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7. ANAESTHESIA

7.1 Chloroform

Chemical Name: $CHCl_3$

Appearance: Colourless liquid melting point 61ºC

Availability: Medical labs, Industry (Pure and commercial form both)

7.1.1 Properties:

1. Evaporates very quickly.

2. Dangerous because there is a very small difference between the lethal and the sleeping

dose.

3. Chloroform reacts with oxygen to form fusogen which is a poisonous gas.

7.1.2 Preparation

Methane Chlorine

Ratio 1: 3

7.1.3 Test Results

1. 2ml given orally to a rabbit. Died in 1/2 minute. Note: $CHCl_3$ used was pure.

2. 1ml given orally to a rabbit. It slept for 1 1/2 hours after which he was OK.

7.1.4 Notes:

1. Chloroform causes general loss of strength and low body temperature.

2. There is a hypothesis that if poison is used on a person after chloroform, more poison

than usual will have to be used.

7.2 Di-phenyl ether

(Maybe ' diethyl ether' is the name ?)

Chemical name: $CH_2=CH-O-CH=CH_2$

Appearance:

Effect: One sniff causes instant sleep.

Availability: Medical Laboratory.

7.3 Halothane

Effect: A very small quantity is stronger than cholorform and is not poisonous.

Halothane, *liquid anesthetic agent. Halothane's chemical formula is $CF_3CHBrCl$. It produces a deep level of unconsciousness when inhaled.(Encarta)*

7.4 Methoxyflurane Penthrane

Chemical Formula:

H F H

top

| | |

H-C-O-C-C-Cl

| | |

H F Cl

Appearance:

Notes: Very modern anaesthesia. Non-toxic.

Sedative

Sedative, any of the drugs used to reduce nervous tension or induce sleep. Often referred to as sedative-hypnotic drugs, these substances generally have a calming and relaxing effect on the central nervous system and muscles when taken in small doses, and a hypnotic, or sleep-producing, effect when taken in larger doses. For centuries alcohol and opium were the only substances known to produce these effects, but in recent decades over 50 other substances have been discovered, each differing slightly in its effect on the user. Among the sedatives prescribed for calming patients are the tranquilizers Librium (chlordiazepoxide hydrochloride) and Valium (diazepam), which are commonly used to relieve emotional stress (*see* Anxiety; Tranquilizer).

Drugs administered to produce sleep include **barbiturates** such as **secobarbital, pentobarbital, and Phenobarbital (long)**, which produce short, medium, and **prolonged durations of sleep**, respectively (*see* Barbiturate). *Chloral hydrate, paraldehyde, antihistamine, and Quaalude (methaqualone) are other sedative-hypnotic drugs.*

Sedatives are habit-forming and can cause severe addiction problems. Easily obtainable from physicians, they have become, since the 1960s, among the most abused drugs. *See* Drug Dependence.

Amobarbital-Secobarbital Oral Uses

This medication is used for seizure disorders. It is also used as a short-term sleep aid (for insomnia), and for tension relief (e.g., before a medical procedure).

Barbiturate

Barbiturate, any of an important group of drugs that depress brain function; they are derived from barbituric acid ($C_4H_4N_2O_3$), a combination of urea and malonic acid. Depending on the dosage or formulation, barbiturates have a sedative (tranquilizing), hypnotic (sleep-inducing), anticonvulsant, or anesthetic effect. Very short-acting barbiturates such as thiopental are injected intravenously to induce rapid anesthesia before surgery. Phenobarbital, *a long-acting barbiturate*, is prescribed with other medications to prevent . Other barbituric-acid derivatives, such as secobarbital, were used as antianxiety medications until the development of the tranquilizer; they are still in use for the short-term treatment of insomnia, although tranquilizers are more suitable sleep inducers. Barbiturates are common drugs of abuse. Taken orally or intravenously, they produce symptoms similar to drunkenness: loss of inhibition, boisterous or violent behavior, muscle incoordination, depression, and sedation. They are physically addicting and produce severe withdrawal symptoms; overdoses can cause profound shock, coma, or death. *See* Drug Dependence.

Tranquilizer

Tranquilizer, common name applied to a class of drugs used to treat anxiety and insomnia (sleep disorder). Originally the term comprised two groups: the major tranquilizers—(1)the phenothiazines, such as chlorpromazine (Thorazine)—useful in the treatment of acutely ill mental patients (*see* Mental Illness); and the minor tranquilizers—the (2) benzodiazepines, such as diazepam (Valium). By popular usage, the term now refers only to the latter group. In the early 1980s, these

minor tranquilizers were the most frequently prescribed drugs in the world. Despite a 30% decline in the number of prescriptions written in the U.S. for benzodiazepines between 1975 and 1980, more than 5 million people were taking some form of them each year. Although they are useful for relief of temporary anxiety and insomnia, a National Academy of Sciences report warned in 1979 that they are not effective for periods longer than two weeks.

The minor tranquilizers are safe when taken alone, but taking substantial amounts of these substances at the same time as alcohol can lead to coma or even death. Long-term administration of larger than usual doses of the benzodiazepines can cause physical dependence, with typical withdrawal symptoms ranging from nightmares to convulsions when the drug intake is stopped.

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History

Despite the synthesis of ether in 1540 by the German scientist Valerius Cordus, the use of anesthetic agents in a medical setting represents a totally American contribution to medicine. Dr. Crawford W. Long, a rural doctor in Georgia, first used inhaled ether to anesthetize a patient for neck surgery in 1842. Unfortunately, his work was not publicized. Dr. Horace Wells attempted to demonstrate the surgical use of nitrous oxide in 1845, but was unsuccessful. In 1846, a Boston dentist named William Morton demonstrated the anesthetic effects of ether in front of a live audience at Massachusetts General Hospital. He anesthetized a patient undergoing resection of a submandibular mass by a prominent surgeon of the time, Dr. John C. Warren. With its publication in the Boston Daily Journal the next day, the medical world came to know of the discovery of surgical anesthesia. Within six months the use of ether during surgery was widespread. The next year, Dr. James Simpson used chloroform to relieve the pain of labor. Nitrous oxide was used frequently as a form of social recreation with occasional reports of surgical procedures (largely dental) performed under its influence. The use of chloroform gained public acceptance after Queen Victoria in 1853 was administered this drug by Dr. John Snow, the first physician to devote his life to anesthesia.

Numerous other developments paved the way for modern anesthesia to flourish. The endotracheal tube was discovered in 1878 which protected against the drug-induced

respiratory failure. Nerve block anesthesia with cocaine was popularized by Halsted in 1885 with epidural and spinal anesthesia emerging shortly thereafter. Intravenous agents became increasingly popularized after sodium thiopentone was first used in 1934. The current concept of “balanced anesthesia” was first introduced after curare was used in anesthetic practice in 1942. Over the next fifty years, many additional anesthetic agents have been developed and refined with anesthesia emerging as an important specialized field in medicine.

Basic Principles of General Anesthesia

Anesthesia is defined as the *absence or abolition of sensation*. This term should be differentiated from analgesia which is defined as the absence or abolition of pain. General anesthesia involves rendering a patient unconscious whereas local anesthesia (or more correctly, local analgesia) is aimed at blocking conduction of nerves to the operative site. In order to provide safe,as well as adequate general anesthesia, the anesthesiologist must combine the need for unconsciousness, the need for analgesia, and the need for muscle relaxation to provide the best operative conditions for the surgeon. This so-called ‘triad of anesthesia’ can be achieved with the use of only one drug, however side effects have limited the successful application of single line agents in modern anesthesia. Therefore, utilizing various drugs for their particular muscle relaxing, sleep producing, and analgesic properties, anesthesia can be safely and properly maintained.

Four main stages of general anesthesia are recognized regardless of the method in which the anesthesia is delivered. These stages are based upon the patient’s body movements, respiratory rhythm, oculomotor reflexes, and muscle tone. In general, a patient in stage one is conscious and rational, however the perception of pain is diminished. Stage one is commonly termed the analgesia stage. Stage two, the delirium stage, is marked by the patient becoming unconscious, however the body responds reflexively and irrationally to stimuli. Breath holding may be present and can result in hypoxia, however tone is maintained in pharyngeal muscles and a patient can maintain and protect their own airway. Pupils generally become dilated and gaze is discongugate. Stage three, the surgical anesthesia stage, is characterized by increasing degrees of muscular relaxation. Protective pharyngotracheal reflexes are absent and the patient is unable to protect the airway. Stage four is medullary depression. This stage is characterized by cardiovascular and respiratory collapse due to depression of the cardiovascular and respiratory centers in the brain stem.

Each anesthetic agent has a varying effect on the pattern of surgical anesthesia. For example, certain agents are highly analgesic (nitrous oxide) whereas others do not show stage I (thiopental). For a particular agent, the stage or depth of anesthesia must be judged with reference to the known sequence of signs for that agent. Various anesthetic agents are used to achieve the aforementioned stages for general anesthesia. These include inhalational agents, intravenous agents, analgesic agents, and muscle relaxants. Local anesthetics represent a category of anesthesia outside the realm of general anesthesia and will be discussed separately.

