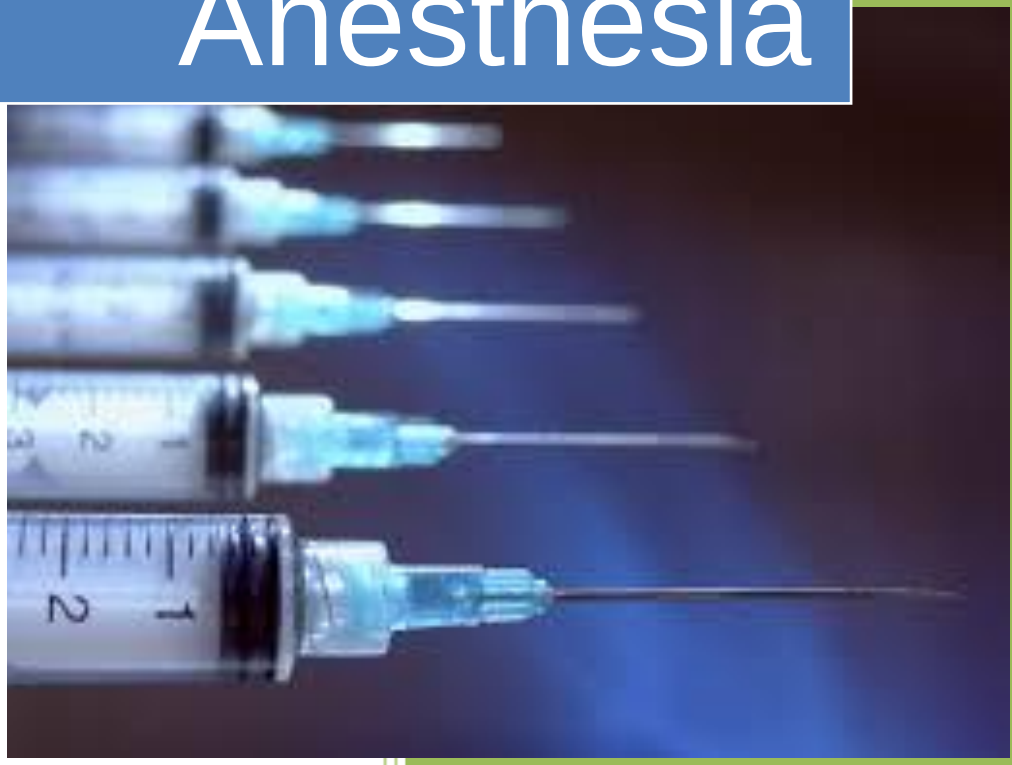
Anesthesia



Research Project

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1. Introduction

One of the branch's of medicine that is really interesting is surgeon and this is probably one of the most difficult jobs related to health. Furthermore, everyone who thinks of surgery, do think about anesthesia. That is why this project is focused on these topics and because these will be probably the study area that the author wishes to accomplish in the near future.

However, considering that most of the people do not understand how anesthesia works and how it can affect a living being when it is being administered. There are a couple of questions to solve: how does anesthesia work? Is it possible to synthesize an anesthetic? Then, it was easy to state the hypothesis:

> It is possible to synthesize an anesthetic which reduces the heart rate or the mobility of microorganisms.

After that point, there were set some objectives to accomplish while doing this research, for example to difference between anesthesia and analgesia, or to analyze and study if the anesthetic obtained by synthesis can affect or not the beats or movement of some microorganisms.

After that, it was needed to fix a methodology to verify or falsify the hypothesis. There was chosen some experiments closed related:

The synthesis of an organic compound that can act as an anesthetic: benzocaine, useful to see if it can reduce the beats or movements of microorganisms.

To ensure that this organic compound was obtained correctly, there were performed a series of complementary studies: X-ray Diffraction to compare to a standard database or the calculated position of the atoms using the Bragg's Law.

Part of these studies would not have been possible without the help of Eugènia Estop PhD, who financed the cost of the X-ray diffraction, and Angel Alvarez PhD, who helped in the process of the diffraction and gave the ideas of using the Miller Indices and creating the software. Both of them are from the Geology Department, *Universitat Autònoma de Barcelona*.

