borne infections of the 1970s and 1980s served as the first impetus to the efforts in blood conservation, only to be replaced with issues of cost, immunomodulation and increased morbidity and mortality associated with allogeneic blood transfusions. While there has been widespread adoption of blood conservation efforts and the experts advise the adoption of multimodal strategies, it should be kept in mind the risks and benefits of many of the blood conservation modalities are still poorly defined.[4,5]

It should be stressed that patient blood management is not limited to avoiding allogeneic blood utilization, but also includes the appropriate utilization of blood and blood products. There are simple rules to ordering and administering blood products that should be established, published, and reinforced at every institution:

- A Transfusion Guideline should be established (Table 2).
- Ordering of a blood product should include the indication for its administration, e.g. transfuse one unit of RBC for a hemoglobin of 70 g/L.
- RBC units should be administered one unit at a time with the patient reassessed before a second unit is administered.

Following these simple guidelines will improve the utilization of blood products and reduce unnecessary transfusions.

Preoperative Blood Management Modalities

Identification and Treatment of Anemia

The incidence of preoperative anemia in patients scheduled for inpatient surgery can be as high as 40%. The etiology of this anemia is multi-factorial, but the two most common causes are iron deficiency anemia and anemia of chronic disease. Importantly, preoperative anemia is the single most treatable risk factor for a blood transfusion; iron supplementation and the use of erythropoietin are the primary modes of therapy of preoperative anemia.

The incidence of preoperative iron deficiency anemia is unknown, but elderly patients have a number of risk factors for iron deficiency, including use of non-steroidal anti- inflammatory drugs (NSAIDs) and poor diet. Iron deficiency anemia typically presents as a hypochromic, microcytic anemia and the mean cell volume (MCV) may be a good predictor of a response to iron supplementation. A ferritin of less than 30 ug/L or a ferritin less than 100 ug/L with a transferrin saturation less than 20% may also indicate iron deficiency.

The routine use of perioperative supplemental iron therapy is controversial in that it has little effect on blood transfusion. However, for patients in whom erythropoeisis is stimulated by recombinant erythropoietin, iron supplementation is recommended. The goal is to add approximately 60-100 mg of elemental iron daily. It is difficult to obtain this amount of iron from diet alone. If oral iron absorption is poor and iron supplementation is still required, intravenous iron sucrose is a safe and effective alternative.

Erythropoietin (EPO) is a naturally occurring hormone secreted by the kidneys in response to low partial pressure of oxygen. EPO stimulates effective erythropoiesis only if there are adequate iron stores, and the use of EPO should be combined with supplemental iron. The efficacy of preoperative EPO has been demonstrated in double- blind randomized controlled trials, increasing preoperative hemoglobin concentration by 15 g/L while reducing the frequency of RBC transfusion by as much as 50%.

While EPO is undeniably an effective therapy in reducing the risk of an allogeneic blood transfusion, there are 2 caveats to its routine use that should be considered. First, it remains an expensive therapy ($500 (CAN) per injection) and second, concerns about the safety of EPO have been identified. The first safety concern is an increased risk of thromboembolic events. The second, and perhaps more worrisome safety concern, is the increased risk of serious adverse events and death when they are used to treat anemia in cancer patients. These risks were identified in studies of long term EPO use (more than 8 weeks) and not in the shorter preoperative period. It is also unclear how these risks balance against the risks of perioperative transfusion.

Preoperative Autologous Blood Donation (PABD)

PABD is a method of expanding the red blood cell mass by removing blood for storage in the blood bank and allowing the patient to replace the sequestered RBCs prior to surgery. While some protocols allow for blood collection from anemic patients (Hb <130 g/L) and allow for blood collection up to 48 hours before surgery, this practice should be avoided, as the patient is unlikely to replace the sequestered RBCs before surgery and the risk of an allogeneic blood transfusion will be unchanged at best.

The overall level of evidence for PABD remains poor. Thus at this time, PABD is not used routinely and only indicated for patients with rare blood types (e.g. multiple alloantibodies) where blood is not readily available through Canadian Blood Services.

Intraoperative Blood Management Modalities

Minimizing Blood Loss

It cannot be overstated that the most effective blood management modality is the strict attention to hemostasis. Equally important are the maintenance of a normal coagulation cascade by equally strict attention to body temperature, pH, and minimizing the use, where appropriate, of anti-platelet and anticoagulant medications.

Controlled Hypotension

Controlled hypotension has been advocated to limit arterial blood loss from the surgical site, particularly from non-compressible blood vessels, e.g. bone. However, there is very little evidence to support the routine use of controlled hypotension, and in combination with anemia, hypotension increases the risk of tissue ischemia and should be avoided.

Acute Normovolemic Hemodilution (ANH)

For ANH, autologous whole blood is sequestered from the patient in the operating room and the intravascular volume is replaced with crystalloid or colloid to maintain normovolemia. As a result, the blood lost during surgery is diluted and the amount of hemoglobin or number of RBCs lost is reduced. The sequestered whole blood is re-transfused if a transfusion trigger is met or the case is completed.

Several meta-analyses have considered the efficacy of ANH, including trials from various surgical procedures.[6,7] Conclusions from these reviews are that:

1. The effectiveness of ANH is dependent on the number of units sequestered and the degree of hemodilution tolerated.

2. The trials included in the review were not blinded resulting in an over-estimated effect size.

3. When the outcome decisions, i.e. allogeneic blood transfusion, were considered under a transfusion protocol, the effect size was reduced. In order to accomplish sufficient hemodilution to reduce the risk of an allogeneic blood transfusion, a prolonged severe anemia would be required and this has perioperative risk in and of itself.

Therefore, **the evidence does not support the routine use of ANH, as it offers only limited benefit in terms of blood conservation and has an unproven safety profile.**

Intraoperative Cell Salvage

Cell salvage is a widely-used intraoperative blood management modality in which shed blood is collected by low pressure suction into a sterile reservoir and mixed with either citrate or heparin. The shed blood is then washed with normal saline and centrifuged to concentrate the red blood cell to a hematocrit of 0.60 to 0.80.

Intraoperative cell salvage use is usually confined to cases where large volume blood loss can occur over a short interval, for example in abdominal aortic aneurysm repairs, liver transplantation and major trauma. The major benefit is the retrieval of red blood cells that would otherwise have been discarded. The potential complications include thrombocytopenia and a dilutional coagulopathy due to the loss of platelets and coagulation factors, but these complications are more due to the blood loss than the cell salvage. Air emboli and bacterial contamination are rarer complications.

The use of cell salvage in cancer surgery remains controversial, as there is no evidence to support the contention that cell salvage may cause the cancer dissemination, but many feel that the benefit has not been established to justify the potential risk. Therefore, the contraindications for use of cell salvage remain the potential presence of malignant cells, bacterial contamination, ascitic fluid or amniotic fluid in the operative field.

Intraoperative cell salvage may be acceptable to Jehovah's Witnesses and the contraindications listed above will have to be reconsidered in light of the morbidity associated with severe anemia.

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Chapter 5

REGIONAL ANESTHESIA

Sections:

1. **Central Neuraxial Blockade: Epidural & Spinal**
2. **Peripheral Nerve Blockade**

Section 5.1

Central Neuraxial Blockade : Epidural & Spinal

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Introduction

Regional anesthesia involves the use of a variety of techniques to block nerves with local anesthetics. Unlike general anesthesia, regional techniques permit the patient to maintain a clear mental status during surgery and can also be used to provide prolonged postoperative pain control. Regional blocks are classified into central neuraxial and peripheral neural blockade. Central neuraxial blockade refers to placement of local anesthetics around the nerves of the central nervous system (e.g., epidural, spinal, and caudal anesthesia), whereas peripheral neural blockade refers to placement of local anesthetic agents onto or near peripheral nerves (e.g., brachial plexus block or ankle block).

In this chapter we provide a basic framework for understanding the use of spinal and epidural anesthesia in clinical practice. This includes the basic and applied anatomy relevant to each technique, indications and contraindications to their use, common side- effects, and associated complications.

Overview of Spinal and Epidural Blockade

Safe and effective use of central neuraxial blockade requires an understanding of the types of patients and procedures for which epidural and spinal blockade are suitable, contraindications to block use, knowledge of spinal anatomy and the technique of block performance, and the ability of the physician to anticipate and treat side-effects and complications of these procedures. Optimal use of these blocks requires an understanding of the methods by which choices of drugs and drug mixtures may be used to refine the type of blockade produced. For instance, varying the concentrations of local anesthetics and the types of drugs used (local anesthetics, opioids, epinephrine, etc) can provide a pregnant woman with a block dense enough that she can neither move nor feel pain during cesarean surgery or with a block light enough that she can walk without pain during early labor.

As with general anesthesia, the anesthesiologist performing regional anesthesia should determine the nature of surgical procedure to be performed, the indication for the procedure, its anticipated duration, and the required patient position during surgery. The medical history, physical examination, and laboratory review should be conducted to determine if any contraindications exist to epidural or spinal blockade. The degree to which patient-related co-morbidities might impact upon successful block placement (e.g., previous spine surgery) or upon preoperative, intraoperative, and postoperative care should also be carefully considered. The risks, benefits, side-effects, and alternatives to regional anesthesia should be discussed with the patient prior to the block, including the use of general anesthesia should difficulties arise. Consent should be obtained for all procedures. Patients undergoing

central neuraxial blockade should receive an intravenous line and co-loading of fluids as well as appropriate monitoring. Oxygen, intubation equipment and vasopressor/resuscitative drugs and equipment should be readily available to treat common side-effects such as hypotension and bradycardia, as well as uncommon events including high spinal blockade, seizures, and cardiovascular collapse.

Spinal and Epidural Blockade for Surgical Procedures

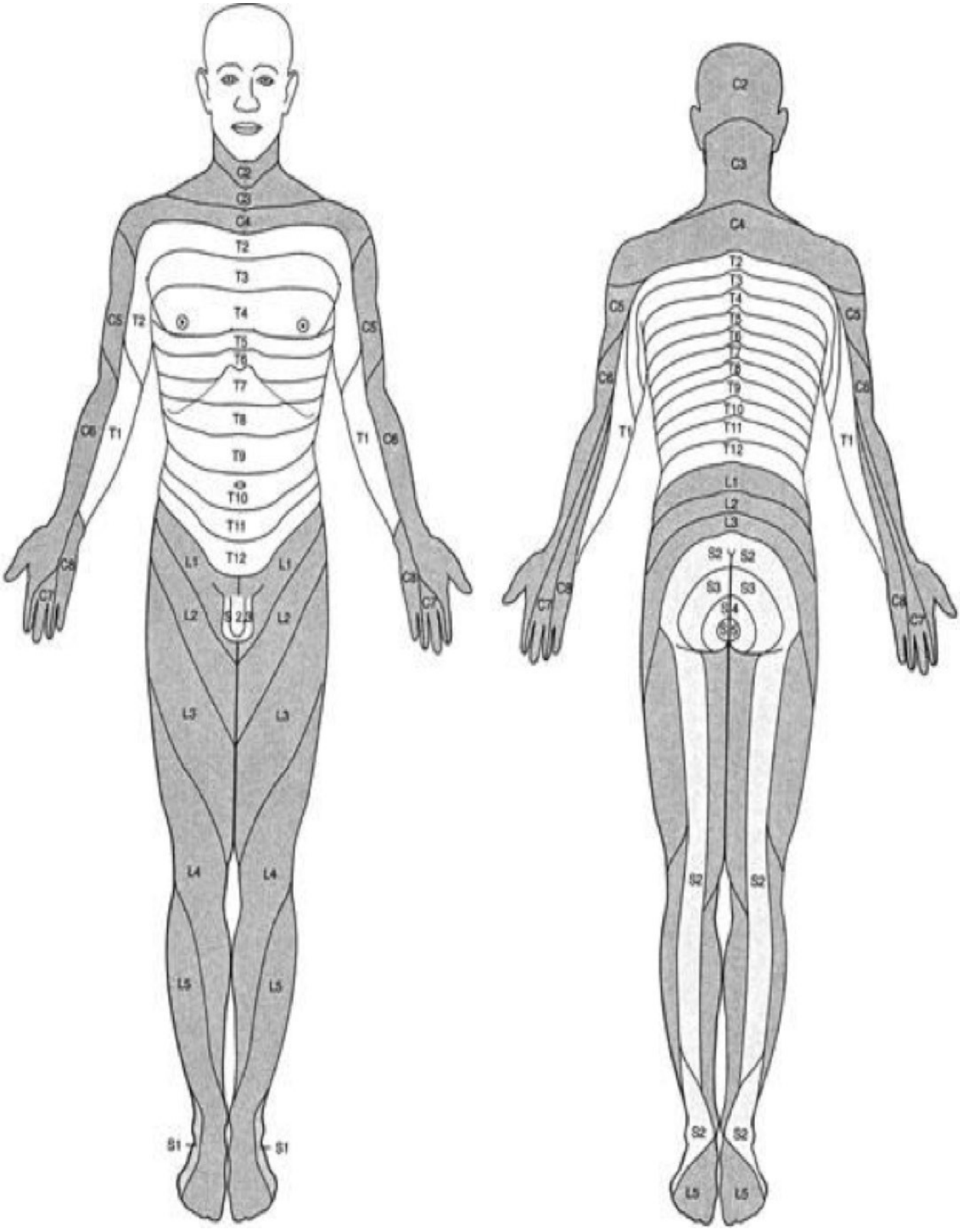
Spinal and epidural anesthesia are best reserved for operations below the umbilicus.[1] These include gynecologic and obstetric surgeries, hernia repairs, hip surgery, lower limb surgeries, urologic operations, and operations on the perineum or genitalia. Spinal and epidural anesthesia are often used to provide surgical anesthesia for older or sicker patients. Spinal anesthesia provides more rapid onset of conditions required for surgery in healthy patients compared with epidurals. In older or sicker patients, or more complicated surgeries, the slower onset of epidural blockade may be preferred over spinal anesthesia since it is associated with less hypotension and reflex tachycardia. Epidurals offer the advantage that placement of the epidural catheter allows for continued maintenance of anesthesia for prolonged periods of time whereas a single spinal injection provides time-limited anesthesia. Epidural catheters are commonly used for labor and delivery analgesia and management of postoperative analgesia. Table 1 lists the minimum suggested spinal levels which need to be blocked to provide spinal or epidural anesthesia for various purposes.[1,2] Figure 1 depicts the cutaneous dermatomes[2] corresponding to sensory innervation by their respective spinal nerves.

TABLE I - MINIMAL DERMATOMAL LEVELS REQUIRED.

Surgical Anesthesia	Pain Relief	Dermatomal level
Lower extremities		T-12
Hip		T-10
Bladder, prostate		T-10
Testes, ovaries		T-8
Lower intraabdominal		T-6
Other intraabdominal		T-4
	First stage labor	T10-L1
	Second stage labor	S2-S4

(Modified from: Nishida T, Pian-Smith M. Spinal, Epidural and Caudal Anaesthesia. In Dunn PF ed. Clinical Anesthesia Procedures of the Massachusetts General Hospital, 7th edn. Lippincott Williams & Wilkins 2007: 247- 272)

FIGURE 1- HUMAN SENSORY DERMATOMES2



Contraindications to Central Neuraxial Blockade

Multiple contraindications exist to the use of spinal and epidural blockade and must be ruled out prior to their use. These are generally divided into absolute and relative contraindications, (Table 2).[2,3]

TABLE 2 - CONTRAINDICATIONS TO CENTRAL NEURAXIAL BLOCKADE.

Absolute	Relative
Lack of knowledge of how to perform the Block	Pre-existing neurologic deficits (demyelinating lesions)
Lack of resuscitative drugs/equipment	
Patient refusal or inability to cooperate	Severe spinal deformity
Severe hypovolemia	Prior back surgery at the site of injection
Localized infection at the insertion site	Prolonged surgery
Frank coagulopathy/bleeding diathesis	Major blood loss or maneuvers that can compromise respiration
Septic shock	
Cardiac lesions with fixed output states (i.e., severe aortic/mitral stenosis)	
Intracranial mass lesion with raised intracranial Pressure	

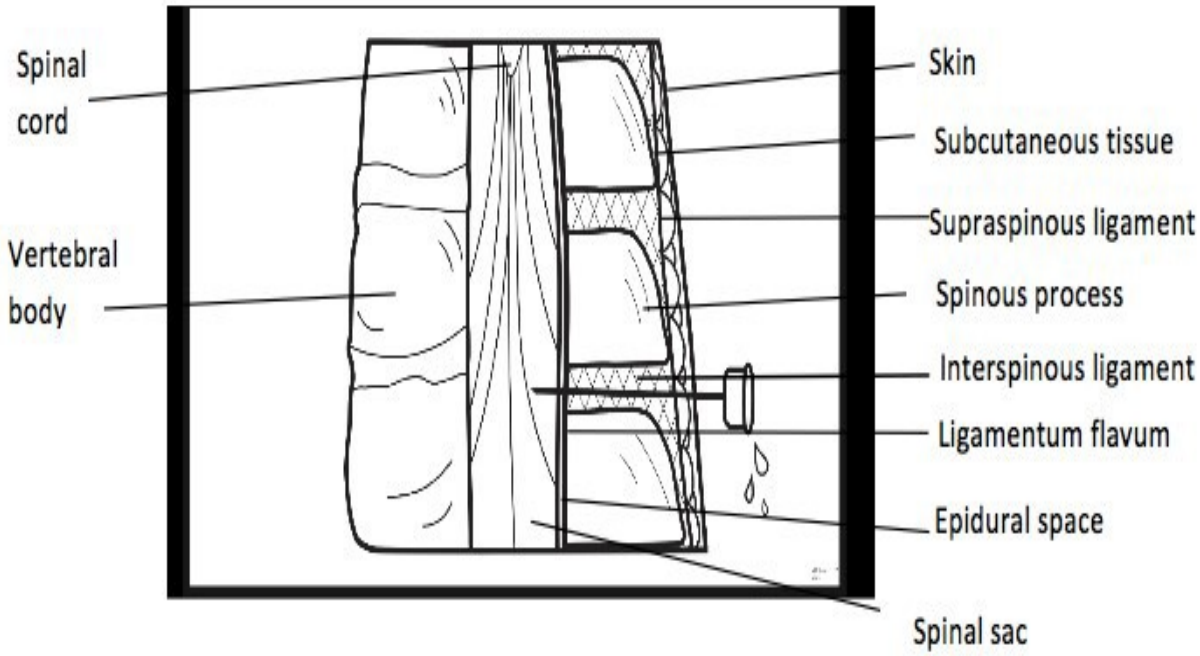
Basic Anatomy for Central Neuraxial Blockade

The greater rate of growth of the vertebral column relative to the spinal cord results in variation in cord length within the vertebral canal over time. In the fetus, the spinal cord extends the full length of the canal, whereas it ends at around L3 at birth and at around L1-2 in most adults. In adults, spinal

needles are commonly placed at L3-4 and L4-5 to avoid injury to the spinal cord. Epidural catheter placement does not require dural puncture as part of the technique (unlike spinal anesthesia). For this reason, the intervertebral level at which the epidural needle is placed is more variable, with needles carefully placed in the middle of the dermatomal segments which are to be blocked, including over the spinal cord.

The following structures are pierced during placement of a spinal needle into the subarachnoid space (Figure 2**):** skin, supraspinous ligament, interspinous ligament, ligamentum flavum, epidural space, dura and arachnoid membrane, and subarachnoid space.[4] Epidural anesthesia involves detecting epidural needle tip entry into the epidural space (just outside the dural sac) and passage of a fine catheter into the space. Unlike the case with spinal anesthesia, dural sac puncture with epidural needles, which are much larger in diameter, is usually unintentional. Epidural catheters permit intermittent injection or infusion of drugs over time during labor, for surgery and for postoperative pain relief.[5]

FIGURE 2: STRUCTURES PIERCED DURING SPINAL NEEDLE PLACEMENT INTO THE SUBARACHNOID SPACE



Determination of the Vertebral Interspace Level for Needle Placement

External bony landmarks are commonly used to locate the desired intervertebral level of needle insertion prior to initiation of epidural and spinal anesthesia. Important landmarks include the prominent spinal process of C7, the wing of the scapula (spinous process of T7) and Tuffier's line. Tuffier's line is located by drawing a line between the left and right iliac crests (L4 spinous process). The mid-lumbar region is the level at which the majority of neuraxial blockades are performed. From this point, other vertebral levels are identified. Needle placement is most commonly performed at the L3-4 and L4-5 interspaces for labor pain relief and cesarean section and higher for abdominal and thoracic surgeries.

Comparison of interspace levels based on external landmarks is variably consistent with levels based on radiologic imaging. Studies examining agreement between the estimated level and the actual (radiologic) level have shown that use of anatomic landmarks typically results in block placement at a level 1-2 segments higher than desired.[7] Experienced anesthesiologists err on the side of caution and will often choose the lower of two interspaces palpated for block placement during spinal needle placement, to avoid potential injury to the spinal cord. In more recent years, ultrasound has become a popular method to confirm intervertebral space levels prior to needle insertion; this modality is

particularly useful in patients with obesity and scoliosis.