Inhalational Anesthetic Agents

Inhalational anesthesia refers to the delivery of gases or vapors into the body via the respiratory tract to produce anesthesia. Through uptake and distribution, some portion of the anesthetic agent is presented to the nervous system, resulting in the absence of sensation. Understanding the induction, maintenance, and recovery from an inhalational anesthetic requires applications of the pharmacokinetics of the particular drug. In general, the aim in giving an inhalational anesthetic is to readily achieve a partial pressure of that anesthetic in the brain sufficient to keep the patient asleep and maintain that partial pressure until the operation is complete. Certain factors such as(1) the solubility of the anesthetic agent,(2) cardiac output of the patient, and(3) alveolar ventilation of the patient will influence the ability of the anesthetic to achieve its result.

An important concept in comparing inhalational anesthetics is knowing their measure of potency called the minimum alveolar concentration (MAC). *It is defined as the concentration of a particular inhalational anesthetic at one atmosphere pressure in which 50 percent of patients do not move in response to a skin incision.* Minimum alveolar concentration is analogous to the ED50 value computed from a pharmacological dose-response curve. Therefore, the potencies (as well as side effects at similar potencies) of different inhalational agents can be compared; so can combinations of agents. In general, a half MAC of each of two inhalational anesthetics is equivalent to one MAC of either. This concept not only has clinical applications but also suggests that the fundamental mechanisms by which these inhalational agents induce anesthesia are similar. The use of MAC in comparing the potency of different anesthetic gases has been criticized because it measures only a single point, the abolition of muscular response to pain. The concept fails to recognize the importance of the slope of the response curve. Other comparisons have been advocated (e.g. MAC/AWAKE ratios) however the MAC is the most widely used.

All the inhalational agents impair respiratory and circulatory function as well as influencing every organ system in one way or another. Some of these actions do not accompany the anesthetic effect but are side effects that must be appreciated when these agents are utilized. The potency, systemic effects, and specific side effects of the most commonly used inhalational agents will be discussed.

Nitrous Oxide

Nitrous oxide (N_2O) was first prepared by Priestly in 1776 (prior to the isolation of oxygen) and its anesthetic properties described by Humphry Davy in 1799. Dr. Davy's thought was that this inorganic gas might "be used with advantage during surgical operations" went unheeded until the mid 1800's. Nitrous oxide is characterized by its inert nature--it undergoes only minimal metabolism. It is colorless, tasteless, and odorless. It does not burn but will support combustion, so it cannot be taken for granted in a high-risk environment (laser surgery). It is stored as a liquid at 50 atmospheres in a cylinder.

Potency

The major difference between nitrous oxide and the rest of the inhalational agents is its low potency. The MAC of this agent is 105%, unreachable at normal atmospheric pressure in oxygen concentrations compatible with survival. The value of this agent is its ability to produce different effects over a wide range of inspired concentrations. It is a weak anesthetic but powerful analgesic. Patients will have some degree of

analgesia at 50% nitrous oxide and may become amnestic at 66 2/3 %. Its drawback is the need for some additional agent to achieve full surgical anesthesia. It is poorly soluble in blood, and thus the onset and recovery times for nitrous anesthesia are brief (three to ten minutes).

S***ystemic Effects***

Despite its relatively low potency, nitrous oxide affects most of the major body systems. It does cause direct mild myocardial depression, and although its general effects on heart rate and blood pressure are innocuous, it can cause major cardiovascular depression in patients with underlying hemodynamic compromise (hypovolemia, myocardial dysfunction, or septic shock). Nitrous has little effect on respiration and does not affect the neuromuscular junction to alter the requirement for a nondepolarizing neuromuscular blocking agent.

Side Effects

There are a number of special concerns with nitrous oxide that are not present with the other agents. Nitric oxide and nitrogen dioxide are both highly toxic to the lung and fortunately have largely been eliminated as impurities from the manufacturing process. There is a very real danger of administering a hypoxic mixture of nitrous oxide-oxygen mixture to a patient. The large volume of gas administered poses another problem. Although nitrous oxide is the least soluble anesthetic agent, it is still much more soluble than nitrogen. This means that the two agents take time to equilibrate across the alveolo-capillary membrane. At the beginning of anesthesia, nitrous oxide leaves the alveoli faster than nitrogen enters the lung, thereby raising the concentrations of oxygen, carbon dioxide, and any other inhalational agent used. Increasing the concentration of other inhalational anesthetics can speed induction at the beginning of a case, a phenomenon known as the *second gas effect*. At the end of anesthesia, the opposite is true. The alveolus fills rapidly with nitrous oxide and the nitrogen in the alveolus is unable to equilibrate as rapidly with the blood. This dilutes the oxygen present within the alveolus potentially creating hypoxemia especially if low levels of supplemental oxygen are used and the patient has a depressed state of consciousness at the end of a case. This phenomenon is termed *diffusion hypoxia* and may be present for up to 30 minutes after administration of the gas. The same principle applies when some portion of the body has trapped air, such as in a pneumothorax, bowel obstruction, air embolism, or with middle ear surgery. The displacement of tympanic membrane grafts is well described with the use of nitrous oxide anesthesia. Nitrous oxide also interferes with cell division. High concentrations will stop white cell formation after 36 hours of administration. It may also inhibit methionine synthetase thereby resulting in a megaloblastic or aplastic anemia. Under a similar mechanism, it can also inhibit vitamin B-12 metabolism producing its associated neurologic deficits.

Halothane 1,2

Fluorinated anesthetic agents were discovered secondary to advances made by development of the atomic bomb. They represented a relatively safe and effective alternative to the flammable, often toxic agents used until that time. Halothane was the first of these gases and for many years has been the most commonly used supplement to nitrous oxide anesthesia. It was synthesized by Suckling in 1956 with the hopes of being an ideal anesthetic agent. It *exists as a volatile liquid with a*

distinctive aroma and is added to the gas mixture delivered to the patient by means of a vaporizer added to the anesthesia machine. It is a comparably stable compound, nonflammable, and easy to vaporize. (Must be kept in dark a tightly closed glass container). Anesthetic doses range from 5000 to 30,000 ppm (parts per million) [ACGIH 1991].

Potency

Halothane has a MAC of 0.75%, indicating that it is highly potent. It has poor direct analgesic properties which makes it a perfect complement to nitrous oxide. Halothane is very soluble in blood and fatty tissues and awaking from halothane anesthesia may be prolonged if attention is not given at the time of emergence.

Systemic Effects

Halothane has profound effects on various body systems. In addition to depressing consciousness, halothane reduces or eliminates the sympathetic response to painful stimuli. This depressant effect on the sympathetic nervous system also reduces the protective baroreflex response to conditions such as hypovolemia. Depression of the respiratory drive is also produced by halothane. Both the central response to carbon dioxide and the peripheral response to tissue hypoxia are depressed. The pattern of respiration produced by halothane is rapid, shallow, and monotonous with no sighs. Such a pattern predisposes to atelectasis. Halothane also depresses protective airway reflexes thereby placing the patient at higher risk of aspiration at induction. Halothane directly decreases myocardial contractility and heart rate and slows conduction through the AV and ventricular Purkinje system. Although some vasodilation occurs with halothane, the hypotension produced by this agent is primarily the result of myocardial depression and decreased cardiac output. Exogenous doses of catecholamines (e.g. during facial plastic surgery) may produce severe ventricular dysarrhythmias due to the myocardial sensitization. Halothane also results in muscle relaxation and can result in potentiation of paralytic agents.

Side Effects

One of the well-known complications of halothane is (1)“halothane hepatitis”. This syndrome appears following exposure to halothane and may produce fever, jaundice, and possibly massive hepatic necrosis and death. The mechanism is not clear but allergic reactions to halothane byproducts are implicated. It is an extremely rare occurrence but is seen in increased frequency in those patients who have suffered hepatic anoxia thereby increasing the concentrations of hepatotoxic metabolites. Halothane is also a well-known(2)trigger for malignant hyperthermia. This anesthetic reaction is usually detected in young fit individuals who have inherited a susceptibility to this problem. It is characterized by masseter spasm, sustained muscle rigidity, myoglobinuria, and a rapidly rising core body temperature. These symptoms and signs are manifestations of a hypermetabolic state initiated by an inhibition of calcium reuptake into the sarcoplasmic reticulum of skeletal muscle. It is universally fatal unless total body cooling, vigorous hydration, and administration of Dantrolene is delivered expeditiously.

A syndrome called "halothane hepatitis" occurs in 1 in 10,000 halothane-induced anesthesia patients; this syndrome involves fever, anorexia, nausea, and vomiting and may progress to hepatic failure and death [Hathaway et al. 1991]. This

syndrome usually occurs in patients who have been anesthetized with halothane more than once in a short period of time [ACGIH 1991

Enflurane

Because of the disadvantages of the available anesthetics at the time, enflurane was developed in 1963 by Terrell and released for use in 1972. It is a stable, nonflammable liquid that is somewhat less volatile than halothane. It has a distinctive pungent odor that creates an unpleasant induction in a non-premedicated patient.

Potency

Enflurane is slightly less potent than halothane with a MAC of 1.68%. Onset and elimination is similar to that of halothane.

Systemic Effects

The respiratory drive is depressed to a greater extent with enflurane than halothane, and the ventilatory response to hypoxemia is also decreased. Enflurane depresses cardiac contractility and heart rate more than halothane and produces a similar baroreflex response depression as halothane although sensitization to exogenous catecholamines is much less with enflurane than halothane. The metabolism of enflurane is one-tenth that of halothane thereby reducing its potential as a hepatotoxic agent. Its metabolism does release one fluoride ion which is potentially nephrotoxic but is rarely sufficient to produce clinical concern except in hyperthyroid patients and in patients taking rifampin. Fluoride toxicity presents as nephrogenic diabetes insipidus and, in extreme cases, high-output renal failure can occur.