2. Objectives

The main objectives of this research project were:

- To know what anaesthesia is.
- To know about anesthesia and its types.
- To difference between anesthesia and analgesia.
- To be aware of the problems that anesthesia can cause.
- To obtain an anesthetic by organic synthesis in the laboratory.
- To use that compound to reduce the beats or mobility of microorganisms.
- To analyze and study if the product obtained is pure or not.

Then, the priority was to synthesize an anesthetic and try to use it properly, but it was difficult to know if it was pure or not. That made necessary to analyse the anesthetic and study it with an X-ray diffraction, which is a technique based on constructive interference of monochromatic X-rays and a crystalline sample.

After that, it was found that it would be interesting to induce the anesthetic to daphnia and paramecium, because it will be helpful to understand how anesthesia works into a living being. The difference between both species would help to determine the effects of anesthesia and the quantity of it that is needed to reduce the heart rate of the daphnia or the mobility of paramecium. This would also help to realize the problems anesthesia can cause, because it is knew that it can be dangerous.

Thus, this research is based on a study of the problems that anesthesia can cause and the way some people with certain diseases have to be administered it. Next, it will be explained how to synthesize benzocaine, a local anesthetic, and what an X-ray diffraction is.

Finally, the anesthetic was administered to daphnia and paramecium. The results were compared to a commonly used anesthetic: Thiopental sodium and a solution of saline serum as a control.

3. Anesthesia for the Patient with Cardiovascular Disease

3.1 Preoperative evaluation and preparation

It should be designed to answer the two questions: Is the patient in the best possible physiologic and physchologic balance, and if not, what can be done to ensure that the patient is in the best possible condition? Specific questions asked during the history, physical examination, and laboratory studies should be designed to clarify the extent of the impairment that the patient suffers respect to the heart and the peripheral vascular system; pulmonary conducting and gas exchange systems; renal functions; cellular metabolism; intravenous, cellular and interstitial volume status; hepatic, metabolic and excretory capabilities; and the extent of neurologic impairment. The most important of these areas for the anaesthesiologist are the cardiovascular system and the lungs.

3.1.1 Congestive Heart Failure

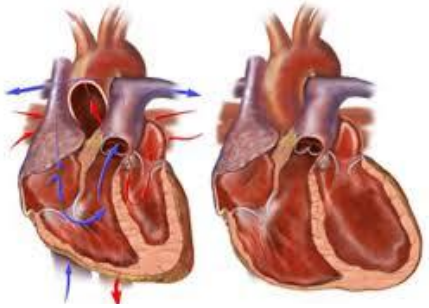

Figure 1. Difference between a healthy heart and a congested heart

Yet it is generally accepted that the risk of anesthesia is greater in patients in congestive heart failure, a weakness of the heart that leads to a build-up of fluid in the lungs and surrounding body tissues. The anesthetic risk is magnified because of the increased probability of hypoxia, reduced cardiac output, overt pulmonary edema, hypotension, malignant arrhythmias and complete cardiovascular collapse (see figure 1). These patients have greatly reduced myocardial reserve and cardiac output. On the other hand, their decreased cardiac output promotes rapid changes in depth of anesthesia, as well as concomitant alterations in cardiovascular dynamics and critical organ perfusion.

Patients in early congestive heart failure, such as the patient in our case report, present signs and symptoms that are subtle and are often missed during a cursory history and physical examination. Occasional coughing, especially at night, as well as insomnia (perhaps due to early respiratory distress), nocturia[1], unexplained fatigue, irritability (perhaps secondary to reduce cerebral blood flow), abdominal discomfort (particularly right upper quadrant pain) and evidence of increased sympathetic activity (such as sweating) are early symptoms of congestive heart failure that can be easily overlooked.

[1] **nocturia**: excessive urinating at night

Therapy for congestive heart failure should include bedrest, a low-salt diet, vigorous diuretic and adequate digitalis therapy, potassium supplementation and pharmacologic therapy or cardioversion for serious arrhythmias. Pericardial and pleural effusions should be treated before induction of anesthesia. Adequate therapy for congestive heart failure can rarely be accomplished in a few hours.