Complications of Spinal and Epidural Anesthesia

Complications of spinal and epidural placement can be related to both the technique of placement and/or the effects of drug administration. These include **block failure** or a**chievement of only partial blockade** of the desired nerves, the latter being more common with epidurals.

Hypotension may occur in the period following both spinal and epidural anesthesia, particularly in patients with high levels of nerve blockade and/or relative hypovolemia. It is more common in patients with spinal anesthesia where it may occur in up to 80% of cases.[13] Hypotension results from pre-ganglionic blockade of the sympathetic nervous system, which may extend several levels higher than the level of somatic blockade, and reductions in preload and cardiac output. It may also be associated with bradycardia. Hypotension may occur in patients undergoing epidural anesthesia but is less frequent (up to 5% of patients)[13] Symptoms of hypotension include lightheadedness, nausea and vomiting. Some patients receiving spinal anesthesia also experience symptoms of difficulty with breathing as the block spreads cephalad. Treatment of hypotension includes intravenous fluids and vasopressors such as phenylephrine and ephedrine. Phenylephrine infusions are commonly used to prevent or treat hypotension after spinal anesthesia, particularly during cesarean delivery. Bradycardia, if present, may require treatment with glycopyrolate, atropine and in more extreme cases epinephrine.

Inadvertent injection of local anesthetic into epidural veins may lead to symptoms of early **central nervous system toxicity**[2] (perioral numbness/tingling, facial numbness, agitation/confusion, **seizures**), **and cardiovascular collapse**, if large enough amounts are injected. For this reason, the epidural catheter is carefully aspirated to identify return of blood. Dosing of drugs is done in fractions (3ml, then 5ml aliquots), often with epinephrine if high concentrations of local anesthetic are used, to assist in early detection of intravascular injection. Inadvertent injection of large amounts of local anesthetic into the dural sac may lead to high spinal blockade requiring intubation, ventilation, and the need for pharmacologic support of blood pressure and heart rate.

Puncture of the dural sac during needle placement may lead to development of **postdural puncture headache (PDPH)**, the most significant common morbidity of central neural blockade. PDPH occurs most commonly after dural puncture with large gauge needles, but also occurs, albeit far less frequently, even with fine gauge spinal needles. These headaches, which are typically postural and occur secondary to cerebrospinal fluid leakage from the dural sac, may respond to simple analgesics (non-steroidal anti-inflammatory drugs, acetaminophen, opioids, caffeine), or may require administration of an epidural blood patch. Inadvertent intrathecal injection of air during epidural needle placement or spinal anesthesia may also result in pneumocephalus, producing a postural "air headache" which closely mimics PDPH from cerebrospinal fluid leakage.

Addition of opioids to drug mixtures given into the epidural or subarachnoid spaces may also lead to opioid induced **pruritus** which can be treated with nalbuphine, naltrexone or naloxone. In large doses, opioids may lead to respiratory depression and/or respiratory arrest.

Permanent neurologic injury after central neuraxial blockade is rare (0.1-0.03 %). This includes **injury to the spinal cord itself and/or nerve roots from direct trauma or neurotoxicity**. Paresthesia caused from insertion of epidural catheters are usually transient in nature if they come in contact with the adjacent nerve roots. The incidence may be as high as 44%,[15] compared to 12% in cases performed under spinal anesthesia.[16] However, direct contact between epidural needles and laterally placed nerve roots is extremely rare.

Meningitis, epidural abscess, cauda equine syndrome and epidural hematoma are also rare complications of central neuraxial blockade. The reported incidence of post-dural puncture meningitis varies greatly between 1:3000 and 1:50,000 and underreporting is probable.[17]

Epidural abscesses following epidural catheter insertion have been reported to be 1:1000. Bacterial contamination can occur through the needle or catheter, epidural solution, or other predisposing factors, including the patient being immunocompromised, development of an asymptomatic epidural or subcutaneous hematoma, multiple attempts at insertion, or hyperhidrosis.[18]

The overall rate of epidural hematoma was 1 in 183,000 women, or 5 per million in an obstetric setting

in studies prior to 1990, whilst rates in larger post-1990 studies were 1 in 168,000 women, or 6 per million.[19] Spinal haematoma is reported more often following epidural anesthesia than after spinal anesthesia. In contrast to the low incidence of spinal haematoma in the obstetric population, the incidence in elderly females is reported to be as high as 1:3600, perhaps due to vascular disease, thromboprophylaxis, and spinal changes due to age-related processes and diseases.[17] **Both epidural abscess and hematoma can lead to paralysis if not recognized and treated.**

Nausea and vomiting are frequently associated with hypotension and are far more common after subarachnoid blocks than after epidural anesthesia. The incidence of nausea following subarachnoid block has been reported to be 14% - 45%.[20] Treatment of hypotension usually relieves the symptoms of nausea. Intrathecal opioids are more commonly associated with nausea and vomiting than epidural opioids, and may require treatment with antiemetics.[21]

Shivering is another common complication of neuraxial blocks, with a higher incidence in patients receiving subarachnoid block compared to epidural blockade, as the shivering threshold is depressed and the body core temperature falls faster and with much greater intensity.[22] The etiology continues to be elusive, but mostly involves a differential inhibition of spinal cord afferent thermoreceptors.[23] It can be effectively treated with small doses of intravenous meperidine.

Horner's syndrome, characterized by ptosis, miosis, enophthalmos, and anhydrosis is usually unilateral but may also be bilateral, and is present in 1% to 4% of patients receiving epidural anesthesia. Most commonly it appears as an isolated finding in the course of a normal block, or rarely as a component of an excessively high block, particularly after a subdural block. Symptoms usually recede within 1-2 hours without sequelae, and are unlikely to recur with subsequent epidural top-ups. The mechanism is blockade of the small-diameter preganglionic sympathetic fibres supplying the muscles of the eye.[24]

Inadequate block or failed block may occur in up to 6% of cases following epidural anesthesia,[25] either due to transforaminal escape of the epidural catheter tip, presence of dorsal midline or lateral septum preventing uniform spread of the epidural solution, catheter malfunction, or presence of anatomical variability of the spine.[26] The incidence of failed subarachnoid block ranges from 0.67% to 15%.

Accidental subdural entry during attempted epidural anesthesia is relatively uncommon, with an incidence of 0.8%,[27] whilst during subarachnoid block it is more common with an incidence of 4%-13%.[28]

Local tenderness and transient backache at the epidural or spinal insertion are relatively common, especially if the insertion has been difficult. However, this usually clears within several days to 3 weeks and may be related to superficial irritation of the skin, periosteal damage, or irritation. These symptoms may also occur as a result of hormonal or mechanical changes associated with pregnancy.[29]

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Section 5.2

Peripheral Nerve Blockade

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Introduction

Peripheral nerve blockade (PNB) offers several important advantages compared to general anesthesia (GA), largely due to opioid sparing. These benefits include a reduction in nausea and vomiting, sedation and pruritis. (SS Liu) These in turn hasten postoperative discharge home, improve rehabilitation, and provide greater patient satisfaction. The key to safe and successful PNB requires a thorough understanding of the clinical anatomy and associated complications of each technique. This chapter reviews the important anatomical, clinical, and technical considerations of the most commonly performed PNB techniques for anesthesia and analgesia in contemporary anesthetic practice.

Methods of Nerve Localization

Successful PNB depends on delivering local anesthetic (LA) injectate close to the target nerve by bringing the needle tip in proximity to the nerve. There are various methods used to localize the target nerve and the most commonly used method at present is ultrasound, which is described below. Regardless of the method used, no PNB should ever be performed without the application of standard monitors and the availability of resuscitation equipment. Despite the time-tested record of safety and low complication rate associated with PNB, the provider must always be prepared for adverse events.

Ultrasound

The recent introduction of portable ultrasound (US) technology has revolutionized the practice of regional anesthesia as US guidance affords real-time visualization of the needle tip, the target nerve, and the local anesthetic injectate. Compared to the aforementioned traditional "blind" methods for nerve localization, the benefits of US- guided nerve localization are (i) improved success, since local anesthetic can be deposited completely around the target nerve under direct vision, and (ii) enhanced safety, since blood vessels, pleura, and viscera are easily identified and avoided. Recent randomized studies have shown that US affords faster onset, greater success, and fewer complications compared to PNS.

Sedative medication is usually indicated for anxiolysis when performing PNB, but must be used judiciously so as to maintain verbal communication with the patient. Complaints of intense pain or paresthesia during injection of LA can suggest potentially damaging intraneural needle placement; this mandates immediate cessation of injection and needle relocalization. Additionally, the vigilant provider must recognize the most severe – and potentially fatal – complication of PNB: LA toxicity. LA toxicity can occur following inadvertent intravascular injection of small amounts of LA or systemic absorption following large amounts of LA, and manifests as confusion, seizures, and cardiac arrhythmias. LA should always be injected incrementally, aspirating on the syringe before injection in order to exclude accidental intravascular placement.

Techniques

Depending on the type of local anesthetic selected for PNB, motor and sensory anesthesia can last up to 18 hours, with opioid-sparing effects up to 36 hours, following a single bolus injection (i.e., "single shot" PNB). For patients where prolonged PNB is indicated, a perineural catheter can be inserted and a continuous infusion of dilute, long-acting local anesthetic can be initiated to significantly prolong postoperative analgesia and facilitate rehabilitation (i.e., "continuous" PNB). For the purposes of this chapter, only single-shot PNB will be discussed.

Upper Extremity Peripheral Nerve Blockade

Brachial Plexus Anatomy

The brachial plexus originates from the C5 to T1 ventral rami, with variable contributions from the C4 and T2 nerve roots. Depending on the desired distribution of anesthesia or analgesia, the brachial plexus can be blocked at any level along its course from the roots in the neck to the terminal nerve branches in the arm, as described in the approaches listed below. For each approach, there are multiple techniques that have been described, including variations in nerve localization methods (see above), anatomical landmarks, needle insertion point, direction of needle advancement, and acceptable endpoint. The techniques described below are those most easily learned and performed, and reflect the author's preferred practice when ultrasound is not used.

Approaches

Interscalene Brachial Plexus Block

Indications: Interscalene brachial plexus block (ISBPB) provides anesthesia at the level of the roots. ISBPB reliably blocks the C5, C6, and C7 roots of the brachial plexus, and is therefore ideally suited for surgery involving the shoulder and lateral aspects of the arm and forearm. Local anesthetic exposure to the C8 and T1 roots is much more variable (delayed, incomplete, or absent). Consequently, ISBPB spares the ulnar nerve in up to 50% of cases and is therefore not recommended for surgery involving the medial elbow, forearm, or hand.

Complications: Complications specific to ISBPB include phrenic nerve blockade and hemidiagphragmatic paresis (100% incidence, 25-30% reduction in FEV1 and FVC), Horner's syndrome, recurrent laryngeal nerve paresis, inadvertent intrathecal or epidural injection, and intravascular vertebral artery injection. Contraindications to ISBPB include moderate or severe COPD and contralateral recurrent laryngeal nerve palsy.

Supraclavicular Brachial Plexus Block

Indications: Supraclavicular brachial plexus block (SCBPB) provides anesthesia at the level of the trunks and divisions. Because the trunks and divisions of the brachial plexus are bunched close together above the clavicle, SCBPB can provide near complete anesthesia of the entire upper extremity below the shoulder. SCBPB is especially useful for elbow surgery, and can be used for forearm, wrist, or hand surgery as well. Because of the relatively high incidence of pneumothorax associated with SCBPB (0.5-6%), various techniques have been described in order to lessen this risk. The application of US for PNB is invaluable for SCBPB, since puncture of the pleura and large vessels can be avoided with confidence.

Complications: Complications specific to SCBPB include pneumothorax (0.5-6%), phrenic nerve blockade and hemidiagphragmatic paresis (28-80%), Horner's syndrome (70-90%), and intravascular subclavian artery injection.

Infraclavicular Brachial Plexus Block

Indications: Infraclavicular brachial plexus block (ICBPB) provides anesthesia at the level of the cords. ICBPB is useful for elbow surgery, and can be used for forearm, wrist, or hand surgery as well. Because the brachial plexus is located lateral to the pleura at this level, the risk of pneumothorax is reduced compared to the supraclavicular approach. US can be particularly useful for ICBPB, since the cords lie relatively deep (4-6 cm) at the infraclavicular level and encircle the axillary artery. ICBPB is also ideal for perineural catheter insertion, since the catheter can be securely fastened to the anterior chest.

Complications: Complications specific to ICBPB are not widely reported but are presumably similar, and perhaps less frequent, than those seen with SCBPB.

Axillary Brachial Plexus Block

Indications: Axillary brachial plexus block (AXBPB) provides anesthesia at the level of the terminal branches of the brachial plexus. AXBPB is useful for surgery of the forearm, wrist, and hand. Because

the musculocutaneous nerve separates from the median, ulnar, and radial nerves in the proximal axilla, the AXBPB often spares the lateral aspect of the forearm. A separate musculocutaneous nerve block is often required, which is easily performed by injecting 5 ml of LA directly into the body of the coracobrachialis muscle.

Complications: Complications specific to AXBPB include systemic local anesthetic toxicity from intravascular injection and local hematoma formation.

Intravenous Regional Anesthesia (Bier Block)

Intravenous Regional Anesthesia (IVRA) refers to the injection of LA intravenously into an exsanguinated limb (most commonly upper extremity) distal to an occluding tourniquet. The mechanism of action includes extravascular diffusion of local anesthetic as well as tissue ischemia.

Indications: IVRA is indicated for procedures <1 hr in duration because of tourniquet pain rather than insufficient surgical site anesthesia.

Complications: Complications specific to IVRA include systemic LA toxicity.

Contraindications to IVRA include uncontrolled hypertension, a fracture at the tourniquet site, and sickle cell disease.

Lower Extremity Peripheral Nerve Blockade

Lumbar Plexus Anatomy

The lumbar plexus arises from the ventral rami of L1 to L4 (Fig. 10 [Brown Fig 11-1]) and innervates the hip joint, the anterior, medial and lateral thigh, the knee joint, and the medial leg and medial malleolus. Depending on the desired distribution of anesthesia or analgesia, the lumbar plexus can be blocked at the level of the roots, which are embedded in the psoas muscle, or at the main terminal nerve branches, i.e. the lateral cutaneous nerve of the thigh (L2-3), the obturator nerve (L2-4), and the femoral nerve (L2-4).

Unlike upper extremity PNB where the proximity to large blood vessels, the pleura, and the spinal cord can cause dangerous complications, lower extremity PNB is accompanied by fewer reported complications. Complications specific to lower extremity PNB tend to be limited to intravascular injection and hematoma formation.

Approaches

Femoral Nerve Block

Indications: The femoral nerve primarily supplies motor and sensory innervation to the anterior thigh and knee joint, therefore femoral nerve block (FNB) is most useful for major knee surgery. Because the lateral cutaneous nerve of the thigh and obturator nerve lie in close proximity to the femoral nerve, it is often possible to anesthetize all 3 nerves with a single injection (i.e., a "3 in 1" block).

Sacral Plexus Anatomy

The sacral plexus arises from the ventral rami of L4 to S3. The roots of the sacral plexus converge to form the sciatic nerve, the largest nerve in the body, which exits the sciatic foramen and descends in between the greater trochanter of the femur and the ischial tuberosity. Midway through the thigh, the sciatic nerve splits into its two major components, the tibial nerve medially and the common peroneal nerve laterally.

Approaches

Sciatic Nerve Block

Indications: The sciatic nerve innervates the posterior thigh and knee joint, and the majority of the

leg and foot. A small portion of the medial lower leg and medial malleolus is innervated by the saphenous nerve, which is a branch of the femoral nerve. Sciatic nerve block (SNB) is ideal for leg, ankle, or foot surgery, and is often used in conjunction with a FNB for major knee surgery.

Popliteal Nerve Block

Indications: The popliteal nerve block (POP) refers to blockade of the sciatic nerve at the level of the popliteal fossa. POP can be used for many types of foot and ankle surgery, including Achilles' tendon repair, but spares the medial leg and medial malleolus (saphenous nerve). Since the sciatic nerve bifurcates into the tibial (medially) and common peroneal (laterally) nerves approximately 5 cm above the popliteal crease, the goal of the POP should be to block the sciatic nerve before it splits into its two components.

Ankle Block

Indications: Ankle blockade is ideal for forefoot surgery. Five nerves innervate the foot and each need to be blocked for complete anesthesia. There are 4 terminal branches of the sciatic nerve (deep and superficial peroneal, tibial and sural nerves) and one terminal branch of the femoral nerve (saphenous nerve).

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Chapter 6

OBSTETRICAL ANESTHESIA

Sections:

1. **Physiological Changes of Pregnancy**
2. **Obstetrical Pain Management**

Section 6.1

Physiological Changes of Pregnancy

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Introduction

Throughout gestation, women undergo profound physiological adaptations that, in part, contribute to the successful outcome of the pregnancy. This chapter will concentrate on those changes that are particularly relevant to the practice of anesthesia.

Cardiovascular system

Within weeks of conception, cardiac output begins to increase significantly. At term it is approximately 50% higher than non-pregnant baseline values. Most of this increase occurs during the first trimester and is secondary to increases in both heart rate and stroke volume combined with a decrease in systemic vascular resistance. During labor, delivery and immediately postpartum, cardiac output increases significantly above the pre-labor values due to increases in sympathetic nervous system activity1 and auto transfusion of blood from the uterus and placental bed. Although most women tolerate the increased cardiac demands associated with pregnancy and delivery, women with pre-existing heart disease may decompensate very quickly, particularly during labor and in the early postpartum period. During this time, to prevent labor-induced increases in maternal catecholamines, optimal care must include the use of effective pain relief, usually through the use of epidural analgesia.

Early in the second trimester, the maternal position is critical to the maintenance of cardiac output. Studies have shown that a phenomenon known as the **supine hypotensive syndrome or aortocaval compression** can occur as early as 13 – 16 weeks gestation[1]. Aortocaval compression increases throughout the pregnancy and is maximal at term. This syndrome is secondary to compression of the inferior vena cava and/or the aorta by the gravid uterus when the parturient adopts the supine position. Compression of the vena cava causes a decrease in venous return and in turn, a drop in cardiac output[1]. The resulting decrease in maternal blood pressure may be accompanied by pallor, nausea, vomiting, bradycardia and a general feeling of unwellness. Placental blood flow may become compromised as it is entirely dependent on an adequate maternal blood pressure. In addition, aortic compression can also cause a reduction in uterine blood flow, as the uterine arteries originate below the site of the obstruction. Both general and regional anesthesia may further compound these changes and limit the mother's ability to compensate. Therefore, it is very important to maintain a left lateral or "wedged" position throughout labor and anesthesia. In this position, the blood pressure measurements should be taken in the dependent left arm and correlate well with those taken in the supine or sitting position[2].

The maternal plasma volume and total blood volume increase throughout pregnancy to reach levels up to 50% greater than baseline while the red cell production increases by only 20-30%. [1-4] This disproportionate change results in hemodilution and the "physiological" anemia that occurs during pregnancy. A hemoglobin less than 11g/dL or a hematocrit below 33% is considered to be indicative of maternal anemia, most commonly secondary to iron deficiency.[2] Fortunately, the total increase in blood volume helps the parturient compensate for the normal blood loss that occurs during vaginal delivery (≤ 500 ml) or cesarean section (≤ 1000ml). However, since uterine blood flow is 500-700 mL/min at term, once delivery is completed, it is important that uterine contraction is established quickly to limit blood loss. Otherwise rapid deterioration can occur.

Respiratory System

Both anatomical and functional changes occur within the respiratory system that impact on anesthesia. Vasodilatation and increased capillary permeability within the upper airway result in mucosal edema and airway stuffiness[2.] Therefore, smaller endotracheal and nasotracheal tubes should be chosen. In addition, intubation, particularly nasal intubation, may be accompanied by increased bleeding.

Early in the first trimester, the relative hyperventilation of pregnancy begins. Minute volume increases approximately 50% by term, mainly due to an increase in tidal volume as opposed to respiratory rate1. The PCO_2 decreases to 30mmHg, producing a mild chronic respiratory alkalosis and a compensatory decrease in serum bicarbonate.[5-7]

In contrast to the increase in tidal volume, the residual volume and functional residual capacity (FRC) both decrease, mostly due to elevation of the diaphragm by the enlarging uterus. At the same time, oxygen consumption increases throughout the pregnancy secondary to the metabolic demands of the growing fetus and uterus, as well as the increase in maternal cardiac and respiratory work[4]. The decrease in FRC and increase in O2 consumption lead to rapid hypoxemia during periods of apnea, for example, during the rapid sequence induction of general anesthesia.