Side Effects

There is one unusual side effect that is not seen with the other agents. At deep levels of anesthesia and with a lowered $PaCO_2$, some patients show an epileptiform pattern on EEG. Even though no post-anesthetic neurologic sequelae have been attributed to this pattern, this drug should be avoided in patients with seizure disorders.

Isoflurane

Isoflurane was synthesized in 1965 by Terrell but its development lagged behind that of its isomer enflurane because of difficulties in its synthesis, purification, and now refuted claims of carcinogenesis. It is nonflammable, and has properties similar to that of halothane and enflurane with a few striking exceptions.

Potency

Isoflurane is less soluble in blood than halothane or enflurane which affords a more rapid induction and recovery from anesthesia. Its disadvantage is its pungent odor which is difficult to administer to a conscious patient. *With a MAC of 1.3%,* isoflurane is less potent than halothane but more potent than enflurane in producing general anesthesia.

Systemic Effects

Isoflurane depresses the respiratory drive and the ventilatory response to hypoxemia in a similar degree to that of halothane, but much less than its isomer enflurane. Although isoflurane is a direct cardiac depressant, cardiac output

decreases less than with either halothane or enflurane. The baroreflex is inhibited but again less than either halothane or enflurane. Isoflurane is much less likely than halothane to produce arrythmias in the presence of circulating catacholamines. Isoflurane does however cause a significant reduction in the systemic vascular resistance, with a marked increase in blood flow to the muscle and skin. It is the most potent vasodilator of the previous three inhalational agents and the hypotension that results with its use is a result of it peripheral effects rather than its direct effects on cardiac depression. Isoflurane results in more muscle relaxation than the others in its class and can cause significant potentiation of paralytic agents.

Side Effects

Isoflurane does not create the elipetiform activity as seen with enflurane and may be used in seizure prone individuals. A major difference in this agent compared with the other is its extremely low level of metabolism in the body, thereby nearly eliminating the possibility of nephrogenic or hepatic toxicity.

Sevoflurane

Sevoflurane is a new fluorinated ether compound that has similar properties to the other fluorinated inhalational agents. It can produce mild respiratory and cardiac depression. It is not bronchoirritative and is characterized by a rapid degree of induction and recovery due to its low lipid solubility. It has a similar biotransformation profile as enflurane and may induce nephrogenic and hepatic side effects.

Desflurane

Desflurane is another new halogenated inhalational agent. It is also characterized by a low blood and lipid solubility which allows for rapid induction and emergence from anesthesia. It does produce bronchoirrative effects with a high incidence of breath holding, coughing, and laryngeal spasm. This agent is not as widely used for induction as the other inhalational agents. It is not metabolized to any appreciable degree and its side effect profile is advantageous.

Penthrane (methoxyflurane)

is a liquid anesthetic that is taken by inhalation. It is particularly good for abdominal, ophthalmic, and neurologic surgery.

There are many ways to design an anesthetic plan to meet the requirements for general anesthesia: muscle relaxation appropriate for the procedure, unconsciousness, and analgesia. Intravenous agents can be used to meet each of these requirements. These drugs are generally classified as nonopioids, opioids, and muscle relaxants.**The nonopioid** intravenous anesthetic drugs principally *provide hypnosis and blunting of reflexes* whereas **the opioids** (narcotics) and neuromuscular blockers *provide analgesia and muscle relaxation respectively*. In most surgical procedures, the induction of anesthesia is carried out by the use of an intravenous agent and is not an unpleasant experience. It has become customary to induce general anesthesia with an intravenous agent regardless of the subsequent agents to be used for maintenance.

NGand other Nonopioid Compounds

Barbiturates are commonly separated into classes based on duration of action and onset. In general, anesthesiologists *prefer to use drugs that have a rapid onset of*

action but a short duration of action. Such drugs allow rapid titration to the required effect and are usually used to induce anesthesia. Thiopental sodium is the prototype drug in this class.

(1)Thiopental

Thiopental is water soluble and stable in aqueous solution for weeks. It is generally prepared as the sodium salt and is quite alkaline in solution with a pH of 10.5. This alkalinity makes thiopental incompatible with many other acidic agents such as opiates, catecholamines, and some neuromuscular blockers. *Because of this alkalinity, thiopental must be injected into a freely flowing intravenous line* as extravasation can produce skin necrosis. Inadvertent intra-arterial injection is a serious complication. A chemical endarteritis occurs and thrombosis of the artery may follow. Tissue ischemia and gangrene are potential complications. The use of less concentrated suspensions of thiopental (2.5%) can decrease this risk and is now the standard concentration used in practice today.

Thiopental is generally delivered as a bolus dose of 3-5 mg/kg. The drug is rapidly diffused into vessel-rich areas such as the brain and unconsciousness ensues within 10-20 seconds (one circulation time). Unconsciousness from thiopental results from dose-dependent suppression of neuronal activity within the central nervous system. This suppression is associated with a general decrease in cerebral metabolic rate. Despite this depression in metabolic rate, thiopental and other barbiturates are poor analgesics and, in low doses, may even increase the perception of pain. The CNS effects of thiopental go beyond producing unconsciousness. Adequate levels of thiopental depress cortical brain activity measured on an EEG to the point of electrical silence. The metabolism when the EEG is flat presumably represents the basal metabolic requirements of cell function. Thus, in patients with severe brain injury and increased intracranial pressure, an induction dose can reduce pressure in most cases.

The effect of thiopental on the cardiovascular system is varied. It may have a profound effect in some patients, whereas virtually no effect in others. Healthy patients may experience a transient decrease in arterial blood pressure with a mild compensatory tachycardia and return of blood pressure to normal. In this situation, cardiac depression is limited. In large doses, or in patients with limited ability to activate a baroreceptor response (patients taking antihypertensives or hypovolemic patients), myocardial depression is more pronounced. Adequate volume repletion and sympathomimetic drugs all play a role in treating the hypotension in these patients.

Thiopental also produces a dose-dependent depression of medullary and pontine respiratory centers. Carbon dioxide responsiveness is blunted as are ventilatory responses to hypoxia.

The short duration of thiopental was originally thought to be a result of rapid metabolism. It is now clear that this is due to the rapid redistribution of the drug into tissues. Metabolism eventually occurs via the liver.

(2)Etomidate

Several newer drugs have been introduced to avoid the drowsiness associated with prolonged metabolism of the barbiturates. Etomidate is one of these newer agents and has a structural appearance similar to ketoconazole. In terms of onset, elimination, and reliability in producing unconsciousness, etomidate is similar to

thiopental. It produces unconsciousness in less than 60 seconds at the usual induction dose of 0.2-0.4 mg/kg. As with thiopental, drug redistribution from the brain to other tissue accounts for its short duration of activity. Bolus doses cause less change in blood pressure and heart rate than thiopental and this drug has less depressant effect on cardiovascular function in patients with depressed myocardial function. It also produces less respiratory depression than thiopental. It does have several disadvantages that limit its use. There is a high frequency of myoclonic movements and pain with injection (due to propylene glycol). It has also been shown to produce cortisol suppression and Addisonian crises when used in debilitated patients.

(3)Ketamine

Ketamine is an alkylamine structurally similar to phencyclidine (PCP) and produces a state of "dissociative anesthesia". An IV dose of 1-2 mg/kg may produce a cataleptic state characterized by intense analgesia, amnesia, and commonly a slow nystagmus with the eyes open. Systemic effects are characteristic of sympathetic nervous system stimulation. The more commonly observed include increases in heart rate, blood pressure, and cardiac output. Respiratory function is not depressed in normal patients and laryngeal reflexes are maintained. The onset of action is rapid (within a few minutes) and consciousness returns within 10-15 minutes although retrograde amnesia may be prolonged. A major disadvantage associated with its use occurs during emergence and consists of unpleasant dreams or even hallucinations. Benzodiazapines greatly reduce these side effects.

(4)Propofol

Propofol is a substituted phenol whose action is characterized by a rapid onset and short duration of action. Therefore, propofol is suitable for induction and can be used as a maintenance agent. The usual induction dose of 1.5-3 mg/kg produces unconsciousness within a matter of minutes and is metabolized quickly by the body. The major hemodynamic and respiratory effects of propofol are similar to those of thiopental. Like, thiopental, propofol decreases systemic blood pressure by dilating peripheral blood vessels. In patients with a blunted sympathetic response, profound hypotension may occur. Propofol mimics the action of thiopental by inducing a short period of apnea after bolus. Side effects are rare; the most common being the venous irritation upon administration (due to the soybean solvent in its emulsion). This can be diminished by the use of a large vein or injecting lidocaine IV prior to its administration.

(5)Benzodiazepines

Many benzodiazepines are available in the United States and are used primarily for the treatment of anxiety disorders. These agents are excellent in producing amnestic and sedative responses. Three benzodiazepines are available for IV injection and are commonly used in anesthesia practice: (1)diazepam, (2)lorazepam, (3)and midazolam. Benzodiazepines induce amnesia and sedation secondary to potentiation of the inhibitory neurotransmitter gamma amino-butyric acid (GABA). Although sleep inducing doses of diazepam (0.3-0.6 mg/kg) or midazolam (0.2-0.4 mg/kg) may produce unconsciousness in *two to three minutes*, these drugs have a slower onset of action and a longer post anesthetic recovery period than thiopental.