3.1.2 Myocardial Ischemia of Infarction

In recent years, optimal preoperative preparation and careful anesthetic and postanesthetic management have reduced the risk of perioperative reinfarction from approximately 40% to less than 10%. Perhaps the most difficult of these patients is to identify the patient who is symptomless and thus unaware of myocardial ischemia (see figure 2). Even a standard electrocardiogram accomplished under resting conditions may not diagnose the pathology.

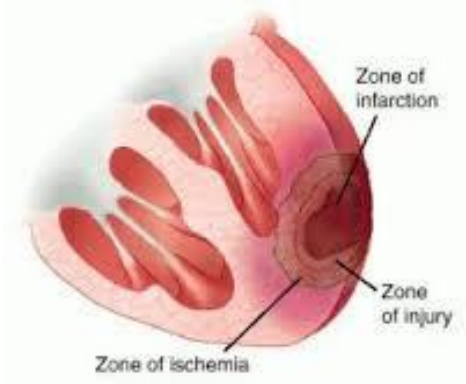

Figure 2. Myocardial ischemia or infarction

However, electrocardiograms performed during stress testing are more likely to demonstrate myocardial ischemia, but they are more time-consuming and costly. The incidence of reinfarction and death decrease as the time between infarction and surgery increases, what means that more time would suppose less risk. Patients operated on within three months of infarction have a reinfarction rate of 37%.

This rate decreases to 16% in patients three to six months after infarction and remains at 4 to 5 percent when infarction has occurred more than six months previously. Therefore, elective operations during the first three-month period following infarction (when most of the healing of the infarcted tissue is taking place) are prohibitively dangerous. Surgery should be postponed for at least six months following the infarction.

3.1.3 Hypertension

Among the known causes of hypertension[2], there are abnormal secretions of hormones from the pituitary, thyroid, adrenal cortex of medulla, ovary and kidneys, as well as pathology in the central nervous system, kidney and adrenal glands. Life expectancy is inversely related to the magnitude and duration of hypertension (see figure 3); what means that when one increases, the other one decreases.

Most patients with known hypertension, therefore, are taking antihypertensive medication when admitted to the hospital for operation. Frequently, the therapy is inadequate and the hypertension is not well controlled. Indeed, it has been estimated that as many as 75% of hypertensive patients are not adequately treated. It is important when it has been admitted to the hospital that the blood pressure is measured frequently in preoperative patients, even though they may not have a history of hypertension.

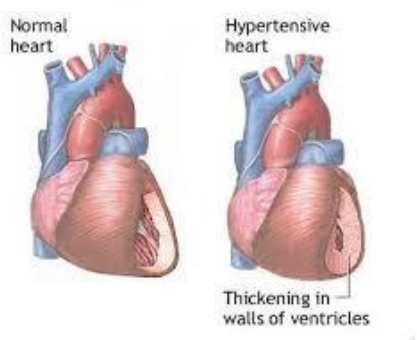

Figure 3. Difference between a normal and a hypertensive heart

A number of studies in the late 1950s and the early 1960s evaluating the advantages and disadvantages of continuing antihypertensive therapy with reserpine and other rauwolfia alkaloids produced conflicting results and conclusions. By 1965, it was agreed that reserpine should not be discontinued prior to anesthesia.

This position was solidified by studies that evaluated the cardiovascular responses of patients who were not hypertensive, patients whose hypertension was untreated or inadequately treated and patients who had their hypertension well controlled with a variety of antihypertensive drugs. It was found that, while cardiac output was reduced by anesthesia to a similar degree in all three groups, untreated patients had a more marked fall in systemic vascular resistance and a much greater reduction in mean arterial blood pressure than the patients in the other two groups. In addition, the untreated hypertensives experienced a 70% incidence of severe dysrhythmias[3] and electrocardiographic evidence of ischemia. This group of patients also experienced severe hypertensive responses during tracheal intubation and during the immediate period surrounding awakening, which were similar to the ones suffered by the hypertensive patients well treated prior to operation. The cardiovascular responses to anesthesia depend on preanesthesia arterial blood pressure rather than on whether the elevation in blood pressure was treated.

[2] **hypertension:** elevated blood pressure
[3] **dysrhythmias:** an abnormal cardiac rhythm

Hypertension leads to an increase in cardiac and vascular abnormalities. It is important that scrupulous attention is focused upon careful evaluation of cardiac and renal function and the cerebral circulation. Cardiac evaluation of these patients will frequently disclose elevation of left ventricular end-diastolic pressure or left atrial pressure.