Dyspnea is a very common complaint during pregnancy, beginning during the first trimester. This is thought to be due to the respiratory stimulant effects of progesterone. However, spirometry remains normal throughout pregnancy. Simple routine tests, such as the one second forced expiratory volume (FEV_1) remain unchanged and therefore can be helpful in the diagnosis of dyspnea during pregnancy[5].

Gastrointestinal System

Important changes that have a significant impact on anesthesia occur in the gastrointestinal tract during pregnancy. Both estrogen and progesterone relax the smooth muscle of lower esophageal high-pressure zone (LEPZ), often referred to as the lower esophageal sphincter (LES), while at the same time the enlarging uterus mechanically displaces the stomach upwards, altering the orientation of the LEPZ[1,2.] As a result, the barrier pressure is decreased and gastroesophageal reflux (heartburn) is a common complaint during pregnancy. In addition, although gastric emptying remains normal throughout gestation, it is markedly decreased with the onset of labour and is further reduced by pain, emotional distress and opioid administration[1,2,6]. In light of these changes, all parturients are considered to be at an increased risk of aspiration pneumonitis after **16 weeks gestation**. However, since the ingestion of clear fluids appears to promote gastric emptying, labouring patients without additional risk factors for aspiration are allowed to consume clear fluids[2]. In the event that general anesthesia is required after 16 weeks, a rapid sequence induction and endotracheal intubation must be performed. Sodium citrate (a non-particulate antacid), metoclopramide (increases gastric emptying), and histamine H_2 receptor antagonists such as famotidine or ranitidine (increases gastric pH) are frequently administered prior to the induction of general anesthesia.

Nervous System Changes

Due to altered pharmacokinetics, changes in hormonal levels and increased plasma endorphins, pregnant women have elevated pain thresholds, particularly near term and during labour[1]. These changes result in an increased sensitivity to intravenous and local anesthetics as well as volatile agents[2,6.] Minimum alveolar concentration (MAC) is reduced by up to 40% [1], spinal anesthetic doses are decreased approximately 25% [1], and small doses of local anesthetics have been shown to spread further in the epidural space of parturients as compared to nonpregnant women; therefore, careful drug titration is mandatory. In addition, hemodynamic stability in pregnant women is primarily dependent on the sympathetic nervous system, particularly during the latter part of gestation[1]. Thus, any drug or procedure that inhibits sympathetic tone, such as a spinal anesthetic, can cause a marked decrease in maternal blood pressure[1].

Hematological Changes

In addition to the physiological anemia of pregnancy, there is also a decrease in total plasma proteins, resulting in a decrease in colloid osmotic pressure. Mild edema is common during the latter stages of

pregnancy. These changes may be further accentuated in preeclamptic patients, thereby increasing the risk of pulmonary edema.

Pregnancy is considered to be a hypercoagulable state which helps limit the blood loss at delivery but also increases the risk of thromboembolism throughout gestation and the immediate postpartum period[2]. There is an increase in platelet activation as well as elevations in the majority of the coagulation factors. Some have described pregnancy as a state of "accelerated, but compensated, intravascular coagulation," that is, increased clotting combined with increased fibrinolysis (clot breakdown)1. Laboratory results show a shortening of the prothrombin (PT) and partial thromboplastin (PTT) times, consistent with activation of the clotting system, and an increase in fibrin degradation products (FDPs), suggesting enhanced fibrinolysis.

Despite the increase in platelet activation and consumption, the majority of women maintain normal platelet counts during pregnancy due to an increase in production. However, a small percentage of otherwise normal women develop gestational thrombocytopenia with platelet counts that can fall below 150,000/mm^3. A few may even go below 100,000/mm^1. Although there is a drop in the absolute levels, hemostasis in these parturients does not appear to be affected. Therefore, in most cases regional anesthesia can be safely administered.

During the first trimester the white blood cell count (WBC) begins to increase and can be elevated to levels as high as 16,000/mm^3. During labour these levels increase even more and do not return to normal for at least 6 weeks postpartum[2].

Renal

Profound changes in the kidneys occur early in pregnancy, particularly regarding renal blood flow which is elevated up to 80% above normal and increases the actual size of the kidneys, the latter resulting in hydronephrosis in a large proportion of pregnant women. Glomerular filtration is also significantly elevated causing physiological glycosuria, mild proteinuria and increased creatinine clearance[1,2]. Therefore, a normal BUN and serum creatinine during pregnancy may be indicative of poor renal function[1,2].

Fetal Considerations

The care of pregnant patients should always take the well-being of the fetus into consideration. The placenta serves as the major interface between the mother and the fetus and provides nutrition, waste elimination and respiratory gas exchange[4]. Unlike many other vascular beds, uteroplacental blood flow is not autoregulated. Consequently, placental perfusion depends mainly on the maternal blood pressure. Hypotension from any cause, such as aortocaval compression, regional anesthesia, pain medications and hypovolemia can result in decreased uterine blood flow, and in turn, fetal well-being. In addition, all practitioners caring for pregnant patients must be cognizant of the potential for transfer of various substances, including anesthetic medications, across the placenta. The effects on the fetus will depend on the characteristics of the agent itself as well as the gestational age of the fetus[6].

Summary

1. The increased cardiac demands throughout pregnancy may not be well tolerated in parturients with pre-existing cardiac disease. Therefore, during labor and delivery, effective pain management to decrease maternal catecholamines is a particularly important aspect of their care.

2. Aortocaval compression occurs early in pregnancy and may be further exacerbated by general or regional anesthesia. An adequate lateral or "wedged" position is imperative to maintaining maternal and fetal well-being.

3. Uterine blood flow at term is 500 -700 mL/minute. Rapid and effective uterine contraction is essential to the prevention of postpartum hemorrhage, one of the leading causes of maternal morbidity and mortality.

4. The combination of a decrease in FRC and an increase in oxygen consumption during pregnancy results in rapid hypoxemia during periods of maternal apnea.

5. After 16 weeks gestation, parturients are at an increased risk for aspiration. Consequently, in the event that a general anesthetic is required, a rapid sequence induction with endotracheal intubation is indicated.

6. Pregnant women have an increased sensitivity to all intravenous and local anesthetics as well as volatile agents; therefore, careful titration during anesthesia is required.

Conclusions

Both the parturient and the fetus undergo tremendous physiological changes throughout gestation. Therefore, in order to facilitate a successful outcome, it is important that the anesthesiologist understands how these changes impact on the delivery of anesthesia.

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Section 6.2

Obstetrical Pain Management

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Introduction

Obstetrical pain management has been an important issue since the beginning of written history. The challenge is to provide satisfactory pain relief that is safe for both the mother and the baby. This chapter outlines the basic approach to pain relief in labour, based on anatomical, physiological, psychological, and pharmacological principles.

Pain Pathways and Characteristics of Labour Pain

It should be noted that the exact pain pathways for the first and second stage of labour have not been completely identified in the human.

During the first stage of labour, pain is generated by the contraction of the lower uterine segment and dilation of the cervix. The pain afferents pass through the paracervical region, via the hypogastric nerve, through the lumbar sympathetic chain to the cell bodies in the T10 to L1 dorsal root ganglia. Much of the pain is transmitted through small, unmyelinated visceral sensory C fibres to the substantia gelatinosa of the spinal cord. Pain associated with the second stage of labour is transmitted by the same pathway, with additional afferents from the vagina and perineum. These are transmitted via the pudendal nerve to the spinal cord at S2 to S4. After modulation in the dorsal root ganglion, pain impulses enter the dorsal grey matter of the spinal cord (Figure 1). The impulses are transmitted cephalad via the ipsilateral and contralateral ventral columns of the spinothalamic tract. The perception of pain, which is rudimentary at the level of the thalamus, becomes more defined and focused by the cerebral cortex (Figure 2).

Knowledge of the pain pathway leads to numerous strategies to alleviate pain. It is also possible to block the pain pathway at more than one level at a time, leading to enhanced pain relief and, often, a reduction in side effects.

FIGURE 1 - CROSS SECTION OF THE SPINAL CORD SHOWING THE PAIN PATHWAYS. COURTESY ANAESTHESIA UK WEBSITE A. HTTP://WWW.FRCA.CO.UK/ARTICLE.ASPX?ARTICLEID=100118. ACCESSED APRIL 5, 2017.

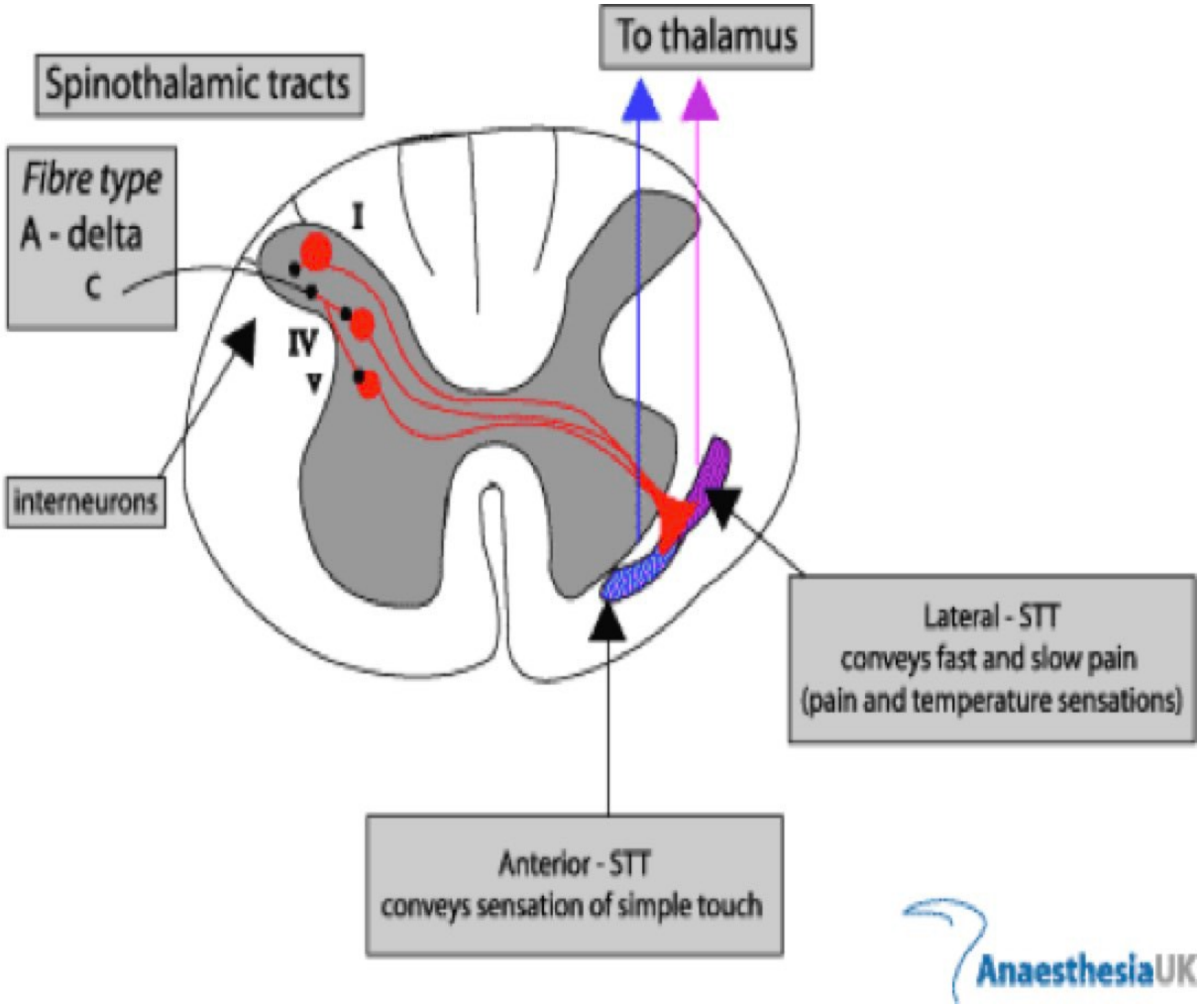
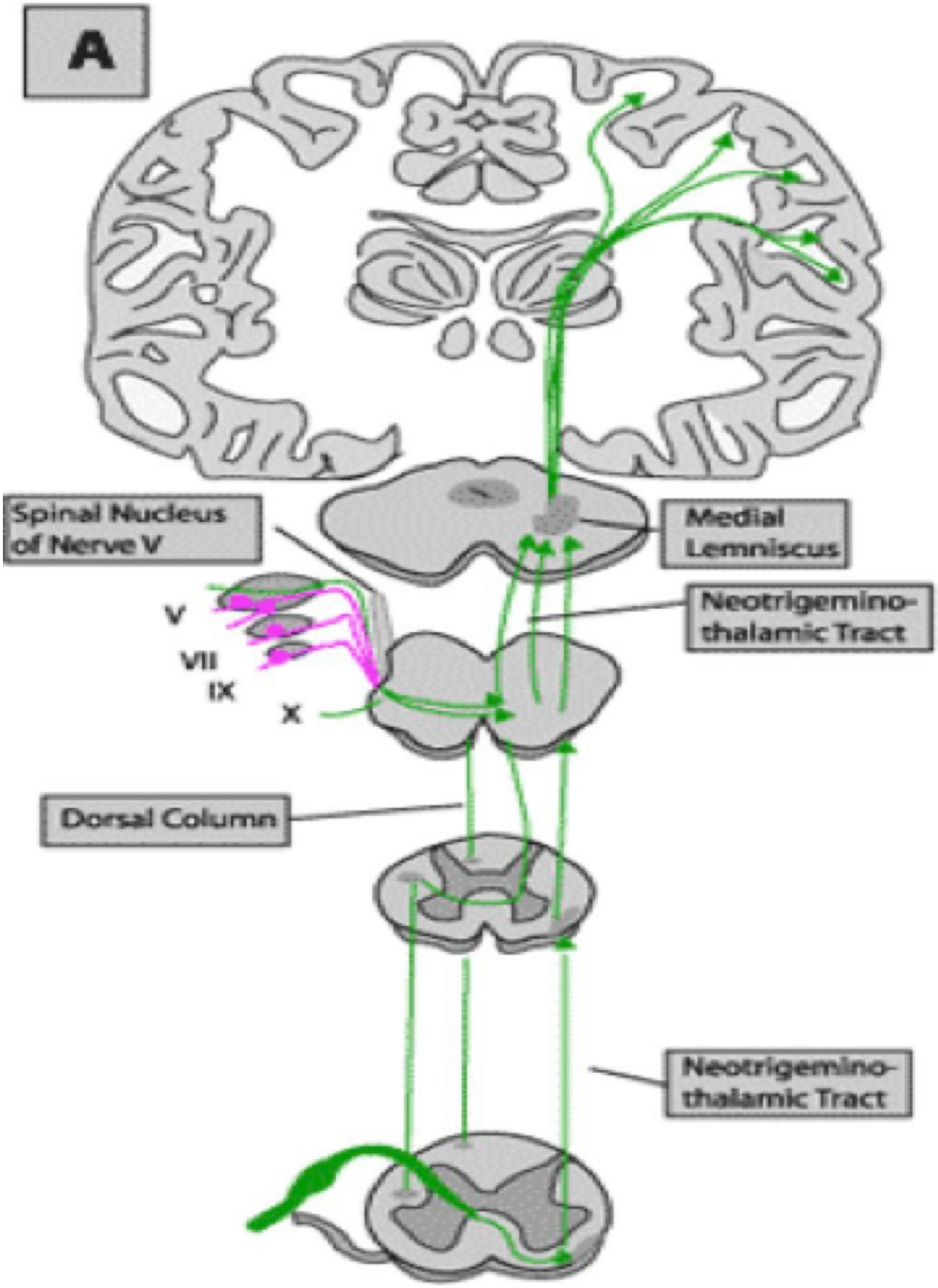


FIGURE 2 - CENTRAL PAIN PATHWAYS. COURTESY ANAESTHESIA UK WEBSITE HTTP://WWW.FRCA.CO.UK/ARTICLE.ASPX?ARTICLEID=100118 ACCESSED ON APRIL 5, 2017.



Modes of Analgesia

It is possible to categorize labour analgesia into various groups based on mechanisms of action. These are outlined in Table 1.

TABLE 1 - TYPES OF LABOUR ANALGESIA.

Category	Examples
Non-pharmacologic	• Childbirth preparation • Emotional support • Touch and Massage • Therapeutic use of heat and cold • Hydrotherapy • Hypnosis • Acupuncture/acupressure • Lamaze • Transcutaneous Nerve Stimulation (TENS) • Intradermal water blocks • Meditation and Imagery
Inhalational analgesia	• Nitrous oxide
Systemic (parenteral) analgesia	• Opioids • Ketamine* (rarely used)
Local anaesthesia	• Local infiltration of the perineum • Paracervical block • Pudendal block
Regional analgesia	• Subarachnoid block • Epidural analgesia o Lumbar o Combined spinal-epidural (CSE)

Non-pharmacologic Analgesic Techniques

These include a wide range of modalities that do not involve the use of drugs. Childbirth preparation,

various breathing exercises and physical comfort measures continue to be used by a large number of women. In contrast to pharmacologic interventions, there are few risks to either mother or fetus **provided that the labour is normal and the woman has freely chosen one of these methods.** Methods such as acupuncture, TENS, and hypnosis have an economic cost. Whether or not there is benefit to their use is controversial, but it is certainly worthwhile if other methods of analgesia are contraindicated (see below). Sterile water injections over the sacrum may transiently reduce back pain, but the mechanism of action is unknown. These methods of analgesia have recently been reviewed.[3]

Pharmacologic Analgesia Techniques

Practitioners must be aware that drugs given to the mother will eventually be transferred to the fetus. Furthermore, some long-acting drugs continue to be transferred to the newborn via the breast milk. In general, drugs that cause maternal sedation may cause neonatal sedation. Some techniques, such as regional anesthesia, may affect the fetus indirectly by causing adverse changes to uterine blood flow, uterine tone or maternal hemodynamics.

Systemic Analgesia

Opioid analgesics are commonly used for labour analgesia. The benefits and side effects of opioid analgesics are shown in Table 2. While there are many drugs in this class, there is no clear evidence that one is better than the other for labour analgesia. Table 3 shows some of the opioids in common use for labour analgesia, their pharmacologic properties and special considerations.

TABLE 2 - OPIOID ANALGESICS: BENEFITS AND SIDE EFFECTS.

Benefits	Side effects
Analgesia Anxiolysis Easy to administer High therapeutic ratio Relatively inexpensive Specific antidote available (naloxone)	**Maternal** • Sedation • Nausea and Vomiting o GI effects o CNS effects •Respiratory Depression (maternal & neonatal) • Biliary Spasm • Venodilation & orthostatic hypotension • Variable effect on labour **Fetal** •Reduced beat-to-beat fetal heart rate variability **Neonatal** • Respiratory depression • Sedation • Potential effect on early breastfeeding

TABLE 3 - OPIOID ANALGESICS IN COMMON USE FOR LABOUR. * = PATIENT CONTROLLED INTRAVENOUS ANALGESIA.

Drug	Usual Dose IM/IV	Onset of Action	Duration of Action	Comments
Morphine	10-15 mg IM 2-5 mg IV	30 min IM 5-10 min IV	2-5 hrs	
Hydro-morphone	1-2 mg IM 0.2-0.4 mg IV	30 min IM 5-10 min IV	2-5 hrs	Very similar to morphine on an equipotent basis.
Fentanyl	25-75µg IV	1-3 minutes	20-60 min	Short-acting, very potent. Action terminated by redistribution. Cumulative effects.
Remifentanil	0.2 to 0.8µg/kg Bolus or 0.05 to 0.5µg/kg/min as continuous infusion	Seconds	3 min	Extremely potent. Rapid metabolism by pseudo-cholinesterase. Administered by continuous intravenous infusion, PCIA* or a combination.

Nalbuphine	15-20mg IM 5-10 mg IV	15 min IM 5-10 min IV	4-5 hrs	Agonist-antagonist activity. Ceiling effect on respiratory depression.

Opioids act on specific receptors in the central nervous system. While there are various subtypes, the μ receptor is primarily associated with analgesia and respiratory depression. These receptors are located in both the brain and spinal cord, particularly in the substantia gelatinosa. Opioid effects can be reversed by specific antagonists at the receptor level (i.e., naloxone).

Small (subanaesthetic) doses of ketamine can be used for analgesia for vaginal delivery. The mechanism of action is different from the opioids because it works at different receptors (N-methyl-d-aspartic acid (NMDA) receptor). Ketamine, therefore, does not cause maternal respiratory depression or hypotension that may be seen with opioids. Analgesic doses are not associated with neonatal depression. However, its use is limited because of the potential for hallucinations. The analgesic effect is not reversed by naloxone.

Modes of Administration

Opioids can be effectively administered through intramuscular or intravenous routes. Patient-controlled intravenous analgesia is a particularly effective way of administering opioids because it allows the patient to rapidly individualize the dose of medication and optimize the interplay between analgesia and side effects. The neuraxial use of opioids is discussed below. Ketamine is given intravenously.