Because of this, benzodiazepines are less commonly used as induction agents, but are commonly used for sedation and to ensure amnesia. Diazepam is commonly used for premedication with a 5-10 mg IV dose. Induction with diazepam varies from 0.2-1.8 mg/kg dose and is marked by variability in onset and prolonged reactions. The effects of diazepam on the cardiovascular system are minimal. Mild decreases in blood pressure and heart rate are indicative of its sedative effect. There have been reports of respiratory depression with diazepam, however this response is dose dependent and can be marked if concomitant doses of narcotics are used. It is known to produce *venous irritation* when injected. *Lorazepam (0.04 mg/kg)* is slow in onset of action (10-20 minutes) and is not typically used as an induction agent. It is commonly utilized as an adjunct to regional anesthesia because of its profound anxiolytic and sedative effects. Pharmacological actions are similar to diazepam but longer in duration. Similar to diazepam, the parenteral[1] form produces venous irritation and pain when injected. Midazolam is water-soluble and has a lower incidence of injection pain. As with the other benzodiazepines, induction with midazolam is slow and recovery is prolonged. Midazolam is twice as potent as diazepam and *doses of 0.1 mg/kg are generally adequate*. Because of its potential for depressing respiration, especially if given with narcotics, the respiratory response of these patients needs to be monitored. Intravenous benzodiazepines should be titrated to effect and the benzodiazepine antagonist (مضاد) flumazenil should be immediately available.

Narcotic Agonists (Opioids) and Antagonists

Narcotics have been used for centuries to control perioperative pain and anxiety. In the past twenty years, very large doses of narcotics have been used not only for analgesia but also to produce unconsciousness and suppress the usual hyperdynamic responses to surgery. The predominant effects of narcotics include analgesia, a depressed sensorium, and respiratory depression. These effects are dose related. Narcotics have minimal effects on the cardiovascular systems of healthy patients. Narcotics do not produce direct cardiac suppression and are widely *used for induction and maintenance of anesthesia* in patients with myocardial disease. In hypovolemic patients, morphine may precipitate hypotension from its vasodilatory effects. Bradycardia with large doses of narcotics can occur due to direct stimulation of the vagal nucleus, however in normal patients cardiac output is not compromised due to an increase in stroke volume. Side effects include nausea and vomiting, chest wall rigidity, seizure activity, and decreased gastrointestinal motility.

The mechanism of action of these agents is receptor mediated. The sites of this receptor activity are opioid-specific and are most commonly found in the amygdala and spinal cord. Many opioid receptors have been identified and three appear related to the analgesic and anesthetic effects of the narcotics. Stimulation of the mu receptor results in analgesia, respiratory depression, euphoria, and physical dependence. Kappa receptors mediate spinal analgesia, sedation, and meiosis. The omega receptors mediate hallucinations, dysphoria, and tachycardia. *Meperidine, morphine, fentanyl, sufentanil, and remifentnil are* commonly used increasingly potent narcotic agonists.

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[1] **injected, infused, or implanted:** used to describe drug administration other than by the mouth or the rectum, for example, by injection, infusion, or implantation

The discovery of a class of compounds that are *specific antagonists* to the action of the opiates has made it possible *to treat opiate overdosage quickly and efficiently*. The standard drug for this use is naloxone. Some of the antagonists also have opiatelike properties, and this has led to the introduction of a new class of analgesics, the mixed agonists-antagonists. It is hoped that these drugs will produce analgesia without euphoria, reducing their potential for abuse. The three drugs of this class approved so far in the U.S.—*pentazocine, butorphanol, and nalbuphine*—are as analgesic as morphine for many uses and induce little or no euphoria. All appear to have a lower abuse potential than morphine or propoxyphene.

(مضاد)

Nalorphine is a concomitant narcotic agonist and antagonist which has less analgesic effects as well as less respiratory depression. Naloxone produces pure antagonistic effects with no known agonistic properties. It reverses analgesia and respiratory depression nonselectively. The duration of action is approximately 30 minutes with a typical dose of 1-2 ug/kg and additional doses may need to be delivered should the respiratory depression recur as the naloxone is metabolized. Hypertensive crises can occur in narcotic dependent patients in whom naloxone is delivered producing acute withdrawal symptoms.

Muscle Relaxants

There is more to anesthesia than simply rendering a patient unconscious and free of pain. In order to provide an optimal surgical field, an anesthetist must also control muscle tone as the current use of inhalational and intravenous anesthetic agents do not fully achieve this goal. Paralytic agents were first described in 1595 as explorers reported the use *of "poisoned arrows" by south American natives.* It wasn't until the 1930's that physicians began using curare in an attempt to treat tetanus. In the 1940's they were shown to decrease the number of bone fractures resulting from electroconvulsive therapy. Finally, in 1942, Dr. Griffin introduced these medications to the surgical community. Thus, it wasn't until the mid 1940's that paralytic agents began to be routinely used. Its inclusion in the Liverpool technique developed during the 1960's led to the popularization of "balanced anesthesia" achieved with the use of multiple agents.

Muscle relaxants produce their desired effect by action at the neuromuscular junction, but also have nonspecific effects at other sites. In order to understand the mechanism of action of neuromuscular relaxing agents, it is necessary to understand the depolarization of nerves and subsequent muscle contraction. In order to achieve muscle contraction an action potential travels down an efferent nerve to the terminal neuromuscular junction or motor end plate. Upon arrival, the action potential stimulates the release of acetylcholine from the synaptic vesicles into the postsynaptic cleft. The acetylcholine subsequently attaches to nicotinic receptors located on the postjunctional membrane. Should two acetylcholine molecules attach to the acetylcholine nicotinic receptor, the receptor will open allowing an influx of sodium ions into the muscle cell and depolarizing the motor end plate. The acetylcholine rapidly diffuses away from the motor end plate and is hydrolyzed by the enzyme acetylcholinesterase. The end-plate potential returns to resting potentials due to an active Na-K pump and prepares for the next stimulus. Neuromuscular

blockade occurs when the normal events are disrupted at one or more sites. The two classes of commonly used neuromuscular relaxing agents include nondepolarizing and depolarizing agents.

Nondepolarizing Muscle Relaxants

All nondepolarizing muscle relaxants bind to and competitively inhibit the end plate nicotinic cholinergic receptor. With the competitive blockade, an increase in the concentration of a nondepolarizing relaxant at the multiple neuromuscular junctions of each myofibril will increase the density of muscle paralysis. Conversely, drugs that inhibit acetylcholinesterase increase the amount of acetylcholine near the end-plate and competitively "reverse" the neuromuscular blockade. Reversal is often monitored by assessing muscular twitch response to electrical stimuli.

Nondepolarizing neuromuscular blocking agents can be classified into (1) intermediate acting (15-60 minutes) and(2) long-acting agents (over 60 minutes). This characteristic is arbitrary as the duration of action is dose dependent. Intermediate acting nondepolarizing agents include ***atracurium, vecuronium, and mivacurium***, whereas the long acting drugs include ***pancuronium, metocurine, d-tubocurarine, and gallamine***. The intermediate acting drugs in comparison to the long acting muscle relaxants have a similar rate of onset of neuromuscular blockade (3-5 minutes) but are relatively independent of renal function for clearance and evoke less circulatory effects. Most of these drugs have hemodynamic effects. *Tubocurarine* is known to block autonomic ganglia which can suppress sympathetic discharge and can decrease systemic vascular resistance. In addition, tubocurarine is known for its potential in mast cell degranulation with subsequent histamine release and severe hypotension. *Pancuronium* is well known for its inhibition of vagal and muscarinic receptors and commonly produces tachycardia with its use.

When muscle relaxation is no longer needed, any residual effects of the neuromuscular blocking agent are "reversed" to ensure appropriate muscle function and to sustain ventilation. Anticholinesterases inhibit actylcholinesterase, thereby increasing the concentration of acetylcholine.

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The three commonly used drugs for this purpose are neostigmine, edrophonium, and pyridostigmine. The increased concentration of acetylcholine may cause bradycardia and hypotension due to stimulation of the muscarinic cholinergic receptors on the heart. These unwanted side effects can be reduced by the preadministration of a muscarinic blocker such as *atropine or glycopyrrolate prior to its administration.*

Depolarizing Muscle Relaxants

Depolarizing muscle relaxants bind and depolarize the end-plate acetylcholine nicotinic receptors. This depolarization continues as long as the receptor is occupied. ***Succinylcholine*** is the only depolarizing muscle relaxant used clinically. Its duration of action with the typical induction dose of 1 mg/kg is very short (five minutes) because of rapid hydrolysis by plasma cholinesterases. Patients with abnormal production of plasma cholinesterase due to genetic abnormalities cannot hydrolyze succinylcholine resulting in prolonged paralysis. A "phase II block" resulting from

repeated dosing can result in repolarization of the end plate that is only made more dense by administration of typical reversal agents. This desensitization is poorly understood, but may result in delay in recovery of muscle tone.