Elevation of left ventricular end-diastolic pressure or left atrial pressure with increases in myocardial afterload induced by systemic vascular resistance, these left-sided pressure elevations promote large increases in myocardial oxygen requirements. These increases coupled with coronary artery obstruction to blood flow can unbalance the myocardial oxygen demand-to-supply ratio.

Blood Pressure Category	Systolic (mmHg)		Diastolic (mmHg)
Normal	less than **120**	and	less than **80**
Prehypertension	**120 - 139**	or	**80 - 89**
Stage 1 Hypertension	**140 - 159**	or	**90 - 99**
Stage 2 Hypertension	**160** or higher	or	**100** or higher

Figure 4. Patients with diastolic hypertension usually have a reduced plasma volume

Patients with diastolic hypertension usually have a reduced plasma volume (see tabulated results in figure 4). Reduction in plasma volume in inadequately treated hypertensive patients undoubtedly contributes to the cardiovascular instability experienced by these patients during anesthesia. The best thing to do in this case would be to increase the intravascular volume before the induction of anesthesia by an adequate preoperative antihypertensive treatment. If that is not possible, then appropriate volume expansion with intravenous fluids should occur before anesthetic induction.

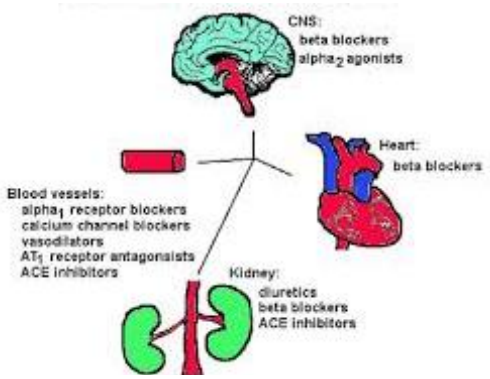

Figure 5. Potential sites of action for antihypertensive drugs

There are many drugs (see figure 5) available to treat hypertension which have different mechanisms of action. However, they can be classified as diuretics, central or peripheral sympathetic blockers, depletors, modifiers, of false transmitters, central nervous system depressant, direct-acting vasodilators, and compounds that influence renin, angiotension, aldosterone, or other hormonal system involved in blood pressure regulations. Many of these drugs alter total body or serum electrolyte concentrations or both, which can lead to serious arrhythmias and myocardial contractility problems during anesthesia.

3.1.4 Arrhythmias

Patients with cardiovascular disease have more arrhythmias preoperatively than patients without cardiovascular disease (see figures 6 and 7). The main causes of arrhythmias preoperatively are myocardial disease with direct or indirect involvement of the conducting system; drug-induced changes in the cardiac conducting system; changes in serum electrolyte concentration, pH, blood gas tension, or hormonal abnormalities and hypertension.

It is important when evaluating a patient with cardiac disease to determine the probable cause of his arrhythmia and to treat the treatable arrhythmias before anesthetic induction. This is because arrhythmias that may have been benign in frequency or type before anesthesia may not remain so during anesthesia.

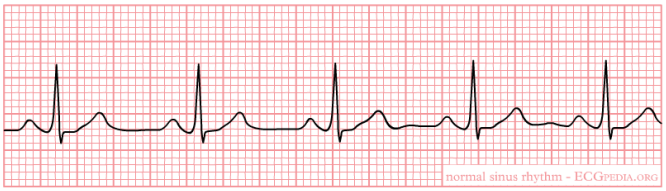

Figure 6. ECG of a person who doesn't have arrhythmias.

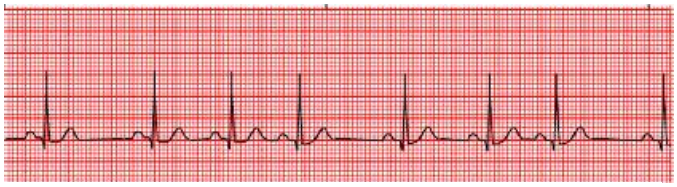

Figure 7. ECG of a person who has arrhythmias.