Inhalational Analgesia

Nitrous oxide is the most commonly used inhalational agent for labour analgesia. Potent inhalational agents such as desflurane and sevoflurane also have analgesic properties. These are rarely used because of the danger of inducing unwanted general anaesthesia and will not be discussed further.

Nitrous oxide (50%) in oxygen (50%) has been used for decades to provide safe and effective analgesia for labour. It is delivered in a fixed ratio either coming from one cylinder (Entonox) or separate nitrous oxide and oxygen cylinders, joined by a mixer (Nitronox). In contrast to potent inhalational agents, nitrous oxide is tasteless and odorless. Nitrous oxide has the advantage of being short acting because it is rapidly eliminated from the body by the respiratory system. It is administered using a demand system that is patient controlled. Unlike opioids, it does not cause respiratory depression in the mother or newborn.

Nitrous oxide has some disadvantages that limit its use in obstetrics. The main problem is pollution and the associated hazards and discomforts for staff. Expensive scavenging and air handling methods are required. The other main limitation is that, in combination with opioids or other depressants, nitrous oxide can induce general anaesthesia and unconsciousness.

Local Analgesia

These include local infiltration of the perineum to facilitate performance of episiotomies and repairs, paracervical blocks for the first stage of labour, and pudendal blocks for the second stage of labour. Usually these are performed by the obstetrician and the quality of analgesia is excellent. However, the analgesia is limited to the part of the body that is blocked. For example, a paracervical block provides relief from uterine contraction pain but does not provide perineal analgesia for the second stage of labour. Bilateral pudendal blocks provide good perineal anaesthesia for the application of forceps, but does not alleviate the pain of uterine contractions. It should be noted that high doses of local anaesthetic may be required and may cause signs and symptoms of toxicity.

Regional Analgesia

Regional analgesia for obstetrics includes epidural, spinal, and combined spinal- epidural (CSE) techniques. These methods are attractive because they are much more effective than other techniques of providing labour analgesia. The drugs used do not cause maternal drowsiness or amnesia and the newborn is not depressed. In this section, we will describe how drugs in the epidural and subarachnoid space can be used effectively for labour analgesia. We will also consider the relevant pharmacology, indications, contraindications, and complications of regional analgesia as it pertains to obstetrics. Lumbar sympathetic blocks are rarely used and will not be considered further.

Regional —analgesia is different from —anaesthesia in a number of key aspects (Table 4). These differences are made possible because of the different types of nerves that are affected. Since labour pain is transmitted by small, unmyelinated C-fibres, a low concentration of local anaesthetic can be used to block them. This concentration would not be effective in blocking the large, myelinated A-α fibres that control the voluntary muscles of the lower extremities and abdomen. Low concentrations are also not effective to block impulses in the A-δ fibres that transmit somatic sensory pain generated by, for example, skin incision.

TABLE 4 - REGIONAL ANALGESIA VS REGIONAL ANESTHESIA

Analgesia	Anaesthesia
Pain relief the only goal	Pain relief is a main goal
Muscle relaxation is an unwanted side effect	Muscle relaxation is an important goal
The dose of drug is not sufficient to perform an operation such as C-section	The dose of drug is sufficient to perform operations
Doses of local anaesthetic do not approach toxicity	Doses of local anaesthetic may approach toxicity
Hypotension is uncommon	Hypotension is common

Epidural analgesia

Ideally, patients will have sufficient information concerning labour analgesia to make an informed choice. This is often written by anaesthesiologists in lay terms and distributed to patients antenatally by obstetricians or posted on a hospital website.[4] Informed consent may be obtained during labour. The anaesthesiologist will discuss the procedure, the benefits, risks and alternatives in the detail appropriate to the clinical situation. While lack of information is not necessarily a contraindication to epidural analgesia (a patient may decline the information), lack of consent is an absolute contraindication. Some examples of absolute and relative contraindications to epidural analgesia can be found in Table 5. Examples of complications, the incidence, usual time of onset and treatment can be found in Table 6. While the list is quite long, the incidence of most complications is quite low. For example, an audit done in Sunnybrook Health Sciences Centre in 2013 showed that 91% of epidurals had no complications. There was a 7% incidence of poor analgesia and 1% incidence for each of dural puncture, high motor block, and hypotension.

TABLE 5 - CONTRAINDICATIONS TO EPIDURAL ANALGESIA.

Absolute contraindications

- Lack of patient consent
- Lack of resuscitation equipment
- Inadequate skill with the procedure
- Infection at the site of epidural puncture
- Severe coagulopathy or full anticoagulation
- Supratentorial space occupying lesion

Relative contraindications

- Hematologic
  - Certain mild coagulopathies
- Cardiovascular
  - Hemodynamic instability, stenotic cardiac lesions
- Neurologic
  - Raised intracranial pressure
  - Progressive neurologic deterioration of unknown etiology
- Musculoskeletal
  - Spina bifida, depending on type and location
  - Severe scoliosis or back surgery (technical problems)
- Obstetrical
  - False labour

TABLE 6 - COMPLICATIONS OF EPIDURAL ANALGESIA.

Complication	Incidence	Etiology	Time of Onset	Treatment
Poor analgesia	1 to 5%	Insufficient drug; misplaced catheter; bladder distension; rapidly progressing labour	Initial failure ~ 20 min but might occur any time during labour	Check for full dilatation, bladder distension, and dislodgement of the epidural catheter. Catheter may need to be replaced
Pruritus	0 to 20%	Neuraxial opioid; more common with subarachnoid administration	Within 20 minutes of opioid administration	Usually none required; low doses of nalbuphine
Intravenous injection	<1%	Epidural needle or catheter in an epidural vein	Immediate	Stop injection. Replace catheter.
Hypotension	~1%	Aortocaval compression; subarachnoid injection; subdural injection.	Up to 20 minutes after initiation.	Stop the drugs. Fluids; left lateral tilt; vasopressors if necessary.
Unacceptable motor block	1 to 5%	High concentrations of local anaesthetic. Prolonged epidural analgesia.	Any time during labour.	Reduce dose/concentration of local anaesthetic if possible. Rule out subarachnoid injection.
Fetal heart rate abnormalities	~5%	Coincidence; hypotension; uterine hypertonus.	Up to 20 minutes after initiation.	Treat hypotension as above; nitroglycerine for uterine hypertonus.

Accidental dural puncture	0.5% to 2%	Epidural needle pierces the dura	At initiation (will cause headache 12 to 24 hrs after)	Initiated epidural at another level. Explain problem to the patient. Follow for headache (if present—treat).
Epidural abscess	1:5,000 to 1:10,000	Endogenous or exogenous organisms	3 days to 1 wk post-delivery	Surgical (rarely non-surgical treatment)
Epidural hematoma	~1:100,000	Coagulopathy; vascular trauma in the epidural space	Within 24 hrs of initiation	Surgical evacuation
Nerve damage	1:1000 to 1:100,000	Usually an obstetric cause. Possible damage to nerves or spinal cord by needle or catheter.	Immediate	Expectant; may recover spontaneously.

Some complications are common during labour and delivery, and often blamed on epidural analgesia. Epidural analgesia does not prolong the first stage of labour, but it may increase the length of the 2nd stage by about 15 minutes. Epidural analgesia does not cause an increased incidence of caesarean section or long term back pain[5;6].

Typically, the anaesthesiologist chooses the lowest concentration of local anaesthetic that will provide labour analgesia while minimizing motor block. When lipid- soluble opioids such as fentanyl are added to the local anaesthetic, the analgesic effect is enhanced because of the opioid receptors located in the substantia geletanosia of the spinal cord. The goal is to obtain a sensory block to the level of T10 in order to block pain generated by uterine contraction.

An epidural catheter is placed in order to provide a route of administration for additional drug. The anaesthesiologist or nurse can give intermittent bolus doses (top- ups). However, continuous infusion techniques are more satisfactory because they provide a more constant level of analgesia. Patient controlled epidural analgesia (PCEA) is the most common form of maintenance as it allows the patient to control dosing. Patient satisfaction is highest with PCEA techniques. Newer techniques such as intermittent mandatory bolus (instead of continuous infusion) are being investigated and show promise.

The dose of local anaesthetic needed to provide analgesia is very low. The usual concentration of bupivacaine or ropivacaine is between 0.05% (0.5 mg/ml) and 0.125% (1.25mg/ml). Approximately 15-20

ml is required to initiate analgesia (7.5 to 25 mg).

Most women use less than 12 mL/hr for maintenance. In contrast, the usual dose of bupivacaine for caesarean section is approximately 20 to 25 mL of 0.5% (5 mg/mL) or 100 to 125 mg.

CSE analgesia

CSE techniques are similar to epidural analgesia, but differ in the way that they are initiated. As with an epidural, CSE starts with the location of the epidural space. Then a small gauge (25 or 27) non-cutting spinal needle is passed through the epidural needle into the subarachnoid space. The initial dose of medication is given through the spinal needle (usually a combination of a small dose of lipophilic opioid and 1 to 2 mg of bupivacaine). The spinal needle is removed and an epidural catheter is placed for maintenance of analgesia. CSE techniques have the advantage of very rapid analgesia with little or no motor block of the lower extremities. The disadvantage is the theoretical risk of 1) piercing the dura and possibly increasing the risk of infection or nerve damage and 2) a somewhat higher incidence of fetal heart rate abnormalities.

Spinal Analgesia

Spinal analgesia is rarely used alone for labour as the duration of labour can vary significantly. Single shot spinal anaesthesia can be used to facilitate forceps delivery if an epidural is not in place.

Summary

Most women require some type of pain relief during labour. There are many options available that may or may not include pharmacologic intervention. Ideally, labour analgesia is safe for mother and infant, is effective, and has little or no effect on the progress of labour. While regional analgesia is far from perfect, it has many of the characteristics of the ideal analgesic technique.

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Chapter 7

PEDIATRIC ANESTHESIA

Sections:

1. **Pediatric Anesthesia**

Section 7.1

Pediatric Anesthesia

Maisie Tsang, MD and Clyde Matava, MBCHB, MMed

Children Are Not Small Adults

Pediatric Anesthesia is a subspecialty of Anesthesia based on the differences of children relative to adults in anatomy, physiology, pharmacology, psychology, and the spectrum of disorders and diseases they may manifest. It is a broad subspecialty covering all areas of surgical practice, procedural sedation, trauma, and resuscitation involving patients from tiny premature infants to adults. This chapter will briefly discuss these differences in order to introduce the medical student to Pediatric Anesthesia. A complete discussion of Pediatric Anesthesia can be found in any one of a number of excellent textbooks on the subject, several of which are referenced in this chapter.

Relevant Anatomy and Physiology of Pediatric Patients:

The Airway and Respiratory System

Airway Anatomy

The neonatal upper airway differs from the adult airway in 5 significant ways:

1) An infant's tongue is larger in proportion to the oral cavity, promoting upper airway obstruction under anesthesia

2) An adult's epiglottis is broad and parallel to the trachea, whereas the infant's epiglottis is narrow and angled posteriorly over the glottic opening. The epiglottis of an infant must be lifted in order to reveal the glottic opening on laryngoscopy.

3) The anterior commissure of an infant's vocal cords is attached inferiorly relative to the cord's posterior attachments, creating the impression of the glottis opening being directed postero-inferiorly. An adult's vocal cords and glottic opening are perpendicular to the trachea. The tip of an endotracheal tube is more likely to get caught up at the anterior commissure of the vocal cords in infants.

4) In an adult, the glottic rim at the level of the vocal cords is the narrowest part of the airway. Though this is controversial in recent MRI studies, traditionally, it is thought that in infants, the non-expandable cricoid cartilage, the only complete cartilaginous ring in the upper airway, is the narrowest part, creating a conical shaped lumen of the larynx. Since this space is non-expandable, it is less able to withstand mucosal pressure without ischemic injury. For this reason, an uncuffed endotracheal tube sized to provide a detectable leak at circuit pressures of 20 cm H_2O or higher was recommended for use in children 8 years or younger. Recently, the role of cuffed tubes for younger patients has been appreciated; caution is taken with monitoring and limiting cuff pressures to under 20cm H_2O.

5) The larynx sits higher in an infant, at the level of C3-4, as opposed to C4-5 in an adult. As a result, the angle between the base of the tongue and the glottic opening is more acute, creating the illusion of an "anterior larynx."

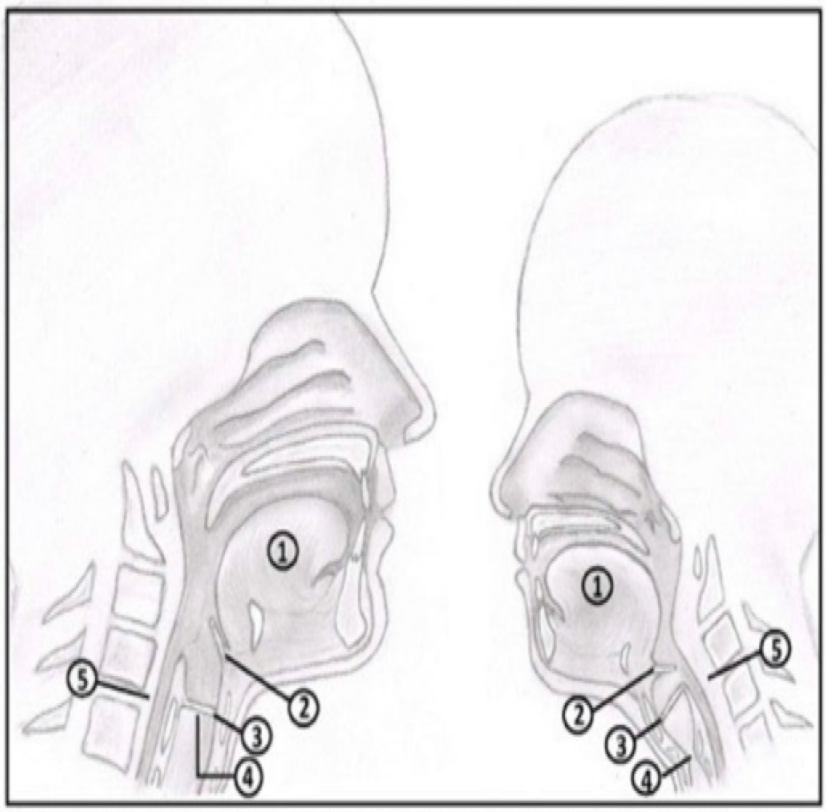

Figure 7.1.1

Anatomical differences between adult and paediatric airways. The numbers relate to the list above. Illustration by Peter Farag.

Respiratory Physiology

Infants and neonates respond differently to chemical controls of respiration, have altered lung volumes, and are more profoundly affected by anesthesia when compared to adults.

Control of Respiration

The chemical control of respiration in children and adolescents is similar to that in adults. Central chemoreceptors respond to changes in pH by increasing ventilation with increased hydrogen ion concentrations. Peripheral chemoreceptors respond to pH, pCO_2, and pO_2 by increasing ventilation in response to respiratory acidosis, hypercapnia and hypoxemia. In neonates and infants, especially those born prematurely and less than 44-weeks post-conceptual age, the response is altered. In these patients, hypoxemia produces a depression in respiratory drive.

Infants and neonates also demonstrate periodic breathing and central apnea. Periodic breathing is

defined as breathing interposed with short apneic spells of 5 to 10 seconds in duration. These may occur during wakefulness or sleep. Periodic breathing occurs in 93% of premature infants, 78% of full term infants, and 29% of infants at one year of age. Central apnea in infancy is defined as apneic spells of 15-seconds duration or more. Shorter duration apneas accompanied by bradycardia, cyanosis or pallor are also diagnostic for central apnea. Central apnea occurs in 55% of premature infants, but rarely occurs in full term babies.

Respiratory Mechanics

Lung development is far from complete in the full-term infant. Alveolar development doesn't begin until 36-weeks' gestation. The respiratory tree, including the terminal bronchioles, is formed by 16-weeks' gestation but the full-term infant has mostly primitive saccules comprising the terminal airspaces from which alveoli later develop. By 18 months of age, the child has an adult number of alveoli and subsequent growth results in increased alveolar size. The lung volume in early infancy is smaller relative to body size in adults. However, the infant's metabolic rate relative to body mass is twice that of the adult. Therefore, the minute ventilation required per kilogram body weight is doubled.

Lung volumes are the result of the elasticity of the chest wall and lungs as well as the tone in the muscles of respiration. The elastic recoil of the chest wall, which produces an outward expanding force on the lungs, is greatly reduced in neonates. The elastic recoil of the lungs, which promotes a reduction in lung volumes and exhalation, is only slightly lower in neonates than in adults. Functional residual capacity (FRC), which is the volume at the end of passive expiration, is a reflection of the balance between chest wall and lung elasticity. In adults, FRC is 40-50% of total lung capacity (TLC), depending on posture. This volume allows normal gas exchange to occur throughout the respiratory cycle. In neonates, passive FRC is only 10-15% of TLC. This reduced FRC is incompatible with normal gas exchange due to premature airway closure with resultant atelectasis and ventilation-perfusion (V-Q) mismatching. The awake infant compensates for this with tonic activation of the diaphragm and intercostal muscles, producing a "dynamic" FRC of about 40% TLC, comparable to adults.

Effects of Anesthesia on the Respiratory System

The pharmacology of anesthetic agents is reviewed elsewhere in this text.

Inhalational agents are potent respiratory depressants through effects on the respiratory centre, chest wall muscles, and a blunting of reflex responses. The muscle relaxing effects of inhalational agents cause hypotonia of the pharynx with potential upper airway obstruction. Ventilatory drive, tidal volume and response to hypercarbia are reduced. The uptake and onset of inhalational anesthetics in children is rapid, owing to the increased alveolar ventilation relative to FRC, and higher proportion of vessel-rich tissues relative to body mass. By similar means, oxygen is depleted rapidly from the alveoli of apneic infants with resultant desaturation.

Intravenous anesthetics also result in respiratory depression. Propofol often produces apnea at induction doses, as well as blunts airway reflexes. Although some apnea and respiratory depression may occur with induction doses of ketamine, the airway is usually maintained.

The Cardiovascular System

Pediatric anesthesia serves patients from pre-term infants to young adults. Knowledge of fetal circulation and the developing function of the heart is necessary to safely deliver anesthesia to infants and children.

Fetal and Transitional Circulation

The primary role of the cardiovascular system is to deliver oxygen to tissues and to remove waste. Gas exchange in utero occurs via the placenta. The fetal developing lungs are inactive. Fetal circulation is designed to maximize oxygen delivery to high demand tissues using the foramen ovale, ductus arteriosus, and ductus venosus to shunt fetal blood. This creates parallel left and right circulations.

Deoxygenated fetal blood is pumped from the descending aorta to the placenta via the umbilical arteries. Fetal hemoglobin (HbF) has a higher affinity for oxygen than adult hemoglobin (HbA). As a result, oxygen is transferred from maternal to fetal hemoglobin in the intervillous spaces of the

placenta. Oxygenated fetal blood returns from the placenta via the umbilical vein. The ductus venosus allows a large proportion of blood returning from the placenta as well as fetal gastrointestinal venous blood to bypass the liver and directly enter the right atrium via the inferior vena cava (IVC).

At birth, the low resistance placenta is clamped and systemic vascular resistance rises. With breathing, pulmonary vascular resistance falls. With these changes, pulmonary blood flow increases and shunting across the ductus arteriosus falls. In the absence of placental prostaglandins and increased arterial oxygen tension, the ductus arteriosus closes. Increased pulmonary blood flow increases the venous return to the left atrium. The foramen ovale, a valve created by overlapping flaps of atrial septal tissue, effectively closes in response to rising left atrial pressures relative to those in the right atrium. While functionally closed, the foramen ovale remains "probe patent" in 50% of children under 5 years of age and 25% of adults.

Following delivery, a quick assessment of neonatal health status is conducted at 1 and 5 minutes of life. This is referred to as the APGAR score and is described below. In some cases, such as preterm delivery, newborns may need to be resuscitated.

		Score		
Sign		2	1	0
A	Activity (muscle tone)	Active	Arms and legs flexed	Absent
P	Pulse	>100	<100	Absent
G	Grimace (reflex irritability)	Sneezes/ cough/pulls away	Grimace	No response
A	Appearance (skin color)	Normal whole body	Only extremities cyanotic	Cyanosis or pale whole body
R	Respirations	Good crying	Slow, irregular	Absent

Table 7.1.1
APGAR score.

Cardiac Function in Childhood

As with adults, cardiac output in children is a product of preload, afterload, contractility and heart rate. Preload affects contractility in adults via the length-tension relationship. Essentially, stretching a muscle

fiber at rest allows it to produce greater force during contraction. Afterload is related to the wall tension in the contracting ventricle and opposes contractility, thus limiting stroke volume.

The immature heart contains more non-contractile protein than the adult heart. It is stiffer and is less able to increase cardiac output in response to increased preload. The negative effects of afterload on cardiac output are increased in the immature heart. The newborn heart under normal conditions works at the upper limits of preload, afterload, contractility and heart rate, so little cardiac reserve remains. Significant reductions in cardiac output are not uncommon in the face of hypoxia, acidosis or under the depressive effects of anesthesia. The limited ability of the fetal heart to increase stroke volume means that heart rate has a significant influence on cardiac output.