There are several characteristics unique to succinylcholine that may cause undesired effects. The sustained depolarization by the administration of succinylcholine typically produces transient fasiculations. Fasciculation of damaged or weakened myocytes may cause myocyte rupture and intracellular extravasation of potassium in patients at risk (burn patients, trauma patients, and patients with neuromuscular disease). Postoperative myalgias of the muscles of the neck, back, and abdomen are occasionally seen with its use. It is speculated that unsynchronized contractions of skeletal muscle fibers may lead to this side effect. Prior administration of low-dose nondepolarizing muscle relaxant (tubocurarine) can attenutate fasciculation, although it requires an increase of the Succinylcholine dose by 50-75%. Sinus bradycardia, junctional rhythms, and even sinus arrest may follow its administration. These responses likely reflect the action of succinylcholine at cardiac postganglionic muscarinic receptors where this drug mimics the normal response of acetylcholine. These effects are more likely to occur with doses given close together. Atropine, the muscarinic receptor blocker, can attenuate these effects if given prior to its administration. Increases in intraocular pressure, intragastric pressure, and trismus have been associated with the use of succinylcholine. Patients who develop severe trismus with the use of this drug should be considered susceptible to the triggering effect of succinylcholine on malignant hyperthermia.

Techniques in General Anesthesia

Prior to the initiation of general anesthesia, a thorough history and physical examination is warranted. Previous reactions to any of the general anesthetics or a family history of reactions should be noted. Any potential cardiac or pulmonary risk factors should be elicited as these two organ systems are the most commonly affected by general anesthesia. An extensive cardiac and pulmonary evaluation should be made in those patients at risk so that potential risk-reducing interventions can be performed preoperatively.

With an adequate understanding of the drugs used in achieving general anesthesia, it is useful to understand the techniques used to induce and to maintain general anesthesia throughout a surgical case. As discussed earlier,(1) induction of general anesthesia is most often accomplished by the intravenous administration of thiopental. (2) Shortly thereafter, succinylcholine is also administered to produce skeletal muscle relaxation so as to facilitate direct laryngoscopy for intubation of the trachea. (3) This injection of drugs (barbiturates, benzodiazepines, opioids, etomidate, ketamine, or propofol) to produce unconsciousness followed immediately by succinylcholine is referred to as a “rapid sequence induction”. Preoxygenation prior to the administration of the drugs minimizes the likelihood of arterial hypoxemia developing during the period of apnea. A dose of tubocurarine prior to the succinylcholine can reduce the fasciculations induced by the depolarizing muscle relaxant. An alternative to this rapid sequence induction is the inhalation of nitrous oxide plus a volatile anesthetic. An inhalational induction is commonly utilized for pediatrics patients, particularly when insertion of an IV catheter is not practical.

After successful induction and intubation of the patient, maintenance of anesthesia aims at the aforementioned goals of analgesia, unconsciousness, skeletal muscle

relaxation, and control of sympathetic responses to the noxious stimuli. These objectives are most commonly met by the use of a combination of drugs discussed earlier. Typically, nitrous oxide is the most frequently used inhalational anesthetic. It is commonly used in conjunction with an opioid or volatile anesthetic. For muscle relaxation, a nondepolarizing muscle relaxant is also commonly utilized to maintain a motionless surgical field.

Local Anesthetics

The introduction of local anesthesia followed that of general anesthesia by about 40 years. In 1884, Koller introduced cocaine as an effective topical anesthetic for the eye. Later that year, American surgeon Halsted employed cocaine to produce the first nerve block by local injection. Because of cocaine's ability to produce psychologic dependence and its irritant properties when used topically, a search was made for improved local anesthetics. In 1905, Einhorn synthesized the first synthetic local anesthetic, procaine, and by 1943, lidocaine was successfully synthesized and employed for use.

Local anesthetic drugs are used clinically to reversibly inhibit the generation and conduction of impulses from an area of the body. Local anesthetics produce conduction blockade of nerve impulses by preventing increases in permeability of nerve membranes to sodium ions. Failure of this permeability to sodium ions slows the rate of depolarization such that threshold potentials are not reached and action potentials are not propagated. This affect affects smaller nerves preferentially resulting in the loss of pain sensation while preserving motor and proprioception ability. It is likely that the local anesthetic enters the sodium channel from the axioplasmic (inner) side of the nerve membrane and attaches to a receptor about halfway down the channel. While the local anesthetic molecule is within the sodium ion channel, it prevents the sodium ion movements necessary for depolarization. Although a local anesthetic drug is injected to produce blockade of nerve impulses, the drug is subsequently absorbed away from the nerve site and appears in the circulation. The concentration of the drug in the blood is directly related to the systemic effects of the local anesthetic. Local injection into highly vascularized areas such as the hypopharynx, nose, and trachea produces maximal levels that approach that of intravenous injection. Topical application, however, results in blood levels that are one-third that of IV injection. Most of the local anesthetics (with the notable exception of cocaine) are vasodilators, thus necessitating the addition of epinephrine or phenylephrine to aid in vasoconstriction. This addition minimizes the risk of systemic toxicity and allows for a bloodless field. Of interest, the addition of 1:100,000 or 1:200,000 provides the same vasoconstricting effects at the doses typically used for injection. The site of metabolism of a local anesthetic drug is determined by the chemical structure of the drug. Local anesthetics can be divided into two groups, depending on whether they have an ester linkage (cocaine, procaine, benzocaine, and tetracaine) or an amide linkage (lidocaine, bupivacaine, prilocaine, mepivacaine). The metabolism of local anesthetics with an ester linkage are metabolized in plasma by plasma cholinesterase (the same agent that metabolizes succinylcholine), whereas the local anesthetics with an amide bond are broken down in the liver by hydrolysis and dealkylation by the cytochrome p-450 enzyme system.

Local anesthetics tend to be linear molecules consisting of a lipophilic end and a hydrophilic end. The lipophilic end typically contains a benzoic acid moiety while the

hydrophilic end contains a hydrocarbon chain that is ionizable. This is of use clinically because the non-ionized form readily penetrates membrane barriers (when the pH is high more is in the non-ionized state) whereas the cationic form binds more readily to the sodium receptor (typically when the pH is lower). Thus, tissue acidosis render local anesthetics ineffective because the local anesthetic is relatively cationic in this state and cannot cross the nerve membrane to bind to the receptor. The addition of sodium bicarbonate into the local anesthetic provides more anesthetic in the non-ionized form which allows it to readily cross the nerve membrane and produces local analgesia for extended periods of time (in addition to decreasing the pain involved with injection of the parent weak acid compound).

The most commonly used local anesthetic is Lidocaine. Lidocaine injection, when coupled with a vasoconstrictor provides quick onset of analgesia with relatively short duration of effect (60-120 minutes). Bupivicaine and Prilocaine are longer-acting agents with special characteristics. Each is slower in onset, but result in significantly longer periods of anesthesia (240-480 minutes). Articaine was introduced in 2000 and boasts a significant decrease in the risk of toxic side effects due to increased metabolism (and decreased ½ life). It is rapidly absorbed with a quick onset of action.

The major systemic toxicity of local anesthetic agents involves the central nervous system and the cardiovascular system. Because local anesthetics cross the blood brain barrier, toxic levels can produce both CNS excitability and depression. Initially, toxicity is manifested by light-headedness, circumoral numbness, and dizziness, followed by auditory (tinnitus) and visual disturbances. Drowsiness, disorientation, and a temporary loss of consciousness may follow. Slurred speech, shivering, muscle twitching, and tremors precede a generalized convulsive state (CNS excitability). Further increases in the local anesthetic dose results in cessation of convulsive activity, flattening of brain wave patterns, and respiratory depression, consistent with generalized CNS depression. Local anesthetics can produce profound cardiovascular changes by direct cardiac and peripheral vascular effects. It is manifested by myocardial depression and peripheral vasodilation. Inadvertent, rapid intravenous injection of an excessive dose can cause significant myocardial contractility and peripheral vasodilation resulting in profound hypotension and circulatory collapse. Other systemic effects of local anesthetics include methemoglobinemia and allergic reactions. Prilocaine, when administered in large doses may result in accumulation of the metabolite, ortho-toludine, an oxidizing compound capable of converting hemoglobin into methemoglobin. With sufficient methemoglobin, the patient can appear cyanotic and the blood chocolate colored. This is easily revered by IV administration of methyline blue. Allergic reactions to local anesthetics are rare, despite their widespread use. Indeed, it is estimated that less than one percent of all reaction to local anesthetics are related to allergic etiology. Preservatives in the local anesthetic (methylparabenor) or breakdown products particularly of the ester groups (para-aminobenzoic acid) can produce typical allergic systems such as rash, laryngeal edema, bronchospasm. It is more likely that a systemic toxicity has occurred should any neurological or cardiovascular symptoms present. Treatment for a true allergic reaction is supportive. As there is no cross reactivity between classes of local anesthetics, the use of an amide local anesthetic may be used when an allergic reaction is documented for an ester group drug.

Preventing Toxicity

Local anesthetic toxicity primarily results from accidental intravascular injection or injection of an excessive dose. This must always be anticipated. Resuscitative equipment (oxygen, airways, bag and mask, suction), CNS-depressant drugs (diazepam, midazolam, and thiopental), and cardiovascular drugs (ephedrine, phenylephrine, epinephrine) should be on hand at all times. An IV should be started prior before any major regional anesthetic is started. Toxic reactions are best avoided by frequent aspirations during injection and slow, intermittent injection of the local anesthesia. When large doses are injected slowly and intermittently, the patient should be asked about symptoms related to CNS toxicity such as ringing in the ears, circumoral numbness, feeling of light-headedness, etc. Further, the slow injection rate allows dilution of the local anesthetic in the blood, so that high concentrations are not reached quickly. If signs or symptoms of systemic toxicity occur, the injection should be stopped immediately. In cases where large doses of anesthetic are used, monitoring should be employed including the maintenance of verbal contact, continuous ECG monitoring, noninvasive BP checks, and monitoring oxygen saturations. If convulsions or cardiac arrest occur due to local anesthetic usage, establishment of an airway, adequate ventilation, and support of circulation is mandatory. If the patient cannot be adequately ventilated, insertion of an oral airway after administration of succinylcholine (20 mg) can be useful. Should mask ventilation not be possible, tracheal intubation should be performed. CNS excitability (seizures) should be treated with small amounts of benzodiazepines (diazepam 5-10 mg). Hypotension is treated with alpha and beta agonists (ephedrine 5-10 mg or phenylephrine 40-80 micrograms). ACLS protocol should be instituted when life threatening cardiac dysrhythmias occur.

Cocaine

The use of cocaine dates back to the sixth century with South American Indians using the drug to induce euphoria, to reduce hunger, and increase work tolerance. Sigmund Freud was the first to report its clinical use. Dr. William Halstead injected cocaine into a sensory nerve trunk and reported on its regional anesthetic qualities. Today it most commonly used as a topical application for accomplishment of anesthesia, particularly in the head and neck region. It has a rapid onset of action and a prolonged duration of activity. In addition, its strong vasoconstriction effects are unique among local anesthetics, providing decongestion and decreased risk of hemorrhage, thereby obviating the need for epinephrine. The mechanism of action of cocaine is similar to other local anesthetics by blocking the sodium channel of the nerve membrane. It also is the only local anesthetic known to interfere with the reuptake of norepinephrine by the adrenergic nerve terminal and, in addition, prevents the uptake of exogenously administered epinephrine. This action leads to increased levels of circulating catecholamines and sensitizes target organs to the effects of sympathetic stimulation-- tachycardia leading to ventricular and atrial ectopy, vasoconstriction leading to severe hypertension, mydriasis, and an increase in body temperature. While theoretically being a contraindication, the subcutaneous injection of lidocaine with various doses of epinephrine in combination with topically applied cocaine is safe. The use of such dilute solutions of epinephrine and its slow release from subcutaneous tissues result in such low concentrations of circulating epinephrine as to be inconsequential if used with cocaine. Many references state that the safe maximal limit for cocaine is 200 mg (a 4% vial). Other authors mention 300-400 mg. Interestingly, the “safe” level for topically applied cocaine has not been based on

scientific evidence, rather on early clinical experience when cocaine was injected for tonsillectomy anesthesia.

Special Anesthetic Techniques in Otolaryngology

Ear Surgery

Ear surgery provides numerous areas of concern for the surgeon as well as the anesthesiologist. A bloodless field for microsurgery is important and various techniques are employed to maintain this state. Preoperatively, local injection with a solution containing epinephrine can produce sufficient vasoconstriction. Maintaining low-normal blood pressure without excessive elevations and keeping the neck veins free of compression can do much to limit the bleeding associated with middle ear surgery. The middle ear is an anatomic air cavity that is prone to diffusion of nitrous oxide. If nitrous oxide is used during middle ear surgery and is not allowed to diffuse out of the middle ear space, an increase in intracavitary pressure can exist which can dislodge a tympanic membrane graft. Simply stopping nitrous oxide 15 minutes prior to placement of the TM graft can prevent this occurrence. Facial nerve monitoring is also an important concern in ear as well as parotid surgery. Eliciting a facial grimace or the use of facial nerve monitors are easily used methods of identifying and avoiding the facial nerve. The judicious use or elimination of muscle relaxants allows the facial nerve to be identified by these methods. The use of potent inhalational anesthetics during ear surgery cases can maintain a relaxed patient with preservation of facial nerve conductance.

Tonsillectomy

The tonsillectomy is a common procedure performed in children and adults, however, numerous challenges are provided in anesthetic management. Patients commonly present with upper airway obstruction from enlarged tonsils, peritonsillar abcess, or sleep apnea syndrome. Careful attention to these possibilities is needed in order to anticipate the possibility of a difficult airway. Teeth should be inspected so that these do not become dislodged during induction or placement of the mouth gag. A patient that bleeds after a tonsillectomy represents a high risk induction. There is high rate of morbidity if not handled appropriately. The patient is at high risk for aspiration of digested blood and for the development of severe hypotension during induction due to hypovolemia. Adequate intravenous infusion should be started immediately. Blood should be immediately available for transfusion particularly if evidence of hypovolemic shock occurs.

The patient who is bleeding should be transported to the operating room in the semi-prone position to facilitate the gravity drainage of blood from the oral cavity. Once in the operating room, the patient should be placed in the same position with the right side down (for a right-handed anesthesiologist). Assistants should hold the patient in this position during induction of anesthesia. A full size smaller tube should be available to deal with potential edema from the previous intubation. A high volume suction must be available. The patient is pre-oxygenated and an inhalation induction is employed. When adequate depth is reached for laryngoscopy, the patient is turned to the full lateral position with no support under the head. This allows the head and bleeding points to be below the level of the larynx. The laryngoscope is introduced and is lifted 45 degrees upward to give adequate view for intubation. An older child or adult may be intubated awake however effective use of topical anesthesia is

unlikely in the face of severe hemorrhage in addition to the higher risk of inducing vomiting with laryngoscopy.

Facial Fractures

In severe facial fractures, the anesthetic management is complicated by the presence of blood, teeth, and bone fragments in the oral cavity and possibly the airway. Severe facial injury can be accompanied by fractures of the larynx or cervical spine. In addition, mandibular or maxillary fractures can present with significant trismus or airway obstruction. If one is called to evaluate a newly injured patient in acute respiratory distress prior to cervical spine X-rays, the airway should be established by cricothyrotomy or tracheotomy without manipulation of the neck. If the patient is known to be free of spinal fracture and is to be intubated for surgery, a decision must be made for oral or nasal intubation versus a tracheotomy. In the patient with severe midface fractures in the cribiform or nasoethmoid complex area, nasal intubation should be avoided whenever possible, both to avoid contributing to infection of the CSF and to avoid inadvertent insertion of the tube into the cranium. In the patient with a midface or mandible fracture, the tube may interfere with surgical manipulation. A major hazard with an endotracheal tube is the risk of carrying foreign bodies into the airway with the tube. In these cases, awake intubation with preparations for immediate tracheotomy should be performed.

Laryngeal Surgery

Surgery of the larynx provides numerous anesthetic considerations for both the surgeon and anesthesiologist. The anesthetic objectives are to maintain oxygenation and ventilation while the surgeon must have access to an unobstructed operating field. Communication is critical so that both goals can be met safely for the patient. For some cases with cooperative patients, topical laryngeal anesthesia can be achieved. Cocaine or aerosolized lidocaine is effective in achieving appropriate anesthesia of this area. Alternatively, a superior laryngeal nerve block can be performed. In most procedures, however, general anesthesia is usually required. The use of a small diameter cuffed endotracheal tube can allow for most laryngeal work to be performed safely and adequately. Should an endotracheal tube be a hindrance to the surgery planned, the intermittent apneic technique, jet-Venturi technique, or spontaneous respiration anesthesia technique can be considered. The use of neuromuscular relaxants and intravenous agents allow for appropriate oxygenation and ventilation in those circumstances where these methods are used. At other times, a small catheter placed just superior to the carina allows for adequate oxygenation and ventilation as well. With any of these methods, pulse oximetry and capnography is essential.

A carbon dioxide laser is also commonly used during laryngeal surgery. The risk of fire is always of concern when the laser is used. Certain measures should be undertaken to help reduce the risk of a fire. It has been determined that polyvinyl endotracheal tubes, even if wrapped in protective metallic tape, should not be used. Instead, laser resistant endotracheal tubes such as the Xomed Laser-Shield or Rusch red rubber tubes should be used and wrapped with metallic tape as an added protective mechanism. The safest anesthetic gas mixture has been found to be 30% oxygen in helium and up to 2% halothane has not been found to add any further fire risk. Additionally, the tube cuff should be protected by inflation with saline colored with methylene blue, neurosurgical cottonoids should be covered with saline, and the

patient’s face should be fully covered with saline impregnated gauze. Finally, the use of pulse mode for laser use provides a significantly decreased risk of laser induced fire than that used in the continuous mode.

Sleeping medecine

Zolpidem, prescription drug used to treat insomnia. Zolpidem works by affecting certain brain sites that influence sleep patterns and control the onset of sleep.

Tablets are taken orally, without food, at bedtime. The usual dosage is 10 mg each night for up to ten nights. Longer treatment is not usually recommended because the drug becomes less effective over time and can cause the patient to become dependent on ever-increasing doses. Zolpidem begins to work within one hour of ingestion to induce sleep..

Temazepam, drug used to treat insomnia. Temazepam works by increasing the action of certain neurotransmitters, brain chemicals needed for nerve transmission. As a result, nerve activity to certain parts of the brain is blocked, producing a calming effect. Temazepam also tends to relax muscles as it helps the patient go to sleep.

Insomnia, condition in which a person has difficulty getting sufficient sleep.

Narcosynthetic Drugs.