Effects of Anesthesia on the Cardiovascular System

Inhalational anesthetics, as in adults, produce a depressive effect on the cardiovascular system in children. Modest decreases in blood pressure occur with all inhalational agents. Isoflurane, and likely sevoflurane, produce a reduction in afterload. Rhythm is also affected with volatiles. Sevoflurane at high concentrations can produce bradycardia. Desflurane can cause tachycardia when MAC is increased rapidly.

Propofol, although less of a depressant on the myocardium as compared to thiopental, generally produces a greater reduction in blood pressure through a reduction in afterload. Propofol may cause bradycardia. Ketamine also reduces myocardial contractility, but blood pressure is usually maintained or increased by its sympathomimetic effects, and heart rate may increase.

Conduct of Anesthesia in Pediatrics

Preanesthetic Evaluation

As with the practice of adult anesthesia, the pre-anesthetic encounter in pediatric anesthesia is designed to achieve multiple goals. The patient's past medical history, past anesthetic and surgical history, functional history, and review of systems is elicited in addition to a physical exam to provide the anesthesiologist with an assessment of the patient's risks and unique considerations. The encounter also allows the anesthesiologist to make the patient aware of the anesthetic procedures and risks in order to generate patient questions and obtain informed consent.

In pediatric anesthesia, the history is obtained in surrogate from the patient's caregiver and the physical examination is often limited by patient cooperation. The history includes:

- Antenatal, birth and perinatal history – Premature? Resuscitation and neonatal supports required? Hypoxic injury?
- Developmental history – Normal growth and development? Genetic or Metabolic issues?
- Functional history – Exercise tolerance? Feeding tolerance? Cyanosis? Frequent chest infections? Sleep apnea? Gastroesophageal reflux?
- History of recent common complaints – Upper respiratory tract infection? Fever? Dentition – Loose or damaged teeth?
- NPO status – Fasted?
- History specific to presenting complaint or diagnosed problems:
    - Congenital Heart Disease? (i.e. Tetralogy of Fallot)
    - Congenital Abnormalities? (i.e. Trisomy 21)
    - Acquired or progressive diseases? (i.e. Duchene's muscular dystrophy)
    - Cerebral Palsy

    - Common recurrent problems in childhood – asthma, croup, previous surgeries

- Previous anesthetics – Airway issues? Adverse events? Postoperative adverse events and pain issues?

The physical examination of children in the preoperative waiting room is often difficult. A general observation of the previously healthy child is often sufficient. A child playing in the waiting area, not observed to have nasopharyngeal secretions, cough, decreased energy, pallor or cyanosis, and with normal body habitus and facies is sometimes best left unexamined to alleviate preoperative anxiety. A child with a history of illness or specific conditions relevant to anesthesia must endure a focused exam.

The pre-anesthetic encounter also affords an opportunity to develop a rapport with the child and identify those for whom pre-operative sedation or parental presence at induction may be appropriate.

Pre-operative Sedation

In patients willing and able to take oral medications, midazolam 0.5-0.75mg/kg may be given at least 10 minutes prior to the patient's separation from parents. For patients unwilling to take oral medications, such as the autistic adolescent, intramuscular ketamine 2-4mg/kg may be required. Alternatively, intranasal midazolam 0.2-0.4mg/kg or dexmedetomidine 1-2mg/kg can be given.

Pharmacology of Anesthestic Agents in Pediatric Patients

A complete description of the pharmacology of anesthetic agents in pediatric patients is beyond the scope of this chapter. In general, the same anesthetic drugs used in adult are used in pediatric practice.

Emergence Delirium

Emergence delirium, or agitation, is a phenomenon of dysphoria independent of pain or anxiety which occurs in children following anesthesia. It has been found to occur with greater frequency after Sevoflurane-based maintenance of anesthesia. The pathophysiology is unclear and the generation of emergence delirium is likely multifactorial. Sevoflurane may produce a residual cortical irritability, as it has been shown to induce epileptiform activity. Conversely, it may be the low solubility and rapid awakening with Sevoflurane that has produced this effect. Propofol, ketamine, dexmedetomidine and other agents have been shown to reduce emergence delirium.

Nitrous Oxide

Nitrous oxide is an old inhalational anesthetic. It has been used successfully and safely for over 150 years. It is a weak agent with a MAC value in adults of 106%. It was particularly useful because of its extremely low solubility and thus rapid onset and elimination. Recent evidence suggests that prolonged nitrous oxide exposure affects bone marrow, immunity and peripheral nerve function in susceptible individuals due to inhibition of methionine synthase. The lack of a unique role and concerns about uncommon toxicity have reduced its use in adult anesthesia.

In children, however, anesthesia is often induced by mask prior to the insertion of an intravenous catheter. Nitrous oxide is odourless and tasteless and can be used briefly, prior to the initiation of a volatile anesthetic. Sevoflurane, while not pungent, still possesses an odour to which children may object. For these reasons, nitrous oxide is still a frequently used tool in pediatric anesthesia.

Neurocognitive Impact of Anesthesia

Postoperative cognitive dysfunction in the elderly is well established after both cardiac and non-cardiac surgery. There is a decade of evidence that anesthetic agents can produce apoptotic changes in neurons in infant and fetal animals. The majority of evidence comes from rodent models. Agents implicated include nitrous oxide, isoflurane and ketamine. There is no evidence for similar effects in human infants or fetuses, although there is much discussion in the literature on this topic. Small studies have suggested short term deficits in memory and impairment on neurocognitive testing but fail to show lasting effects.

At present, any risk which does exist is best reduced by exposing infants to anesthesia only when

necessary.

Laryngoscopy and Airway Devices in Pediatric Anesthesia

Endotracheal intubation, laryngeal mask airways (LMA) and mask anesthesia are all commonly used in pediatric anesthesia. Endotracheal intubation can be achieved by direct laryngoscopy, fibre-optic endoscopic intubation, video-assisted laryngoscopy, intubating LMA, and a variety of other devices adapted from adult airway management.

Pediatric Positioning for Laryngoscopy

The differences between the pediatric and adult airway are described above. These differences result in changes in optimal positioning for bag-mask ventilation and intubation. An infant's large occiput results in C-spine flexion at rest when under anesthesia in the supine position. To open the airway, we need to achieve a modest "sniffing position," often by padding under the shoulders. An excessive sniffing position will close the hypopharynx and impair spontaneous or bag-mask ventilation. Optimal positioning, as in adults, best aligns the oropharyngeal, pharyngeal and laryngeal axes to ease laryngoscopy.

Straight vs Curved Blades

In infants and young children, the epiglottis is long, floppy and is angled posteriorly over the glottis inlet. The laryngoscope blade must be placed under the epiglottis to lift it out of the view of the larynx. The straight blades (Miller, Wisconsin, Wis-Hipple) are designed for this purpose.

In older children, the curved Macintosh blade can be used as in adults. Familiarity with the straight blade technique in older children and adults may prove valuable in the approach to the difficult airway.

ETT Size and Insertion Depth

Historically, in pediatric patients under the age of 8, an uncuffed ETT is used. The sizing is directed at allowing positive pressure ventilation and application of sustained airway pressures as needed, while maintaining a small leak at pressures of 20 cm H_2O or greater. This leak, which involves air loss around the ETT, is evidence that undue pressure is not being applied to the tracheal endothelium. Microcuffed ETTs of smaller diameter are available for use in infants and younger children. Proponents of cuffed tubes in younger patients point out that the uncuffed tube is a round object in an irregular tube. A leak doesn't preclude excessive pressure of the tube on the airway at points of contact. They suggest that a smaller cuffed tube, with the cuff inflated at low pressure to take the shape of the airway, may reduce subglottic injury.

Infant ETT sizing is described in Table 7.1.2. Beyond the age of 2, the following formula is used to predict the appropriate inner diameter (in millimeters) of the ETT in pediatric patients:

Uncuffed ETT size in mm = (age in years/4) + 4

This formula is useful up to the age at which the adolescent approaches adult size. Before this time, typically beyond age 8, a cuffed ETT is used. The inner diameter of the cuffed ETT selected should not be greater than one half size smaller than the appropriate uncuffed tube. The appropriate maximal tube sizes are the same as in adults; approximately 7-8 mm in diameter in females and 8-9mm in diameter in males.

ETT depth, from the lips to mid-trachea in infants, is described in Table 7.1.2. Beyond one year of age, the ETT depth may be estimated by the formula:

ETT depth cm = (age in years/2) + 1

Age	Weight (kg)	ETT ID (mm)	ETT depth (cm)
Premature	< 1	2.5	7 – 8
Premature	1 – 2.5	3.0	8 – 9
Full Term	2.5 – 3.5	3.5	9 – 10
3 months	3.5 – 5.0	3.5	10 – 11
6 months	5.0 – 8.0	3.5 - 4.0	11 – 12
1 year	8.0 – 11.0	4.0 – 4.5	12 – 13

Table 7.1.2

Endotracheal tube depth in infants.

Laryngeal Mask Airway

The laryngeal mask airway (LMA) is a supraglottic airway device which may be used with low pressure ventilation or in the spontaneously breathing patient under anesthesia. It is a useful tool in the management of the unexpected difficult airway. It does not protect against laryngospasm or aspiration of gastric content. LMA sizes are based on patient weight. The weight of a pediatric patient should be obtained but can be estimated by the following formula:

Est weight = Age x 2 + 9

Patient Weight (kg)	LMA Size	Maximum Cuff Volume (mL)	Largest ETT that will pass through
<5	1	4	3.5
5 – 10	1.5	7	4
10 – 20	2	10	4.5
20 – 30	2.5	14	5
30 – 50	3	20	6 with cuff
50 – 70	4	30	6 with cuff
70 – 100	5	40	7 with cuff
> 100	6	50	7 with cuff

Table 7.1.3

LMA sizing based on patient weight.

Problems Encountered in Pediatric Airway Management

Preschool children contract upper respiratory tract infections (URTIs) 8-10 time per year and are affected by them for 1-2 weeks with each occurrence. URTIs predispose patients to adverse events under anesthesia, particularly laryngospasm and bronchospasm.

Laryngospasm is an upper airway protective reflex which produces tight closure of the vocal cords. This can occur at light planes of anesthesia both during induction and on emergence. It often occurs in response to stimuli, either of the glottis directly or in response to pain. It is significantly more likely to occur in the setting of a URTI. It is a complete closure of the upper airway and is an emergent situation for the anesthesiologist. It may be relieved occasionally with physical maneuvers, jaw thrust or pressure on the mastoid process. It may also be relieved by deepening the anesthetic or using a paralytic agent.

URTIs produce a state of increased airway reactivity for up to 3-4 weeks following the resolution of acute symptoms. During this time, the patient may be predisposed to bronchospasm under anesthesia, especially when the trachea is intubated.

A delay of elective surgery of between 2-6 weeks has been advocated after URTI. However, if a child has 8-10 colds per year lasting 1-2 weeks and we adhere to an empiric delay of 6 weeks following each, the surgery will never take place. A survey of pediatric anesthesiologists reveals that most will undertake an anesthetic in the face of mild symptoms of an URTI. This means the absence of systemic signs such as fever, wheeze, lower respiratory tract findings, copious secretions, sleep apnea, prematurity, or other complicating factors.

Perioperative Fluid Management

In 1957, Halliday and Segar published their studies on the energy and fluid requirements in children. These results led to the development of maintenance fluid administration empiricisms. The electrolyte composition of the maintenance fluid suggested by Halliday and Segar was model after human milk. Nevertheless, maintenance fluid administration was, for decades, based on the 4 -2 – 1 rule and comprised of hypotonic fluids.

4 – 2 – 1 rule for maintenance IV fluid therapy:

- 4ml/kg/hr for the first 10kg of body mass
- 2mg/kg/hr for the next 10 kg of body mass
- 1mg/kg/hr for body mass beyond 20kg

Antidiuretic hormone secretion is increased by stress pain, anxiety and the use of opiates and inhalational anesthetics. Hyponatremia is the most common electrolyte disorder in the perioperative period in pediatric patients. Serious hyponatremia, less than 120mmol/L, can lead to transient or permanent brain damage due to cerebral edema. This disorder is largely caused by the administration of hyponatremic fluid at a time when free water elimination is reduced.

Current recommendations suggest the use of isotonic fluids in the perioperative period and in critically ill children. In normovolemic children, the maintenance rate should be decreased by 30-50% to further prevent free water overload. Children receiving parenteral fluids should have serum electrolytes measured regularly. Dehydration should also be assessed regularly. The following table depicts this assessment.

Characteristic	Mild (<5%)	Moderate (5-10%)	Severe (>10%)
Heart rate	↑	↑↑	↑↑↑
SBP	Normal	Low normal	hypotensive
Urine output	↓	↓↓	↓↓↓ or anuria
Mucous membranes	Slightly dry	Dry	Very Dry
Anterior Fontanelle		Sunken	Very Sunken
Eyes		Sunken	Very Sunken
Skin Turgor		↓	↓, with tenting
Thirst	↑	↑↑	↑↑↑
Level of Consciousness			Lethargy/coma

Table 7.1.4

Assessment of dehydration severity.

Volume replacement is with isotonic solutions, colloid or blood products based on the degree of hypovolemia and anemia. Fluid compartments vary with age. Total body water is as high as 80% of the body weight of a neonate. This falls in the second 6 months of life to approximately 60% that of adults.

Blood volume per mass is highest in the preterm infant and falls throughout childhood to adult levels. As in adults, replacing blood loss with crystalloid requires volumes 3-4 times the estimated blood loss. Colloids, such as albumin and pentaspan, as well as blood products, replace blood loss in a 1:1 ratio.

Age	Blood Volume (mL/kg)
Premature Newborn	100
Newborn	90
Infant	80
Child	75
Adult	65 - 70

Table 7.1.5

Blood volume by age.

Postoperative Pain Management

In children, as in adults, pain management is multimodal. Non-pharmacologic therapy, acetaminophen, nonsteroidal anti-inflammatories, opiates, and atypical analgesics such as gabapentin are all used. Regional and neuraxial anesthesia is increasing in popularity. Epidural and caudal blocks have long had a place in pediatric pain management. The introduction of the ultrasound has broadened the scope of pediatric pain management to include a variety of peripheral nerve blocks. Ultrasound is of particular importance in the safety of regional anesthesia in children, since in most cases our patients are sedated or under general anesthesia when the block is performed.

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Chapter 8

PAIN MANAGEMENT

Sections:

1. Acute Pain
2. Chronic Pain

Section 8.1

Acute Pain

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Summary

1. Acute pain can cause serious medical problems including cardiovascular, respiratory, and gastrointestinal complications. Unrelieved severe acute pain is highly predictive for development of chronic pain.
2. Mild-moderate acute pain is easy to treat in the majority of cases.
3. Use multimodal analgesic therapy to achieve better pain outcomes and fewer side effects.
4. For mild pain use an NSAID alone or acetaminophen as required.
5. For moderate pain, use a compound drug such as acetaminophen + oxycodone IN ADDITION TO A REGULAR NSAID at set times.
6. For severe pain use intermittent boluses of intravenous opioids at **therapeutic** doses. Consult the acute pain service but think about patient-controlled intravenous analgesia, local anesthetic techniques, and alternative analgesics.
7. Consider the adverse effects of opioids (nausea, constipation, pruritus).
8. Include non-pharmacologic complementary therapy for comprehensive pain relief.

Is Acute Pain Really a Problem?

Growing evidence suggests that many individuals suffer moderate to severe pain after surgery and that in the last ten years the problem has become worse.[1] In many patients, pain can last up to a week following the surgical procedures, and if severe acute pain remains uncontrolled, it can trigger the development of persistent post-surgical pain[2]. Advancements in anesthesia and surgical methods have increased recovery times and facilitated earlier hospital discharge times. As a result, many people are managing their own pain at home, often with the assistance of their community health clinicians such as family doctors, nurse practitioners and pharmacists. Some patients may not have adequate community support systems for pain management, and this can result in limitations in function and delayed recovery from pain. A gap in adequate service for pain management is being addressed by the development of hospital based outpatient transitional pain service programs.

Patients often list pain after surgery as a major concern, yet many don't know this particular type of pain can usually be easily controlled. A good prior knowledge of how to control pain lessens patient anxiety, which in itself can reduce pain and allows individuals to take control of their recuperation process after major surgery.

Why Do We Need to Treat Pain?

Severe postoperative pain causes an increase in sympathetic nervous system activity that can lead to hypertension and tachycardia. Increased myocardial work can progress to perioperative myocardial ischemia and infarction in high-risk patients. Excessive pain can result in poor respiratory effort, leading to pulmonary atelectasis and risk of postoperative pneumonia. Poor mobility caused by excessive pain can predispose individuals to greater risk of thrombotic complications, such as deep venous thrombosis or pulmonary embolism. Finally, inadequate perioperative pain control can lead to persistent post-surgical pain; particularly in high risk procedures such as thoracic, cardiac, breast or hernia surgery.[3]

Good perioperative pain control can facilitate return to normal activity, as well as reduce the morbidity associated with suboptimal control.

TABLE 1 - PHYSIOLOGIC CONSEQUENCES OF POOR POST-OPERATIVE PAIN CONTROL.[4]

Pulmonary	Difficulty in coughing leads to atelectasis and pulmonary infection.
Cardiovascular	Sympathetic stimulation leads to increased myocardial oxygen demand and ischemia.
Endocrine/Metabolic	Catabolic hormone release leads to sodium and water retention and hyperglycemia.
Thromboembolic	Restricted mobility, combined with activation of acute phase proteins, leads to increased risk of deep venous thromboses and pulmonary embolism.
Gastrointestinal	Pain decreases gastric motility and intestinal function and leads to postoperative ileus.
Immunologic	Pain can reduce immune system function, leading to increased risk of infection.
Psychologic/CNS	Unrelieved pain causes sleep deprivation, anxiety and fatigue. Severe prolonged acute pain can lead to chronic pain.

Assessing Acute Pain

"Pain is whatever the experiencing person says it is, existing whenever he says it does" (McCaffery 1968)

Pain is a common symptom which is sometimes overlooked by healthcare providers. There remains a perception amongst some healthcare professionals that poor pain control is not harmful or even worse, that it is necessary for recovery. Many patients are reluctant to report pain and this sometimes makes pain assessment especially difficult. Certain populations are at higher risk of poor assessment and treatment, including children, the elderly and those who aren't able to communicate their pain intensity. Be aware that many patients will not report symptoms to their doctor or nurse ("he/she is busy enough already") unless directly questioned.

There are many methods used to assess pain intensity. The most reliable and valid method to quantitatively assess pain in adults is (Numeric Rating Scale (NRS) where patients express their pain as a score from 0 to 10, where 0=no pain; 1-3=mild pain; 4-6=moderate pain, and 7-10 = severe pain (RNAO, 2013). Other scales such as the Visual Analogue Scale and Simple Verbal Descriptive Scale can also be used.

In the simplest form of assessment, it is sometimes easiest to ask if the pain is mild, moderate, or severe (or of course, no pain). There are several scoring systems used to classify the character of pain (i.e., stabbing, burning, aching, etc.) and the best known is called the McGill Pain Questionnaire, developed by Professor Ronald Melzack from McGill University in Montreal. This tool is most used to assess neuropathic pain and more commonly used for pain-related research studies.

More importantly pain should be assessed regularly, with a consistent approach and treatment should be quick with adequate doses of analgesics once the assessment is finished.