For several years pentothal sodium, a barbiturate, has been used intravenously to induce narcosis, not up to the point of complete sleep, enabling the psychiatrist to induce the patient (1)to reveal unconscious, hidden complexes which dominate in disguised states conscious mentation.(2) The drug has also been used in the same fashion to produce "confessions," particularly in Iron Curtain countries. In 1950 Dr. Douglas G. Kelley, a California psychiatrist, successfully used somnoform (a mixture of ethyl chloride, methyl chloride, and ethyl bromide), a well-known anesthetic. Dr. Kelley, however, employs this drug as an inhalant and claims the level of the patient's unconsciousness is better controlled than by intravenous medication.

Phencyclidine (PCP), general anesthetic that has become a major drug of abuse because of its potent psychological and behavioral effects. Introduced in the 1950s as a relatively nontoxic animal anesthetic, PCP has harsh side effects that make it unsuitable for anesthesia in humans. Within a few years, however, illegal PCP was sold as a substitute and adulterant for such hallucinogens as lysergic acid diethylamide (LSD), mescaline, and tetrahydrocannabinol (THC). Customary users of other hallucinogens usually did not like the severe psychological effects of PCP; it became popular among teenagers in the 1970s, however, under such street names as “angel dust” and “hog.”

Users have more sharply contrasting responses to PCP than to other drugs of abuse. It has profound effects on thinking, time perception, sense of reality, and mood; dreamlike states, euphoric or depressed moods, and bizarre perceptual experiences are reported. Negative aspects of PCP ingestion include disorientation, confusion, anxiety, irritability, paranoid states, and dangerously violent behavior. Hostility and belligerence can remain long after the drug is no longer measurable in the blood. Chronic users may also experience depression or a schizophreniclike state

that can last months after discontinuation. Death can result from acute effects such as depression of breathing and disturbed heart function. PCP abuse continued in the 1980s and 1990s, and it remains a serious public health problem.

Anesthesia

I INTRODUCTION

Anesthesia, absence of physical sensation in part or all of the body. The term more commonly refers to a reversible condition that is induced using anesthetic drugs. These drugs may be injected, inhaled, or applied directly to the surface of the body. Each year about 40 million patients in the United States receive anesthetic drugs for surgery, obstetrics, dentistry, or other medical procedures. Induced anesthesia may be local, involving only part of the body, or general, involving lack of sensation in the entire body as well as a loss of consciousness. Localized anesthesia can also be a result of natural causes, such as nerve injury, leprosy, or diabetes. The lack of sensation caused by these conditions is not easily reversible, and patients' unawareness of pain and other sensations can put them at risk of serious harm. This article focuses on induced anesthesia used in medical procedures.

II PAIN PATHWAYS AND ANESTHETIC ACTION

Anesthesia is distinct from analgesia. An analgesic, or pain-relieving drug such as aspirin, may relieve a headache, but a person who takes an aspirin still feels other physical sensations, such as pressure, heat, cold, and vibration. In contrast, anesthetic drugs block all physical sensations, though for medical purposes their ability to block pain is among their most important effects. Pain is a crucial warning system that tells us when our bodies are in danger, but without anesthesia, pain would make surgery and various other medical procedures much more difficult—or even impossible.

The sensation of pain results from communication between nerve cells in the brain, spinal cord, and elsewhere in the body (*see* Nervous System). The process begins when certain nerve cell endings, known as pain receptors or nociceptors, are stimulated. Pain receptors are located in the skin, joints, muscles, the linings of the body cavities, and elsewhere in the body. Nerve impulses travel from pain receptors along nerve fibers to the spinal cord and then to the brain. Pain impulses are relayed through a brain structure known as the thalamus and then to the cerebral cortex, the area of the brain that interprets messages and generates the conscious sensation of pain. At several points along their journey from pain receptor to cerebral cortex, pain impulses can be modified. For example, chemicals known as endorphins, the body's natural painkillers, interact with nerve cells in the brain and spinal cord to dampen the sensation of pain.

The various drugs used in anesthesia work by several different mechanisms to block the transmission or perception of pain and other sensations. Some sleep-producing drugs used as part of general anesthesia are injected into a patient's veins. These drugs are taken up by organs, muscles, and brain tissue and interfere with the complex and poorly understood biochemical mechanisms of consciousness. *Anesthetic drugs that are inhaled dissolve in the blood and circulate to the brain*. There they interact with brain cells, especially cells in the cerebral cortex that are involved in sensory perceptions.

Opiates, a family of opium-derived pain relievers that includes *morphine, codeine, and fentanyl,* act like the body's own natural endorphins *to dampen the*

sensation of pain. Drugs used as local anesthetics block pain impulses in a specific part of the body, preventing these nerve impulses from reaching the brain. These drugs interfere with the chemicals inside nerve fibers that are involved in transmission of nerve impulses.

III GENERAL ANESTHESIA

General anesthesia, which is usually used for major surgery, produces an *absence of pain* and *sensation in the entire body, loss of consciousness, muscle relaxation*, and amnesia. These effects make complicated surgical procedures easier to perform. For instance, muscle relaxation and loss of consciousness prevent movement by the patient, helping doctors perform more accurate surgery. Surgery under general anesthesia is less traumatic for the patient because he or she remembers nothing about the procedure.

Anesthetic drugs *must be administered throughout the length of an operation* in order to *maintain the proper depth of general anesthesia*. Most commonly, general anesthesia is produced with a combination of several different drugs, each used for a specific effect, such as producing sleep, pain control, or muscle relaxation. General anesthesia often (1) *begins with the injection of a sedative* medication, such as midazolam. A patient may also receive medications to reduce the production of saliva, which could cause choking, and of stomach acid, which could damage the lungs if inhaled. Propofol and sodium pentothal are common sleep-inducing drugs that are administered intravenously. These drugs act rapidly but their effect does not last long, so they are often used for the *early stages of anesthesia*. Anesthesia is then maintained for the length of the surgical procedure with longer acting drugs. Isoforane and desflurane are sleep-inducing drugs that are inhaled. *They are mixed with oxygen in an anesthesia machine*, then inhaled *by the patient through a facemask*. Nitrous oxide, a gas that produces light anesthesia when inhaled alone, is often used in combination with other anesthetic drugs to increase their effect. Commonly used *muscle relaxants include* (1)curare and (2)vecuronium, which work by blocking impulses from nerves to muscles. These drugs paralyze muscles throughout the body, including those involved in breathing. For this reason, doctors place patients who are under general anesthesia on a breathing machine. A pain-blocking drug such as *fentanyl* is also injected as part of general anesthesia.

Anesthetic drugs can have various side effects, including nausea and vomiting or changes in blood pressure, breathing, and heart rate. In addition, many surgical patients already have other illnesses, such as problems with the heart, blood pressure, lungs, kidney, liver, or nervous system. These problems can make anesthetic drugs more dangerous. *To detect and correct* any *complications* that may develop, an anesthetized patient's *blood pressure, heart rate and rhythm, blood oxygen concentration, breathing rate, exhaled carbon dioxide, and temperature are monitored throughout surgery*. The patient is also observed for signs such as *tearing, sweating, and wrinkling of facial muscles that can indicate anesthesia depth may be lightening*.

Using a combination of anesthetic drugs enables doctors to use lower doses of each drug and maintain the proper depth of anesthesia while minimizing the risk of side effects. This strategy, along with better monitoring of anesthetized patients and the development of improved anesthetic drugs, has greatly improved the safety of anesthesia in recent years. In the last decade alone, the number of deaths attributed

to anesthetic drugs has dropped 25-fold, to about 1 in every 250,000 general anesthesias.

Anesthesia is reversed simply by halting the administration of anesthetic drugs. Any remaining anesthetic gases in the body are gradually exhaled, and as their concentration in the body falls, consciousness returns. The muscle relaxant circulating through the body is removed by the liver and kidneys, and its effects can also be reversed with other drugs. Medications to control pain continue to be given after the operation.

LOCAL ANESTHESIA

Local anesthesia is commonly used for a variety of relatively minor procedures, such as dentistry, sewing up wounds in the emergency room, and operations on the toes and fingers and other superficial areas of the body. Local anesthesia is less complicated and often safer than general anesthesia because it involves fewer drugs and has less effect on blood pressure, heart rate, and breathing because there is no loss of consciousness. In dental procedures, local anesthesia is advantageous because protective reflexes such as the gag reflex, which helps prevent choking, remain intact.

Local anesthetics are most commonly *administered by injecting them into the part of the body that needs to be anesthetized*. They can be injected directly into the tissue being operated on, a technique known as local infiltration. Or, they can be injected near the nerves that carry pain impulses from a particular part of the body, a technique known as nerve block. Topical anesthesia is the application of a local anesthetic directly onto the surface of a mucous membrane, such as the eye or the lining of the throat or nose.

Regional anesthesia is produced by injecting a local anesthetic around the spinal area, thus anesthetizing a larger area of the body than in local anesthesia. Spinal anesthesia is a type of regional anesthesia in which the anesthetic is injected into the fluid around the spinal cord. Epidural anesthesia is a similar technique, but the anesthetic is injected into the spinal canal between the membranes that surround the spinal cord. Spinal and epidural anesthesia block sensation everywhere in the body that is lower than the site of injection. These techniques are frequently used in childbirth and in surgery on the lower half of the body, such as prostate gland removal and surgery on the hips or knees.