Pain classification

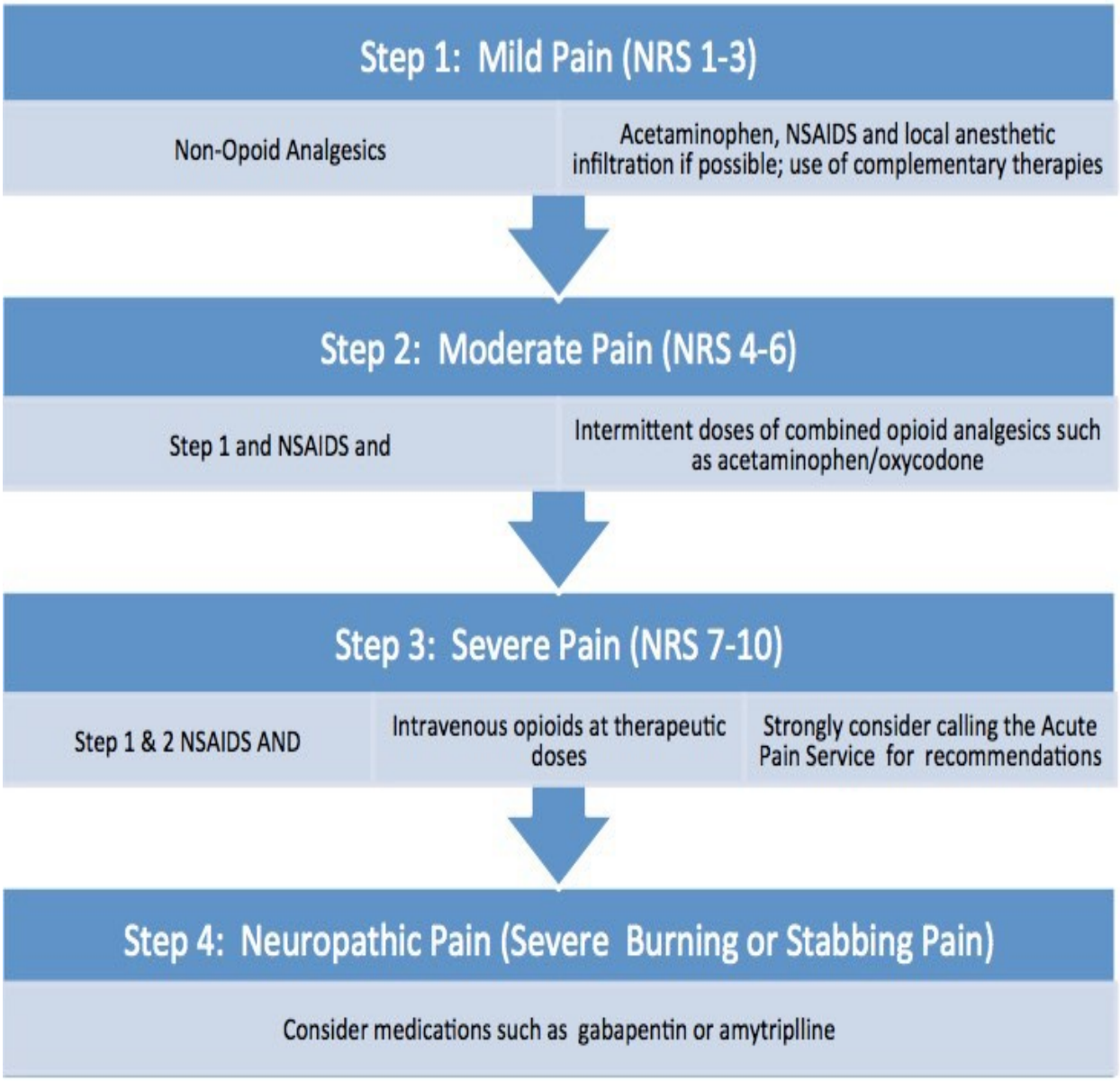
Three types of pain are commonly described:

1. **Somatic pain**: the most commonly described pain occurring after peripheral injury. The pain is commonly described as sharp or aching, and is the commonest pain after injuries such as fractures and surgical incisions. It is often treated with NSAIDS, acetaminophen, and/or opioid analgesics.

2. **Visceral pain:** this is pain related to irritation of the visceral nervous system that innervates the pleura, peritoneum and other structures such as the pericardium. Common types of visceral pain include angina pectoris and abdominal pain related to cholecystitis, and appendicitis. The pain is usually described as a centrally located and poorly defined aching-type pain with a colicky quality (comes in waves or spasms).

3. **Neuropathic pain:** this type of pain is related to nerve irritation, and can happen when any injury or surgery is near a peripheral nerve. The pain is often described as stabbing or burning in quality and is often difficult to treat. This pain is sometimes amenable to treatment with opioid analgesics such as morphine, but other commonly used analgesics for this type of pain include the anticonvulsants such as gabapentin and pregabalin and tricyclic antidepressants such as amitrypytiline and nortriptyline.

FIGURE 1 - TREATING ACUTE PAIN.



Many patients can benefit from simple analgesic regimes for mild pain (NRS 1-3). This type of pain is often easily controlled with intermittent acetaminophen (500mg-1g every 6 hours as required) or a non-steroidal anti-inflammatory drug such as ibuprofen (200 mg to 400 mg every 8 hours). Patients with liver impairment should avoid acetaminophen while patients with peptic ulcer disease, severe asthma, renal dysfunction, or bleeding problems should avoid NSAIDS. However, patients who are at risk of bleeding can safely take a newer cyclooxygenase-2 (COX-2) inhibitor, such as celecoxib (100 to 200 mg twice daily for acute pain up to 5 days) because these medications do not impair platelet function. However, recent evidence has shown that the COX-2 inhibitors may cause cardiac complications if used for prolonged periods of times and, therefore, their use is limited to short term management of acute pain.[5]

Patients with moderate pain (NRS 4-6) will benefit from combining a regular dose (every 8-12 hours) of a non-steroidal anti-inflammatory drug (NSAID), with an opioid/acetaminophen combination used for breakthrough pain as necessary. Examples of these compound analgesics include Tylenol #3 (acetaminophen 500 mg / codeine 30 mg / caffeine 15 mg) and Oxycocet (acetaminophen 500 mg / oxycodone 5 mg). This combination, also known as multimodal therapy, maximizes pain control while reducing opioid-related adverse effects such as sedation, nausea, and constipation. For mild to moderate

postoperative pain, always consider whether local anesthetic infiltration or a nerve block technique may benefit the patient. Care should be taken to avoid exceeding the maximum daily dose of acetaminophen (4 g in healthy adults), especially when using compound analgesics.

Patients in severe pain (NRS 7-10) need rapid relief of symptoms. The easiest method to do this is to give a bolus of intravenous opioid (drugs and doses are suggested in Table 3) and reassess pain within fifteen minutes. If pain is still severe, give a further intravenous dose of opioid every fifteen minutes until pain is controlled.

Patients who have severe pain that is not easily controlled by the above methods or require repeated treatments should be seen by the hospital acute pain service, where available. Patient-controlled intravenous opioid analgesia is a very useful and safe method of treating severe pain, and the acute pain service can help provide and monitor this treatment. Patients who are more likely to have severe postoperative pain can sometimes be predicted in advance of surgery. Table 2 lists some predictors of severe postoperative pain.

TABLE 2 - PREDICTORS OF SEVERE POSTOPERATIVE PAIN.

- Patients with pre-existing chronic pain
- Patients taking > 30 mg oral morphine equivalent per day e.g. > 6 Oxycocet per day
- Patients having major spine, thoracic or abdominal surgery or surgery around nerves

Neuropathic Pain

Neuropathic (severe burning or shooting) pain can be difficult to treat with standard analgesics such as NSAIDS and opioids. This type of pain often occurs after major surgery or trauma, especially when the injury is close to neurological structures such as nerves or the spinal cord.

Two classes of drugs, primarily used for other health conditions, have also been helpful in the management of neuropathic pain. The Canadian Pain Society recommends use gabapentinoids (gabapentin and pregabalin) as first line therapy, and tricyclic antidepressant drugs (TCAs) such as amitriptyline or nortriptyline, gabapentin and pregabalin. More recently, cannabinoids such as Nabilone have also been recommended as third line therapy for management of neuropathic pain[8].

Classically, the TCAs are used to treat burning pain and the anticonvulsants to treat stabbing or shooting pain. However, there is considerable crossover in their effectiveness for each type of pain.

Amitriptyline is used in much lower doses than those normally used for depression. Typical doses start at 10 mg and increase in 10 mg increments until effective. It is usually taken at night because sedation is common with these drugs. In addition, TCAs have adverse anticholinergic effects (e.g. tachycardia, dry mouth, and urinary retention) and, therefore, care should be taken in elderly or at-risk subjects. It should also be used with caution in patients who have had a history of cardiac arrhythmias.

Gabapentin is usually started at 100-200 mg every 8 hours and increased every 2-3 days until an effective dose is reached. The commonest adverse effect is sedation and therefore slow titration is recommended in practice.

TABLE 3 - DRUGS AND DOSAGES FOR MANAGING PAIN. THE STEPS IN THE LEFT COLUMN RELATE TO FIG1.

	Suggested Agents	Doses	Cautions	Adverse effects
Mild Pain (Step 1)	Acetaminophen po Ibuprofen po Celecoxib po	500 mg-1g q6-8h 200-400 mg q8h 100-200 mg q12h	Liver disease/elderly Platelet, asthma or COPD, severe cardiac disease, hypertension, renal disease or history of peptic ulceration	Negligible at therapeutic doses See cautions as over
Moderate Pain (Step 2)	Acetaminophen 500mg/Codeine 30mg po Acetaminophen 500mg/Oxycodone 5mg po +/- local anesthetic	1-2 tablets q4h 1-2 tablets q4h	Liver disease in elderly & history of allergy to opioid analgesics	Gastric irritation with codeine. Constipation, itching, nausea, sedation, respiratory depression, especially at higher doses with both medications
Severe Pain (Step 3)	I.V. Morphine or Hydromorphone Call APS Consider local anesthetic techniques	0.1-0.15 mg/kg 0.02-0.03 mg/kg	Reduce dose in elderly and supervise closely until pain controlled	All adverse effects as Step 2 except no gastric irritation
Neuropathic Pain (Step 4)	Amitriptyline po Gabapentin po	10-50mg qhs 100-300mg q8h	Cardiac Disease Elderly more prone to sedation	Anticholinergic effects and sedation, especially at higher doses

Treating Opioid-Related Adverse Effects

Opioid analgesics are useful in the treatment of pain; however, all have adverse effects that are dose-related. In all patients if possible, opioids should be used in combination with acetaminophen or a NSAID because this will reduce the required dose of opioid and the risk of adverse effects. This technique of combining multiple medications, described earlier as multimodal analgesia, enables the use of a lower dose of each with improved overall effect.

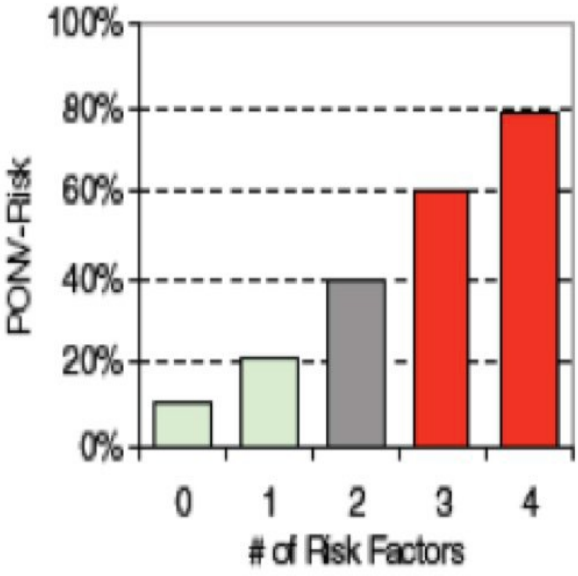
Numerous side-effects can be caused by opioids, including nausea, vomiting, itching (pruritus), sedation/respiratory depression, constipation, delirium, and myoclonus. Constipation, delirium, and myoclonus tend to occur with long-term treatment, and/or with very high doses of opioid. It is important to realize that side effects such as nausea, vomiting, and sedation can have numerous triggers, and a thorough assessment will help decide which factors are most likely to contribute to these side effects in each individual.

Nausea and Vomiting

Despite increased attention to the problem of postoperative nausea and/or vomiting(PONV), it still occurs in approximately 30% of all patients after surgery, and in up to 80% of patients considered high risk.[6] Efforts to reduce PONV have focused on identifying patient risk factors, reducing baseline risk factors, and using appropriate medications for prophylaxis (prevention) and treatment.

FIGURE 2 - IDENTIFYING PATIENT RISK FACTORS.[7]

Risk Factors	Points
Female Gender	1
Non-Smoker	1
History of PONV	1
Postoperative Opioids	1
Sum =	0 ... 4



The risk of PONV increases as more risk factors are present. It is important to remember risk factors can only be used to indicate what groups of patients are at risk for PONV, not which individuals are at risk.

Several strategies can be adopted to reduce PONV. These include avoiding general anesthesia if possible, using propofol, avoiding nitrous oxide and volatile anesthetics, and minimizing the use of neostigmine and postoperative opioids. As mentioned earlier in the chapter, a multimodal approach to postoperative pain management can reduce the use of postoperative opioids.

For patients at high risk for PONV, it is recommended that they receive anti-emetics prophylactically. See Table 3 for possible prophylactic and treatment interventions for PONV. It is important to understand that multiple mechanisms of action contribute to the experience of PONV, and that no

single drug exists that can exert an effect on all the known mechanisms.

TABLE 4 - PROPHYLAXIS AND TREATMENT OF PONV.

Prophylactic use of antiemetics for patients at high risk for PONV	**Treating Established PONV** **(* must wait 6 hours before re- administering a medication already used prophylactically)**	**Potential side-effects**
Dexamethasone 4 mg	Dexamethasone is not usually used for established PONV	None noted with single dose of 4 mg
Ondansetron 4 mg (or other 5HT-3 receptor agonist)	Ondansetron 1 mg every 6 hours as needed	Headache, elevated liver enzymes, constipation
Droperidol* 1.25 mg	Droperidol is not usually used for established PONV	QTc prolongation with high doses
	Dimenhydrinate 12.5-25 mg every 4 hours as needed	Sedation
	Prochlorperazine 5-10 mg every 6 hours as needed.	Sedation, extrapyramidal symptoms at high doses

* Droperidol has an FDA Black Box Warning and is used with caution

! The prophylactic medications can be combined (usually no more than 2 of the drugs are combined at once)

! Other medications used for established PONV that have established efficacy include transdermal scopolamine and haloperidol

Pruritus

Pruritus is a rare side effect of opioids. In fact, the relationship between opioids and pruritus remains somewhat of a mystery. Diphenhydramine (Benadryl), an antihistamine, at doses of 12.5-50 mg every four hours as required, is the most common drug intervention utilized, even though the effect of histamine release on opioid-related pruritus is not certain. Given how rare this side effect is, and the fact that pruritus is more of an annoying but self-limiting side effect, it is unlikely much research will occur in this area.

Sedation/Respiratory Depression

As with nausea and vomiting, many factors can contribute to sedation, including the use of opioids. Minor sedation usually requires no treatment other than observation and intermittent stimulation. If opioids are being used and the patient is pain free, the dose should be reduced.

Respiratory depression is a much more serious, yet thankfully rare, side effect of opioid administration. **It can lead to death if not recognized in time.** Patients at risk for respiratory depression are patients without previous exposure to opioids, and those with conditions that already cause respiratory compromise. This includes sleep apnea, severe asthma, or other disorders of the respiratory system. Opioid-related respiratory depression is classically defined as occurring in a patient with a respiratory rate of <10 breaths/min, and being significantly sedated (constantly drowsy and very difficult to rouse).

Should a patient present with these symptoms, opioids should be held and **naloxone** (an opioid antagonist) should be administered in small doses until the respiratory rate increases and/or the sedation level is reduced. In adults, the usual dosing is 0.04 mg intravenously every 3-5 minutes. **It is important to remember that naloxone is extremely short-acting** and patients need to be observed for repeated episodes of reduced respiratory rate or increased sedation, particularly if the opioid was a sustained release formulation, or was given by the epidural or intrathecal route.

Identifying Patients at Risk for the Development of Chronic Post-Surgical Pain (CPSP): The Development of a Transitional Pain Service

The development of persistent post-surgical pain should be considered as a possibility at the time acute pain is present, especially after surgery. Some patients will leave hospital after surgery and still have significant pain challenges, yet community services for management of acute pain remain limited. To address this gap, and to help prevent the transition of pain from an acute to chronic state, novel interprofessional programs are being developed. For example the **Transitional Pain Service (TPS)**, based at Toronto General Hospital, a hospital-based, interprofessional specialty pain service cares for mainly post-operative patients with the mission of providing pain management and support for opioid weaning for up to six months after major surgery.[8] As patients face daily struggles with pain and psychosocial problems, they may require more than the daily recommended dose (50 - 90 mg – depending on the guidelines). A 50 mg daily dose of a morphine equivalent (MEQ) is considered the new standard safe dose as per the 2016 U.S. CDC guidelines and 90 mg in Canada based on the new Canadian guidelines [9].

As has been reviewed through this chapter, the management of acute pain is essential for proper recovery from painful procedures. Patients in whom acute pain is well controlled may have a lesser chance of developing persistent post-procedural pain. The balanced use of multimodal analgesic and non-analgesic therapies is also critical to ensuring that acute pain is well managed, and that healing following a painful procedure is promoted.

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Section 2

Chronic Pain

Dr. David Flamer (MD, FRCPC) & Dr. Philip Peng (MBBS, FRCPC)

Introduction

Chronic pain affects one out of every five Canadians and is a significant burden on the lives of patients, their families and the utilization of health resources. Chronic pain has adverse effects on physiologic status, functional capacity, psychosocial well-being, economic productivity, and quality of life. Management of chronic pain requires a multidisciplinary approach to help target each of these important domains. Anesthesiologists are in a unique position to participate in multidisciplinary pain management because of broad training in a variety of patients, including surgical, obstetric, pediatric, and medical subspecialties, as well as expertise in clinical pharmacology and regional anatomy. Other disciplines often involved in pain management include psychiatry, neurology, addiction medicine, physiotherapy, and psychology. The challenge for a pain physician is to recognize the complex interplay of the biological, social, and psychological factors that comprise the pain syndrome.

Chronic Pain Definitions (www.iasp-pain.org)

The International Association for Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage." This definition acknowledges both the physiological and psychological components of pain. Chronic pain is defined as pain that persists beyond the usual course of an acute pain syndrome. In general terms, chronic pain is defined as pain lasting more than 12 consecutive weeks.

Pain can be classified according to pathophysiology as nociceptive, neuropathic, or as mixed pain syndrome.

Nociceptive pain is pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors. It can be somatic or visceral (e.g. pancreatitis) in origin. Somatic pain is sub-classified as superficial (e.g. arising from skin or subcutaneous tissues) and deep (e.g. arising from bones, joints, and ligaments).

Neuropathic pain is pain caused by a lesion or disease of the central or peripheral somatosensory nervous system. Examples of neuropathic pain include peripheral mononeuropathy (eg. carpal tunnel syndrome), polyneuropathy (e.g. diabetic neuropathy or HIV-associated neuropathy), and central pain syndromes (e.g. phantom limb pain or post-stroke pain).

Allodynia is defined as pain due to a stimulus that does not normally provoke pain (e.g. light touch causing pain).

Hyperalgesia is an increased painful response to a normally painful stimulus (e.g. pin-prick).

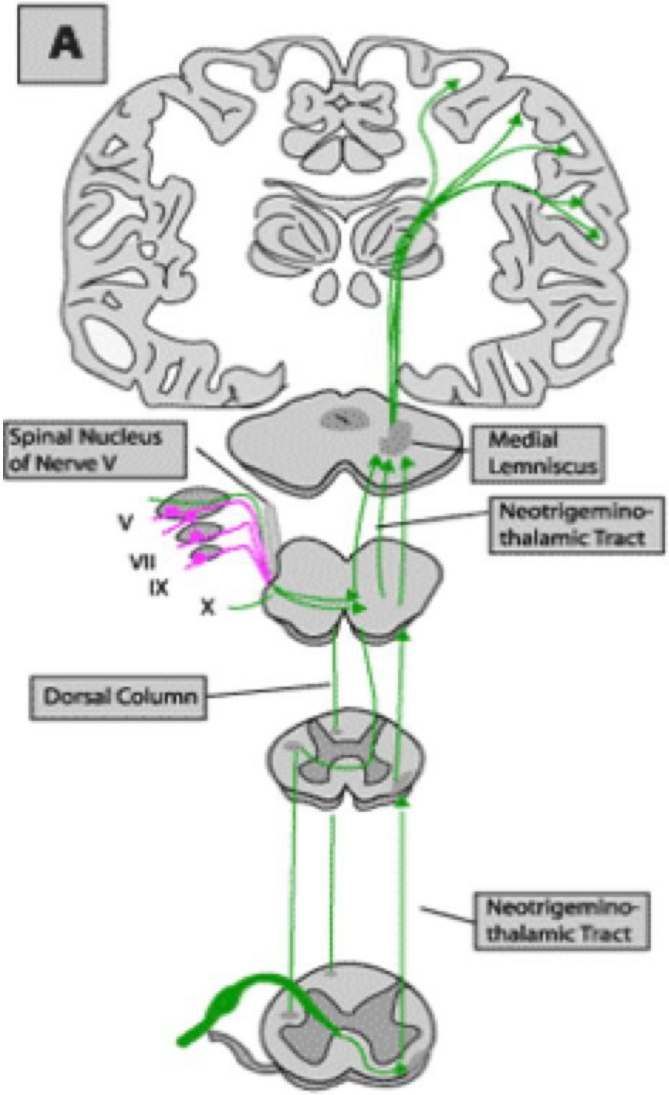
Pathophysiology

The pain pathways have been identified and their anatomy detailed, but an understanding of intrinsic changes to the sensory apparatus, both central and peripheral, is still developing. The transmission and interpretation of pain involves complex pathways that are modulated at multiple levels in the central nervous system.