The earliest known local anesthetic was cocaine, but it is rarely used today because it can cause convulsions and nervousness, and it is addictive. The most commonly used local anesthetic today is lidocaine. Procaine, more commonly known by its brand name *Novocain*, is sometimes used as a local anesthetic, particularly in dental procedures. However, it does not last as long as lidocaine, and it is more toxic. Bupivacaine is a very long acting local anesthetic that is useful for long operations and provides a greater duration of pain relief after surgery. To help allay patients' anxiety, a sedative is often given as a part of local anesthesia.

All local anesthetics can be toxic if injected in too high a dose. Particularly when used as part of spinal or epidural anesthesia, local anesthetics may cause a dangerous fall in blood pressure. Many people experience nervousness and discomfort when local anesthetics are injected with epinephrine, a drug that constricts blood vessels to help keep the anesthetic in the area where it is needed. However, true allergic reactions to local anesthetics are very rare.

ANESTHESIOLOGY

An anesthesiologist is a medical doctor specially trained to administer anesthesia (*see* Medicine). In the United States, an anesthesiologist must complete

two or three years of residency training in an anesthesiology hospital program after finishing medical school and the required internships. An anesthetist is any person who administers an anesthetic, regardless of qualification. Nurses trained to give anesthesia under the direction of a physician or to assist an anesthesiologist are called nurse anesthetists.

In the operating room, an anesthesiologist is in charge of administering anesthetic drugs and is responsible for recognizing and treating complications that may develop during surgery, such as a heart attack or a sudden change of blood pressure. The anesthesiologist is trained to understand how anesthetics work and how they may interact with each patient's health problems and other medications they may be taking. Before surgery, the anesthesiologist makes sure patients are healthy enough to undergo surgery and answers questions from patients and their families. After surgery, the anesthesiologist monitors the patient as he or she gains consciousness and decides when the patient may be moved out of the recovery room or, in the case of outpatient surgery, sent home. Trained to deal with emergencies in the operating room, anesthesiologists are often called on to help with resuscitation in the emergency room and with care and stabilization of patients in the intensive care unit.

VI ALTERNATIVES TO ANESTHETIC DRUGS

Although today's anesthetic drugs are usually effective and safe, the risk of side effects and, in very rare cases, permanent organ damage or death, causes some patients concern. While scientists continue to search for better and safer anesthetic drugs, some doctors and patients have begun to investigate alternative means of inducing anesthesia.

Acupuncture, an ancient Chinese technique that involves inserting special needles at specific points on the body, is sometimes used for surgical anesthesia. The needles are rotated manually or, more often, connected to a device that sends electrical current along the needles and into the body. Acupuncture is thought to block pain by causing the release of pain-blocking endorphins and preventing pain impulses from being transmitted along the spinal cord to the brain. It can be used alone or in combination with sedatives or painkillers. Acupuncture is used as part of surgical anesthesia in most Chinese hospitals today. Scientific studies have been unable to establish how effectively acupuncture can block pain during surgery. However, the technique has been shown to reduce the nausea and vomiting that sometimes occur as a side effect of general anesthesia.

Another alternative means of inducing anesthesia is hypnosis, which can be useful for patients who cannot tolerate anesthetic drugs. However, it requires a great deal of preparation by the patient. Before surgery, a patient must go through several training sessions with a hypnotist. Only about 10 percent of people are capable of reaching a state of hypnosis deep enough for surgery to be performed. Hypnosis is also useful as an addition to anesthetic drugs. It can help allay patients' anxiety before surgery and help diminish complications such as nausea, vomiting, and pain afterwards. Hypnosis is helpful in easing the pain of childbirth and promoting healing in severely burned patients.

VII HISTORY OF ANESTHESIA

Minor surgery has been performed for thousands of years, often with opium, alcohol, or *Cannabis* used to stupefy the patient. However, these drugs were unable to block the pain and shock of surgery to enable lengthy operations or operations involving the interior of the body.

Modern anesthesia—the ability to produce a controlled, reversible state of unconsciousness, amnesia, and muscle relaxation—began in the mid-19th century. Nitrous oxide was first used as an anesthetic in 1844 by the American dentist Horace Wells. In 1846 American dentist William Morton used ether to produce general anesthesia for surgery. Crawford Long, an American surgeon, had been using ether since 1842, but he did not publish his results until 1849. British physician Sir James Simpson first discovered the anesthetic properties of chloroform in 1847. Chloroform anesthesia became more popular after another British physician, John Snow, administered it to Queen Victoria of England for childbirth in 1853.
Anesthesiology became an established branch of medicine in the United States during the early 20th century. The American Society of Anesthesiologists, which sets standards of safety and ethics for anesthesiologists, was founded in 1905. The Board of Anesthesiology, which maintains educational standards, was established in 1938. Anesthetic drugs were also improved throughout the 20th century. The first intravenous anesthetic, sodium pentothal, was introduced in 1932 by American physician John Lundy. The muscle relaxant curare, originally used in hunting by Native American tribes in South America, was first used in surgery in 1942. Better inhalation anesthetics were also developed to replace ether, which is flammable, and chloroform, which is toxic.

Behavior modification.

At the Iowa State security medical facility, inmates who break rules are given injections of *apomorphine*, a drug that brings on 15 minutes of violent vomiting. Other drugs used at other U.S. prison facilities include *succinylcholine*, which produces a terrifying feeling of suffocation; *Anectine*, a derivative of the poison curare, which causes loss of all muscular control; and *Prolixin*, a powerful tranquilizer with neurologically significant side effects.

flunitrazepam

Intramuscular may serve as a convenient, rapid, safe, and effective adjunct to neuroleptics in reducing aggressive behavior in emergency psychiatric settings. was obtained within 30 minutes

Alprazolam

drug used to treat anxiety, panic attacks, and certain phobias. It has also been used to treat depression, irritable bowel syndrome, premenstrual syndrome, and problems associated with alcohol withdrawal. Alprazolam works by depressing the activity of the central nervous system.

Alprazolam is a prescription drug available in tablet form that is taken orally, with or without food, usually three times a day. Dosages may range from 0.25 mg to 10 mg, depending on the severity of the patient’s condition. The drug takes effect after one or two hours. Because drowsiness is a common side effect, patients taking this drug are advised not to drive, operate dangerous machinery, or engage in other risk-related activities.

An overdose of this drug can cause sleepiness, confusion, coma, or even death, especially when combined with alcoholic beverages. Alprazolam should not be used by pregnant or nursing women, as it may harm the baby. No safe dosages have been established for children under 18 years of age.

Possible side effects of alprazolam include blurred vision, stuffy nose, headache, drowsiness, diarrhea, constipation, nausea, chest pains, fainting, muscular weakness, decreased sex drive, irritability, or depression. Side effects are more likely to appear when the drug is first used or when dosage is increased, but they may lessen or disappear with continued use of the drug. Lowering the dosage or eliminating the drug can also produce side effects, especially after prolonged use (more than four weeks). This set of side effects may include blurred vision, diarrhea, loss of appetite, muscle cramps, twitching, or seizures.

Patients who are sensitive to or allergic to tranquilizers should not use alprazolam. In addition, it should not be used by anyone with myasthenia gravis (chronic muscle weakness), or with narrow-angle glaucoma, an eye disorder. This drug may interact adversely with a variety of medications, including carbamazepine, cimetidine, digoxin, disulfiram, various antihistamines, antidepressants, oral contraceptives (see Birth Control Pill), and other tranquilizers.

Brand Name:Xanax

Diazepam

Diazepam, mild tranquilizer drug, used to treat anxiety and nervous tension. It may also be used to treat acute alcohol withdrawal, insomnia, muscle spasms, and certain types of seizures. Classified as a benzodiazepine, diazepam works by blocking nerve activity in certain parts of the brain, producing a calming effect.
Diazepam is available by prescription in tablet, capsule, and liquid form. With the exception of one form of liquid made for injection, all are taken orally. Depending on the patient's condition, the prescribed dosage may range from 2 mg to 10 mg 2 to 4 times daily, with a maximum recommended dosage per day of 60 mg. Diazepam may be taken with or without food. Relief of symptoms is usually apparent within three to five days. Because this drug may be addictive or habit-forming, prescribed treatment is typically no longer than three weeks.
Patients with **mental illnesses or with acute narrow-angle glaucoma (an eye disorder) should not take this drug.** Diazepam should be used with caution by patients **with impaired liver or kidney function,** severe **depression, or epilepsy**. It is not safe for use during pregnancy, while breast-feeding, or in children under six months of age. It should not be combined with alcoholic beverages.

Side effects of this drug may include drowsiness, lightheadedness, fatigue, or poor muscle coordination. Patients who experience these symptoms should not drive, operate dangerous machinery, or engage in other risk-related activities while taking diazepam. Other side effects include blurred or double vision, confusion, depression, dizziness, headache, slurred speech, nausea, constipation, skin rash, or low blood pressure. Patients taking diazepam for an extended period (more than four weeks) may experience withdrawal symptoms if use is stopped abruptly; these symptoms may include abdominal cramps, sweating, vomiting, tremors, or convulsions. An overdose of this drug may cause sleepiness, confusion, or coma.

Diazepam may interact adversely with a wide variety of drugs. These include other tranquilizers, anticonvulsant drugs, antidepressants (especially MAO inhibitors), barbiturates, narcotics, and birth control pills. Other potentially adverse drug interactions include cimetidine, digoxin, fluoxetine, ranitidine, and rifampin.

Brand Names:*Valium*, *Valrelease,Dizac*

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