From a simplistic view, pain is conducted along a three-neuron pathway that transmits noxious stimuli from the periphery to the cerebral cortex. Nociceptors are free or specialized nerve endings sensitive to tissue trauma. The sensory system of pain consists of nociceptors and primary afferent neurons that synapse in the dorsal horn of the spinal cord. The primary afferent neuron synapses with second order neurons whose axons cross to the opposite side of the spinal cord and ascend to the thalamus and

sensory cortex via the lateral spinothalamic tract. The second order neurons synapse in thalamic nuclei with third order neurons, which in turn project to the cerebral cortex (Figure 1).

FIGURE 1 - PAIN PATHWAY. PICTURE COURTESY OF WWW.FRCA.CO.UK



Pain management strategies focus on the four elements of pain processing: transduction, transmission, modulation, and perception. *Transduction* is the event whereby a noxious stimulus in the periphery is converted into an action potential. Targeting this element includes the use of NSAIDs, membrane stabilizing agents, opioids, and topical agents. *Transmission* occurs when the action potential is conducted through the first, second, and third order neurons. An example of targeting this element involves the use of local anesthetics, such as a peripheral nerve block or a neuraxial block. *Modulation* involves altering the afferent neural transmission along the pathway, often in the dorsal horn of the spinal cord. This is accomplished with the use of medications such as spinal opioids, alpha-2-agonists, and NMDA antagonists. *Perception* of pain is the final element whereby painful input is integrated in the somatosensory and limbic cortices, which can be modified with the use of parenteral opioids and other types of medications.

Gate Control Theory

Described by Melzack and Wall in 1965, this theory proposed that the transmission of nerve impulses from afferent fibers to spinal cord transmission (T) cells is modulated by a gating mechanism in the dorsal horn of the spinal cord. This gating mechanism is influenced by the relative amount of activity in large and small diameter fibers, such that larger fibers tend to inhibit transmission (close the gate). In

addition, the spinal gating mechanism is influenced by nerve impulses descending from the brain. When output of spinal T cells exceeds a critical level, it activates the action system, or those neural areas that sub-serve the complex function of an individual's behavioural response and the resulting characteristics of the painful stimuli. This theory emphasizes the modulation of inputs at the level of the spinal cord and the dynamic role the brain plays in pain processing, rather than being a passive component. It altered the earlier view that "it is all in the brain," and emphasizes that psychological factors are now seen to be an integral component of pain processing. This has paved the way for the development of new psychological strategies in chronic pain management.

A practical example of this theory is explained why rubbing over a painful area can sometimes relieve pain. Aß fibers stimulated by touch compete with the noxious impulses being transmitted by C fibers at the dorsal horn of the spinal cord for passage up to higher centers, thus closing the gate. This concept forms the basis of neuromodulation (e.g. TENS machine and spinal cord stimulation) and can partly explain many other physical interventions used in the management of chronic pain. The higher centers also exert descending control over the pain pathways at the level of the spinal cord, normally serving to inhibit pain transmission.

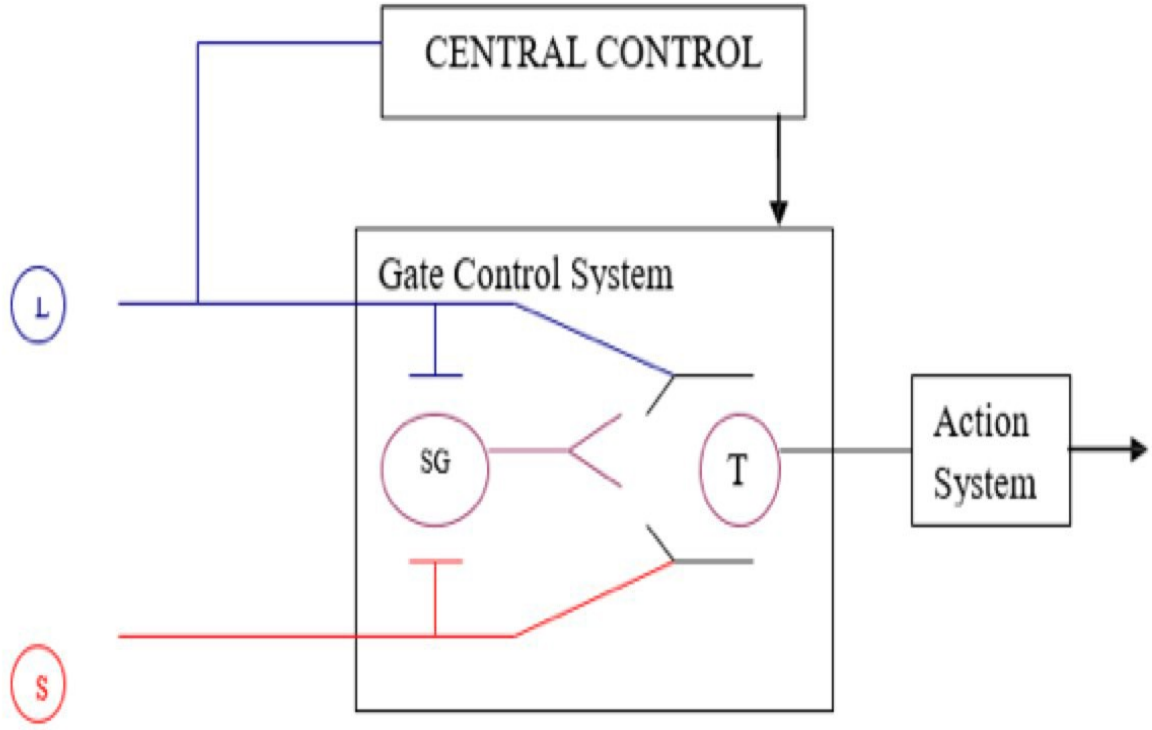


Figure 2: Gate Control Theory
L – Large diameter fiber, eg, Aβ
S – Small diameter fiber, eg, C
SG – Substantia Gelatinosa
T – First central transmission cell in spinal cord.

Sensitization

Following repeated or prolonged exposure to a barrage of noxious stimuli, changes occur in both the peripheral and central pain processing pathways. Peripherally, tissue injury releases local mediators of

inflammation due to repeated noxious stimuli. This causes direct excitation and activation of afferent C fibers. It leads to increased firing at lower thresholds and an increased response to a given stimulus. Furthermore, abnormal sodium channels may be expressed along the peripheral nerve, resulting in ectopic impulse discharge.

As a result of the central sensitization process, the pain signal will be amplified, modified and memorized. *Amplified* refers to the increase in signal intensity and field of pain perception. *Modified* refers to changes in character of the pain signal. An example of a modified pain signal is allodynia, in which a non-painful stimulus results in a painful response. *Memorized* refers to the retention of pain even after the source of the pain signal disappears. An example of this phenomenon is phantom limb pain, which is the persistence of pain from a limb even after the amputation of that limb.

Assessment of Patients with Chronic Pain

It is recommended that patients with chronic pain be managed using a multidisciplinary approach. In addition to improving pain symptoms, the goals of therapy are to restore function as much as possible, minimize side effects from medications, and manage common co-morbidities associated with chronic pain such as depression, anxiety, and sleep disturbance. A detailed history relating to the pain complaint should be taken, with an effort to further relevant details such as the location of pain, type and quality (eg. neuropathic vs. somatic), severity, alleviating and aggravating factors, and timing of onset. In addition to information relating to the pain, a comprehensive assessment will also include an inquiry about pain as it relates to:

- Impact on activity and participation
- Impact on self (mood, energy levels, sleep) and interpersonal relationships
- Past pain experiences
- Existing medical co-morbidities
- Treatment history (pharmacological, non-pharmacological, interventional, alternative)

When relevant, it is important to screen for opioid addiction risk. This can be accomplished with the use of validated risk assessment tools, such as the *Opioid Risk Tool* or the *Screener and Opioid Assessment for Patients with Pain (SOAPP)*. Furthermore, when appropriate, it is important to screen for "red flags" that may indicate a more acute and worrisome cause for pain. For example, in a patient with chronic low back pain, it may be important to rule out cauda equina syndrome by inquiring about bowel and/or bladder dysfunction, saddle anesthesia, and onset of lower extremity weakness.

When taking a pain history, validated pain scales can be used to help assess the severity of symptoms. One commonly used scale is the *visual analogue scale* (VAS). The *McGill Pain Questionnaire* can used to describe the multiple dimensions of pain: intensity, character, affective, and cognitive components. *The Brief Pain Inventory* can be used to assess additional domains including sleep, anxiety, and depression.

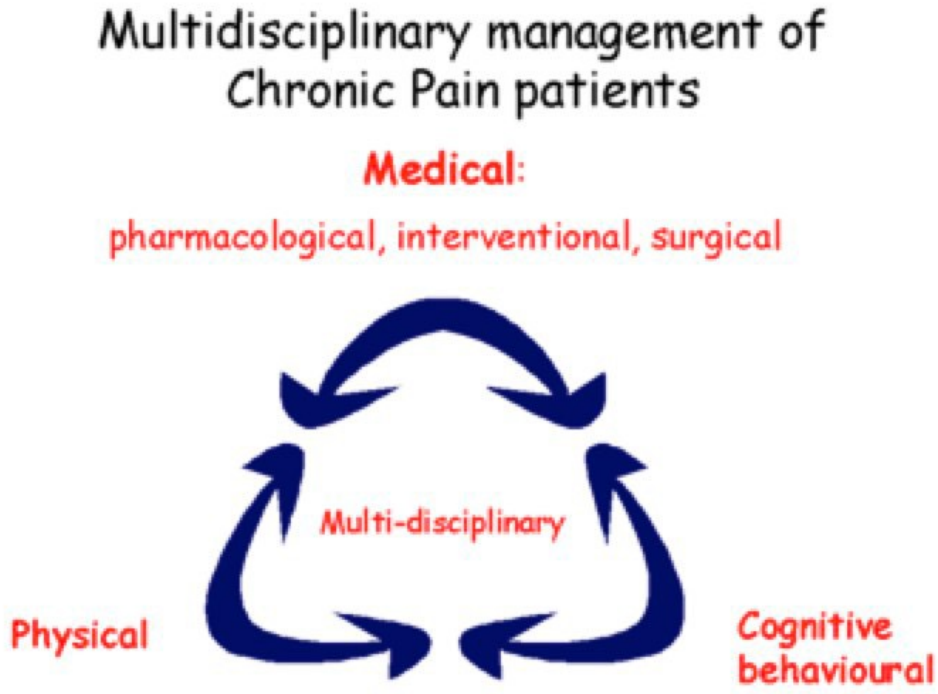
Physical examination of the patient includes assessment of gait, body posture, use of any appropriate walking aids, and display of any significant pain behaviors. A detailed pain-focused examination is carried out with the main emphasis on the neurological and musculoskeletal systems.

When relevant, appropriate investigations are reviewed and ordered. These may include various imaging modalities (plain x-rays, computerized tomography (CT), magnetic resonance imaging (MRI), or ultrasonography), nerve conduction studies/electromyography (EMG), or blood tests (eg. vitamin B_{12}, thyroid, renal function).

TABLE 1- EXAMPLES OF VARIOUS THERAPIES FOR CHRONIC PAIN MANAGEMENT.

	Medical Therapy		Physical	Psychological
Pharmacological	Interventional	Surgical		
Opioids Anticonvulsants Antidepressant Topical agents Membrane stabilizing agent	Epidural steroid injection Peripheral nerve/ joint injections Spinal cord stimulation	Rotator cuff repair Knee replacement surgery Spine surgery	Physiotherapy TENS Heat/cold therapy Massage therapy Strength exercise Acupuncture	Cognitive behavioural therapy (CBT) Mindfulness Meditation Hypnosis

FIGURE 3 - MULTIDISCIPLINARY APPROACH TO CHRONIC PAIN MANAGEMENT.



Management Strategies

In formulating a management plan, the biopsychosocial model should be utilized to help manage the various elements of a complex pain syndrome (Table 1 and Figure 3). When appropriate, patients should be encouraged to optimize their functional capacity with the use of physiotherapy, strength training, stretching, massage therapy, and weight loss. Activities such as aquafit and Tai Chi have proven to be beneficial for patients suffering from chronic pain. Psychological therapies can be beneficial to many patients, and when available should be offered. These options may include cognitive behavioral therapy, mindfulness, and psychiatric or addiction counseling.

When initiating pharmacotherapy, patients should be counseled about the various classes of medications, including the benefits, risks, and possible adverse effects of each type of medication. If opioid therapy is to be considered, it is critical to assess for addiction risk and to have an "opioid contract" completed with the patient to address boundaries relating to prescribing. Patient factors such as age, co-morbidities, and a history of substance use disorder must be addressed.

Guidelines for managing chronic non-cancer pain are available to help advise practice (see reference list). Typically, initiation of pharmacotherapy would involve the use of non-opioid analgesics. If required, progression to opioid therapy may be an option. At each follow-up visit, it is important to inquire about:

- Analgesia: efficacy of pain relief with any changes that were made since the last visit
- Activities: any improvement in functional status
- Adverse effects
- Ambiguous: assess compliance and any aberrant behaviors that would suggest misuse
- Affect: inquiry about mood disorders such as depression or anxiety

When choosing a medication, one should begin with a low dose to minimize side effects and increase

slowly, if needed, to attain maximal benefit. First line therapy may include non-opioid analgesics as such acetaminophen and non-steroid anti-inflammatories. When first-line therapy is inadequate, additional non-opioid analgesics may be appropriate. Depending on the type of pain (eg. neuropathic or somatic), options would include the use of antidepressants, anti-convulsants, or weak opioids. Antidepressant options to consider include tricyclic antidepressants (eg. nortriptyline) and selective norepinephrine and serotonin reuptake inhibitors (eg. duloxetine). Anticonvulsant therapy, with gabapentin or pregabalin, have a unique effect on voltage-gated calcium channels and may be a useful adjunct in patients suffering from neuropathic pain, such as sciatica. A weak opioid, such as tramadol, not only binds to the μ opioid receptor but also inhibits the reuptake of serotonin and norepinephrine, and may be an option.

The opioid family acts on the μ opioid receptor to provide analgesia. Examples of medications would include morphine, hydromorphone, and oxycodone. These medications can be administered as short-acting agents or in a long-acting formulation. Opioid use for moderate to severe pain should be approached cautiously. Adverse effects related to chronic opioid use can be significant. Common side effects would include constipation, nausea, and respiratory depression. Other potential inadvertent effects would include cognitive impairment, urinary retention, sleep-disordered breathing, and hypothalamic-pituitary-adrenal dysregulation. Physical dependence, as well as the increasingly common risk of fatal overdose, has been a growing concern over recent years, and updated prescribing guidelines are being developed to help guide a safer prescribing practice. For many of these reasons, high-dose opioid administration should be reserved for cancer-related pain.

Interventional management options for chronic pain can provide an additional tool for optimizing patient outcomes. Depending on the pain syndrome, options could include epidural steroid injections (caudal, interlaminar, or transforaminal approach), medial branch blocks for facet joint-mediated pain, radiofrequency neurolysis, peripheral nerve blocks, joint injections, and neuromodulation (spinal cord stimulation), among others. The goal of interventional therapy is to improve pain and function. These procedures are performed under fluoroscopic- or ultrasound-guidance to guide needle placement, improve accuracy, and minimize risk. Medications that can be injected include local anesthetics, corticosteroids, and neurolytic agents, such as alcohol or phenol, when appropriate (cancer-related pain).

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Chapter 9

POST-OPERATIVE MANAGEMENT

Sections:

1. **Post- Anesthetic Complications**

Section 9.1

Post -Anesthetic Complications

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Introduction

Anesthetic complications are an inevitable part of anesthetic practice. They can occur despite good knowledge and management, and may not always imply negligence. However, most occur due to human errors, often in association with poor monitoring, equipment malfunction, and organizational failure. Studies in the early 1990s[1,2] on postoperative anesthetic complications showed that 20- 25% of patients in the post- anesthesia care unit suffered from adverse events related to anesthesia. Recent studies3 also showed similar results even though there have been major advances in monitoring, drugs, and patient management. The most common postoperative anesthetic complications are shown in Tables 1 and 2.

TABLE 1 - COMMON POSTOPERATIVE ANESTHETIC COMPLICATIONS.

Respiratory System
- Aspiration of gastric content
- Hypoxemia, hypercapnia, hypocapnia
- Airway Obstruction
- Laryngospasm

Cardiovascular System
- Arrhythmias
- Myocardial ischemia
- Hypotension, hypertension

CNS and MSK
- Residual motor weakness
- Confusion
- Agitation and delirium
- Coma
- Convulsions
- Hypothermia/hyperthermia
- Adverse drug effects
- Complications related to regional anesthesia

TABLE 2 - MINOR POST-ANESTHETIC COMPLICATIONS.

- Sore throat (30%-70%) following general anesthesia
- Hoarse voice
- Laryngeal granuloma
- Headache (60%)
- Anxiety
- Dental damage
- Corneal Abrasion
- Backache
- Myalgia (greater risk after succinylcholine)
- Shivering
- Drowsiness and disorientation
- Anorexia
- Thrombophlebitis/bruises

Respiratory System

Nearly two thirds of major anesthesia-related PACU incidents are related to the respiratory system.[5] These events are mainly due to aspiration, upper airway obstruction, hypoxemia, and hypoventilation.

Aspiration of Gastric Contents and Management

Postoperatively, nausea vomiting in the setting of unreliable airway reflexes may make patients more susceptible to the risk of aspiration. Severe cough and bronchospasm are usually the first indicators of aspiration. When large quantities of gastric contents are aspirated, respiratory obstruction, hypoxemia, and atelectasis occurs. Subsequently the patient can develop a chemical pneumonitis.

In a patient who is vomiting, immediate head down position and tilting to one side helps keep the laryngeal inlet at a higher level than the pharynx and prevent the entry of gastric content into the trachea. If aspiration is suspected,[6] the following treatments should be considered, endotracheal intubation and suctioning of the trachea, delivery of supplemental oxygen, and bronchodilators. There is no indication for prophylactic antibiotics[7,16].

Airway Obstruction

This is a common and dangerous post-anesthetic complication. Airway obstruction causes inadequate ventilation, which leads to hypoxemia and hypercapnia. The most common cause of postoperative airway obstruction is pharyngeal obstruction. Reduced muscle tone from the residual effect of muscle relaxants or inadequate recovery from anesthetic agents causes upper airway obstruction. The triple maneuver of head tilt, jaw elevation, and anterior displacement of the mandible is an easy method of relieving most upper airway obstructions. If the obstruction is not immediately reversible, a nasal or oral airway can be inserted. Other causes of upper airway obstruction include soft tissue trauma and edema, neck hematoma, pooled secretions, laryngospasm, and laryngeal nerve injury (following surgery on the neck).

Hypoxemia

Hypoxemia is reduced oxygen content in the arterial blood (defined as $SaO_2 < 90\%$, $PaO_2 < 60$ mmHg or a fall > 5% in SaO_2). Hypoxemia produces cyanosis, tachycardia, and arrhythmias. In spontaneously breathing patients, tachypnea may occur. When persistent or severe, hypoxemia causes bradycardia, hypotension, and cardiac arrest. Causes of hypoxemia are shown in Table 3. Management of hypoxemia is directed at identifying and correcting the underlying cause.

TABLE 3 - CAUSES OF HYPOXEMIA

Hypoxic inspired gas mixture • Equipment failure - empty oxygen cylinder Hypoventilation • In patients who need ventilatory support in the postoperative period, ventilatory failure, low tidal volume, tracheal tube obstruction, circuit leaks • Respiratory depression or airway obstruction Ventilation perfusion mismatch • Inadequate ventilation – airway obstruction, pulmonary edema • Inadequate perfusion – low cardiac output, pulmonary embolus[6] Others • Methemoglobinemia[7] • Malignant hyperthermia

Hypoventilation

Hypoventilation is defined as reduced alveolar ventilation resulting in an increase in arterial carbon dioxide tension ($PaCO_2$). During the postoperative period, hypoventilation occurs because of poor respiratory drive, reduced respiratory muscle function, or as a direct result of acute or chronic lung disease. Central respiratory depression is seen with all anesthetic agents. The site of incision may also affect the ability of the patient to take a large breath as measured by vital capacity. Patients undergoing upper abdominal surgery have the greatest reduction in vital capacity, as much as a 60% reduction on the day of surgery. Obesity, gastric dilation, tight dressings, and body casts also inhibit respiratory muscle function and can predispose to CO_2 retention. Failure of reversal by neuromuscular blocking drugs may result in inadequate respiratory muscle function postoperatively. Such failure can be due to inadequate excretion of the drug, as in renal failure, or the presence of other drugs that potentiate neuromuscular blockade, such as gentamicin, neomycin, clindamycin, or furosemide.

Measurement of $PaCO_2$ is the best method of detecting hypoventilation in the postoperative period. Vital capacity should be at least 10 mL/kg body weight and inspiratory force should be numerically greater than -20 cm H_2O before patients are fit for extubation. If these minimum values cannot be maintained, the patient should receive controlled mechanical ventilation until awake enough to generate adequate respiratory muscle function.

Cardiovascular System

Cardiovascular events form the second major group of postoperative complications. They can be hypotension, hypertension, arrhythmias, and myocardial ischemia. Surgical and patient factors contribute more to cardiovascular complications than anesthesia- related events.

Hypotension

Hypotension in the postoperative period can result from

A. Reduced cardiac output.

1. Hypovolemia due to hemorrhage or fluid loss

2. Decreased venous return due to obstruction by pulmonary emboli, venacaval or aortic obstruction, pericardial effusion, or tamponade

3. Reduced myocardial pumping action due to arrhythmias, myocardial infarction, ischemia or acidosis

B. Peripheral vasodilation, due to residual anesthetic agents in the absence of surgical stimulation, septicemia, allergic reactions to drugs, and re-warming of the patient[9].

Early identification and treatment is vital, as hypotension can lead to decreased organ perfusion and ischemic damage. A 12-lead ECG, arterial blood gas, or chest radiography may be indicated. The usual first step in the treatment of hypotension is administration of fluids, as hypovolemia is the commonest culprit. An inotropic agent such as dopamine may be necessary to increase cardiac output further and to raise the arterial blood pressure.

Hypertension

Hypertension is a common event in the postoperative period. Hypertension may be due to several factors such as pain, hypercapnia, hypoxemia, excessive intravascular fluid volume,10 sympathomimetic drugs, malignant hyperthermia, and tumors like pheochromocytoma. More than 50%11 of patients have pre-existing hypertension and most may have missed their morning medications before surgery. Hypertension increases the myocardial work and predisposes patients to ischemia[12] and infarction. Treatment of acute hypertension involves identifying and treating the cause. If hypertension persists, antihypertensive medications need to be administered.

Sodium nitroprusside is a rapid-acting agent and very effective. Alternatives to nitroprusside are trimethaphan, hydralazine, and beta-blocking drugs such as metoprolol, labetalol, and esmolol.

Arrhythmias

The common postoperative dysrhythmias are sinus tachycardia, sinus bradycardia, supraventricular tachyarrhythmias, ventricular premature beats, and ventricular tachycardia.

Dysrhythmias are usually short-term events in the post-anesthetic period and disappear when the precipitating event is treated. Sinus bradycardia is benign unless it causes hypotension. Tachycardia in patients with risk of cardiovascular events, or when predisposing to myocardial ischemia, should be treated with beta-blockers.

Musculoskeletal and Central Nervous System

Motor Weakness

Persisting motor weakness is often a result of incomplete reversal of muscle relaxation. Certain factors like electrolyte imbalance, calcium channel blockers, hypothermia and certain antibiotics may delay recovery from the effects of muscle relaxants.

Clinically, the patient may be somnolent with shallow breathing or may be agitated with uncoordinated movements. Residual paralysis compromises cough, airway patency, ability to overcome airway resistance, and airway protection. Reduced ventilation leads to carbon dioxide retention, hypercarbic encephalopathy, and respiratory failure.

Delayed Recovery

There is no general consensus as to when a patient is recovered from anesthesia, but in general more than 90% of patients regain consciousness within 15 minutes of discontinuing anesthetic agents. Unconsciousness persisting greater than this period is called delayed recovery.[13] Causes of prolonged recovery from anesthesia are given in Table 4 and management of prolonged recovery is shown in Figure 1.

TABLE 4 - CAUSES OF DELAYED RECOVERY.

Drugs

1. R[redacted]iazepine volatiles, or [redacted]g drugs
2. E[redacted]l dose(s)

Patient Factors

1. Very young and very old
2. Obesity
3. Poor physical status

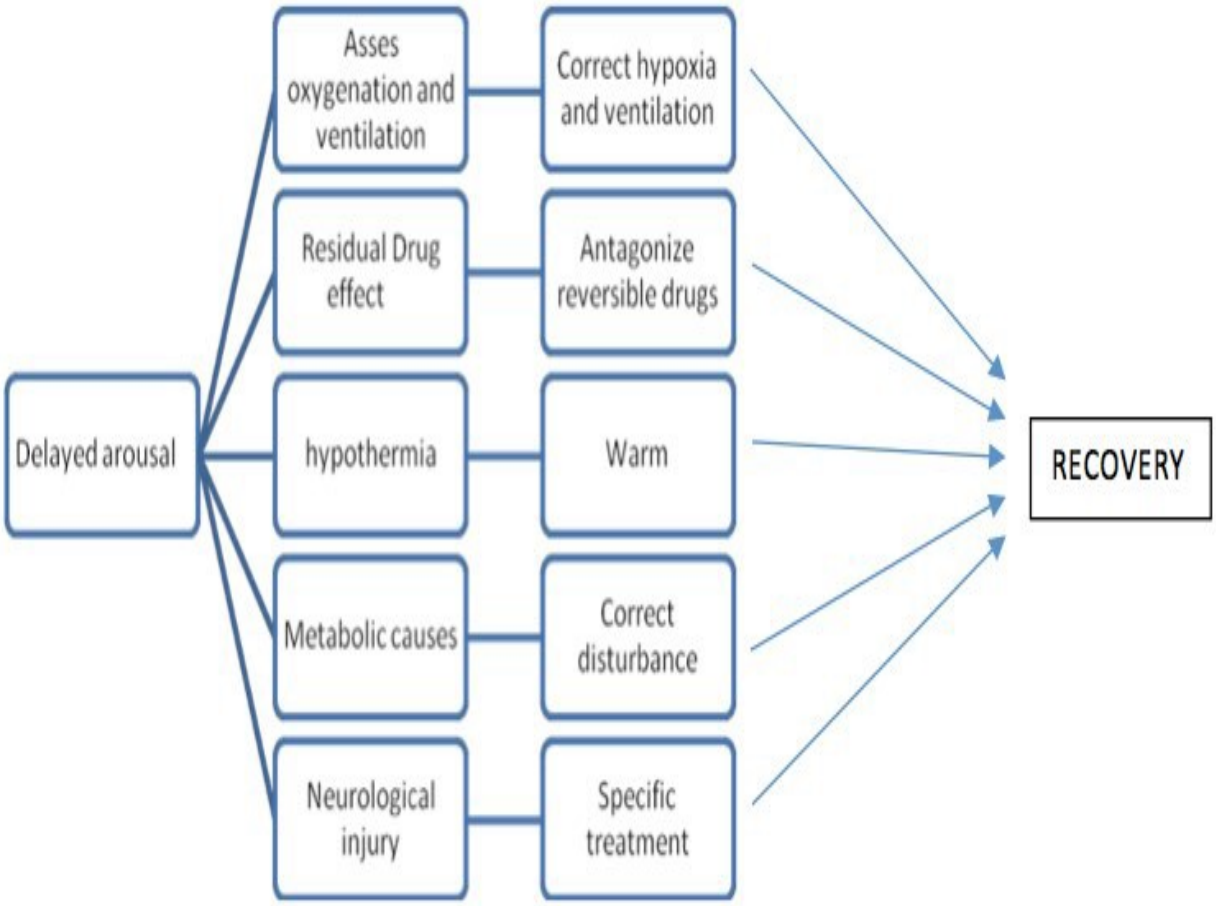
Metabolic

1. Hypoxia and h[redacted]
2. Hypoglycemi[redacted]
3. Electrolyte im[redacted]

Neurological

1. Intracranial hemorrhage
2. Cerebral ischemia
3. Subclinical seizures or post-ictal
4. Cerebral vascular accident

FIGURE 1 - MANAGEMENT OF DELAYED RECOVERY.



Postoperative Delirium

Postoperative delirium is a transient mental dysfunction that can result in increased morbidity, delayed functional recovery, and prolonged hospital stay. This is commonly seen in the elderly.[13] The reported incidence varies widely between 1% to 60%.

The implications of postoperative delirium include

1. Delayed functional recovery
2. Increased length of hospital stay
3. Higher postoperative complication rates
4. First sign of catastrophic event, e.g. MI, sepsis

Prevention

1. Identifying and addressing underlying medical problems
2. Avoiding precipitant medications
3. Optimizing fluid status
4. Aggressive treatment of pain
5. Ensuring tranquil postoperative care setting

Pharmacological treatment is with physostigmine, haloperidol, and benzodiazepines.

Postoperative Nausea and Vomiting (PONV)

Nausea and vomiting[3] are the most common post-anesthetic complications. The reported incidence is variable, from 10-80 %, due to the presence of a large number of risk factors[1] in a varying patient population. The major risk factors are shown in Table 5. The risk of PONV can be reduced by adequate prophylaxis in patients who have risk factors.

Implications of PONV

Aside from unpleasantness for the patient and staff, PONV poses medical risks. Increased intra-abdominal pressure and forceful vomiting jeopardize abdominal suture lines or can disrupt hemostasis at the surgical site of neurosurgical, head and neck, thoracic and intraabdominal surgeries. The elevated central venous pressure increases morbidity after ocular, tympanic, or intracranial procedures. PONV also increases the risk of aspirating gastric contents, especially if airway reflexes are impaired. Movement during PONV worsens postoperative pain and accentuates autonomic responses. Finally, PONV can delay discharge or necessitate the admission of ambulatory patients.

Management of PONV

Although routine anti-emetic prophylaxis is clearly unjustified, patients at high risk for postoperative emesis should receive special considerations. Identification of at-risk patients (Table 5) is the keystone in management. The consensus guidelines[4] published in 2003 recommended double or triple anti-emetic combinations for patients that are moderate or high-risk. Measures like the use of regional anesthesia, propofol, intra-operative supplemental oxygen, adequate hydration, avoidance of nitrous oxide and volatile agents, minimizing perioperative opioids, and minimizing use of neostigmine can significantly reduce the baseline risk. Dexamethasone, 5-HT3 antagonists, droperidol and dimenhydrinate are used in the treatment of PONV.

TABLE 5 - RISK FACTORS FOR POSTOPERATIVE NAUSEA AND VOMITING[13]

Patient-specific factors 1. Female sex 2. Nonsmoking status 3. History of PONV or motion sickness Anesthetic risk factors 1. Use of volatile anesthetics within 0 to 2 h 2. Nitrous oxide 3. Use of intraoperative and postoperative opioids Surgical risk factors 1. Duration of surgery (each 30 min. increase in duration increases PONV risk by 60%, so that a baseline risk of 10% is increased by 16% after 30 min) 2. Type of surgery (laparoscopy, ear-nose-throat, neurosurgery, breast, strabismus, laparotomy, plastic surgery)

Hypothermia and Shivering

The intraoperative loss of heat manifests as shivering in the postoperative period. Studies have identified a host of different precipitating factors including male sex, duration of anesthetic, spontaneous breathing techniques, the use of volatile agents, and anticholinergic pre-medications.[14]

Postoperative Pain

Postoperative pain is one of the greatest fears for patients, and one of the most important considerations for anesthesiologists. Acute postoperative pain is due to tissue injury, nociceptor sensitization, and activation of central pathways. Postoperative pain depends on the site and type of surgery, age, gender, bodyweight, and psychological makeup of the patient. Effects of postoperative pain are many. Uncontrolled postoperative pain produces neuroendocrine responses, leading to sodium and water retention, hyperglycemia, increased free fatty acids, ketone bodies, and lactate. It also produces hypercoagulability. The increased sympathetic response increases myocardial oxygen demand. Respiratory functioning is also affected, especially in upper abdominal surgeries. Chronic effects of postoperative pain include the development of chronic pain and delayed rehabilitation.

Opioids, NSAIDS, local anesthetics, and non-pharmacologic methods such as cryotherapy, TENS (Trans Cutaneous Electrical Nerve Stimulation), acupuncture, and psychotherapy are used in the management of postoperative pain.

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Text Books for Additional Reading

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Chapter 10

QUALITY IMPROVEMENT

Sections:

Section 10.1

Quality Improvement

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Are Quality Improvement and Quality Assurance the Same Thing?

Quality Improvement (QI) offers a formal approach to the analysis of performance and subsequent systematic efforts to improve and optimize said performance. QI is process directed and prospective, whereas Quality Assurance (QA) is often retrospective and incident-directed. One easy distinction between QA and QI is to remember that QA often answers the question 'did we do a good job?' whereas QI addresses the question, 'how can we do better?' QI involves both prospective and retrospective reviews. It is aimed at improvement -- measuring where we are, and figuring out ways to make things better. It specifically attempts to avoid attributing blame, and to create systems to prevent errors from happening. QI activities can be most helpful in improving how our systems and processes work. Trying to find where the weaknesses in a system are, and designing better ways to do things is a challenge but also an opportunity to "think outside the box' and embrace innovation. In industry, quality efforts typically focus on targets such as product failures or work-related injuries and, in its administration, we can see how factors like increasing efficiency or reducing redundancies and duplication of work would be of great interest.

Exercise: Take a moment to consider the following statements and ask yourself whether each statement was written with a focus on QA or QI:

1. 'A patient has a bad outcome after elective surgery due to surgical site infection. Was the surgeon at fault for potentially unsterile technique or was the anesthesiologist at fault for not administering perioperative antibiotics at the correct time?'

2. 'In our hospital, prescribing errors with CPOE (What does CPOE mean?) are most common in the months of July and January. We recommend residents need to be more careful when they first begin prescribing medications in our hospital.'

Answer:

- The first statement seeks to identify a singular source of error (if indeed any error even took place) and limits itself to identification and allocation of fault without any further aspiration toward improving future outcomes. As such, this statement is more in keeping with a historic M&M-type approach and has no real basis in either QA or QI

- The second statement leans more toward QA than QI in that it has identified a trend of error and risk within local care. It has successfully identified an opportunity to improve the quality of healthcare delivered but does not offer any suggestions, resources or process that could reasonably be expected to affect the outcome next time this issue is reviewed. As a further exercise, can you rewrite the second statement to shift its focus from one of QA to that of QI?

Why Does Quality Even Matter?

The *Excellent Care for All Act (ECFAA)*, which came into law in June of 2010, puts Ontario patients first by strengthening the health care sector's organizational focus and accountability to deliver high quality patient care. ECFAA is based on strategic directions that exemplify good governance and high quality patient care. It helps define quality for the health care sector, reinforces shared responsibility for quality

of care, builds and supports boards' capability to oversee the delivery of high quality of care, and ensures health care organizations make information on their commitment to quality publicly available [2].

Requirements for Health Care Providers

The legislation sets out a number of requirements for health care providers (currently only applicable to hospitals in Ontario within the meaning of the Public Hospitals Act). The legislation requires that hospitals :

- Establish quality committees that report on quality-related issues
- Put annual quality improvement plans in place and make these available to the public
- Link executive compensation to the achievement of targets set out in the quality improvement plan
- Put patient / care-provider satisfaction surveys in place
- Conduct staff surveys
- Develop a declaration of values following public consultation, if such a document is not currently in place
- Establish patient relations processes to address and improve the patient experience.

Where Does QI Begin?

If we wanted to get a sense of the quality of healthcare delivery, how might we go about it? We could ask providers if they are following the latest guidelines for a specific disease. We could also ask providers to keep track of errors or "near misses" that result from deviations from said guidelines. However, these methods are fraught with problems of validity and reliability. Self-reporting of errors is shown to be low and, particularly if there is a potential punitive response, reporting is infrequent and inaccurate; this leaves us with a deficit in how we can accurately assess quality. The key to measuring quality in healthcare is to identify areas of importance to all stakeholders, to identify appropriate 'items of measure' that reflect the contribution of process, systems, personnel and resources to the overall outcome, to measure, reliably and objectively, the process outcome in such a way that opportunities for improvement become evident, and, to report process measures in a fashion that is transparent and easily understood by all stakeholders. When this process is conducted in a reliable, fair manner the results are most often greeted as an opportunity to improve patient outcomes and the real work of QI can begin.

Following are some examples of QI processes but with reasons why they may not be the ideal measurement of QI:

- Asthma staging: This may be helpful but is more a measure of disease severity than disease control.
- Hemoglobin A1C: gives you an assessment of diabetic control but does it tell you whether patient is supplied with all information necessary for better lifestyle and disease control? Does it even accurately reflect patient compliance with dietary restriction, regular glucose check and appropriate insulin dosing?

Each of these measures is valid for a specific purpose, however, understanding that value and its limitations determine if it is the correct measure to use for what we really want to evaluate. These challenges are at the heart of healthcare QI. A useful way to begin to consider and practice QI is to set a Key Performance Indicator (KPI). Many Hospitals now have public statements committing to QI and improved patient outcomes. Recent examples in Toronto are at sites such as The Hospital for Sick Children and Sunnybrook Health Sciences Centre who have made commitments to reducing preventable harm below certain target levels in the next two fiscal years 3. Within this framework, KPIs such as the incidence of patient harm from adverse drug events, the incidence of harm from patient falls, surgical site infection rates, etc. all contribute to overall hospital performance. KPIs can

also be set by clinical units such as Out-patient and ambulatory units where measures such as 'wait-time from referral to first assessment' are often used as measurable, reportable key performance indicators. As we can imagine, KPIs can be influenced by any number of factors, therefore a KPI can be seen as an appropriate way to measure and report the overall functioning of a unit, department or hospital by choosing an outcome that is influenced by its personnel, resources, processes, volume of work, and, unforeseen factors. To positively influence and improve the performance of KPIs, Quality Indicators (QIs) are carefully chosen. For example, most intensive care units (ICU) publicly report central-line infection rates, ventilator-associated pneumonia rates, urinary catheter infection rates. These are all Quality Indicators and their performance all contribute to the ongoing KPI of 'Reducing Preventable Harm within ICU'. Another approach is to measure a number of QIs, and group the reporting of these measures together into a regular report that measures performance of both QIs and KPIs. Such reports can be in the format of Quality Scorecards, which typically report current performance relative to recent performance and goals that have been set for said indicators and overall performance. More dynamic versions of these scorecards that are updated on a case by case or daily basis are dashboard indicators where one can assess the effects of a single day or patient experience on overall performance.

How Do We Measure Quality?

I have mentioned the phrase 'measure of Quality' many times so far and there are three types of measures used in quality work:

1. **Structure:** Physical equipment and facilities
2. **Process:** How the system works
3. **Outcome:** The final product or results

Structure and process are easier to measure but outcome is often most important. Structure is a relatively easy concept to define as it is typically physical in character and therefore lends itself to simple measurement (e.g., buildings, raw material, parts, or in our experiences for example, medical equipment). Defining process and outcome therefore becomes key in understanding a QI project. Process is the systematic provision of Healthcare and how that system works whereas Outcome refers to the overall Health status and whether Process has conferred demonstrable advantages or gains. These distinctions are more complex than at first appreciated.

Consider, as an example, the prevention of heart disease. The overall goal is to reduce morbidity and mortality (i.e. promote longevity). The disease process itself is very slow, in other words it takes decades for our 'measurement' (i.e. death) to show up. So what can we measure instead in a timely fashion? This leads us to the concept of proxy measures; using a proxy measure means when we can't measure exactly what we need, we measure what we can. In this regard, sometimes we have to use a process measure instead of an outcome, or we use a measurable process in place of one that is tougher to get at.

Example: We may be interested in how effective the members of our practice are in counseling for smoking cessation. Since details of that are embedded in free text in medical records, to enable us to make use of computer records we may choose instead to look at:

- How many patients had "tobacco abuse" coded as a diagnosis
- How many received prescriptions for Zyban or nicotine replacement

While these clearly do not represent exactly what we want to look at, the presence of either does suggest that smoking cessation counseling occurred.

Example of Proxy measures: These are used to measure something that is close enough to reflect similarly on what we really need to examine. To assess care for the prevention of coronary artery disease we could measure the percentage of patients over 35 with cholesterol screening performed, and, the percentage of 'positive results' subsequently counseled on healthy diet, exercise and pharmacologic methods of cholesterol management. Since it is impossible to measure outcomes that don't occur, we use measures of care that have been shown in other research to be effective in

achieving our goal e.g. the percentage of hypertensive patients with blood pressure at or below goal, or the percentage of diabetic patients with LDL less than or equal to 100.

It is also useful to 'link measures' wherever possible in order to give a more complete overview of how a healthcare system or process is working. An example of this would be linking smoking counseling, blood pressure control and HBA1C levels for a group practice to ED visits for that practice's patients per year. Patients may visit ER departments for a variety of reasons but patients who belong to a practice that sets out to deliver care as set out by the dimensions of quality are likely in better health and this would hopefully lead to less impact on acute care of patients visiting the ED setting for issues that could have been better managed earlier by an efficient high-quality practice.

Conclusion

There is a great deal more that could be included within an introductory chapter to QI: how to carry out a QI project, the use of run charts and statistical process control charts to analyze data, SQUIRE guidelines for writing QI papers, using multiple QI indicators and KPIs to create a quality program. As it is impossible to cover all aspects of QI in this brief report, for extra reading on those topics I would highly recommend reading the following manuscripts from Cincinnati Children's Hospital[4] and The Hospital for Sick Children [5], and browsing the American Society for Quality website [6].

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