3.2 Anesthesia for the Cardiac Patient

3.2.1 Premedication

The fear of surgery in patients with cardiac disease can cause increases in heart rate, peripheral vascular resistance and myocardial contractility that may predispose to myocardial ischemia. It is even more important than usual, therefore, to sedate patients with cardiac disease before operations. On even greater importance is the caution that the anaesthesiologist dealing with the cardiac patient must offer extensive emotional and psychologic support during his preoperative visit. If a patient is going to receive a regional anesthetic, he should be told that the anesthetized sill area remains numb for some time after the completion of surgery.

It is well known that patients who receive a supportive, sympathetic and frank preoperative visit, require significantly less postoperative analgesic medication and receive an earlier discharge from the ICU and from the hospital than patients who receive a preoperative visit that is cursory or no preoperative visit at all. This is of great importance in patients with cardiac disease, not only does good sedation relieve anxiety and secondarily reduce myocardial work requirements, but it also allows for a smoother induction of anesthesia.

Patients with heart disease are often particularly sensitive to anesthetics and other central nervous system depressants. This appears to be especially true with patients with a markedly decreased cardiac output. Patients with severe reductions in cardiac output should not receive premedication. Those patients with reduced arterial oxygen tension should receive premedication with oxygen supplementation.

3.2.2 Monitoring During Operation

Figure 8. Monitoring During Operation

The minimum monitoring includes determination of the electrical activity of the heart, esophageal temperature and heart sounds (including heart rate), indirect arterial blood pressure, central venous pressure, arterial blood gases and pH, and urine output (see figure 8). Any patients with more than minimal cardiac disease will also receive and indwelling arterial catheter for direct systolic, mean and diastolic pressure measurement as well as frequent or continuous arterial blood gas, pH and electrolyte analysis.

The pulmonary artery flows directed catheter is one of the most important monitoring tools developed in the last 10 years. Besides providing pulmonary artery and right atrial pressures, this instrument has enabled monitoring of the left ventricular filing pressures and thus left ventricular function. The catheter can also be used for determination of the cardiac output. In addition, measurements of pulmonary artery or mixed venous oxygen tension are an extremely sensitive index of the adequacy of cardiac output for total body metabolic needs. Recent studies suggest that total body, and even better, specific organ metabolic-perfusion rates are superior in assessing the adequacy of the circulation and predicting early degeneration of circulatory adequacy than standard blood pressure, blood gas, pH or even cardiac output monitoring.

Perhaps the greatest concern to the modern clinical anaesthesiologist is not *what* to monitor but *when* to initiate monitoring. The conservative approach has always been to begin all monitoring as soon as possible (i.e. in the induction or operating room before induction of anesthesia). A recent work suggests that this approach may induce significant iatrogenic complications and may produce more problems in some patients than the value of the information, resulting from the monitoring technique. In a study, in which arterial blood pressure and pulse rate responses to pulmonary artery catheterization were measured in heavily premedicated patients, it was found that all patients sustained marked increases in systolic artery blood pressure, pulse rate and the rate pressure product index. The greatest increases were seen in patients with coronary artery disease and in this group, 50% of those not receiving propranolol experienced angina.

This study raises the serious question of whether invasive monitoring should be instituted in certain groups of cardiac patients before induction of anesthesia. Similar alterations in cardiovascular dynamics were observed during catheterization of a peripheral artery in the operating room. On several occasions, this has produced myocardial infarction and death in patients with coronary artery disease. Some clinicians have suggested that invasive or semi-invasive monitoring devices should be inserted on the evening before operation.

3.2.3 Induction

The ideal anesthetic induction technique would provide a rapid, excitement-free passage from awareness to adequate maintenance levels of anesthesia with significant muscle relaxation but without any alteration in all cardiovascular variables (see figure 9). Unfortunately, such an ideal anesthetic induction agent is not currently available.

The speed of induction is the least important of all of the above criteria for the ideal induction. The most important criteria are stability of circulatory dynamics and absence of excitement. In considering the technique of choice, it is extremely important to recall the specific pathology of the patient involved. A rapid induction with a sleep dose of thiopental followed by paralysis with succinylcholine and endotracheal intubation is obviously not the technique of choice for the patient with coronary artery disease with angina. This technique will often produce tachycardia and hypertension during or shortly after insertion of the endotracheal tube into the trachea.

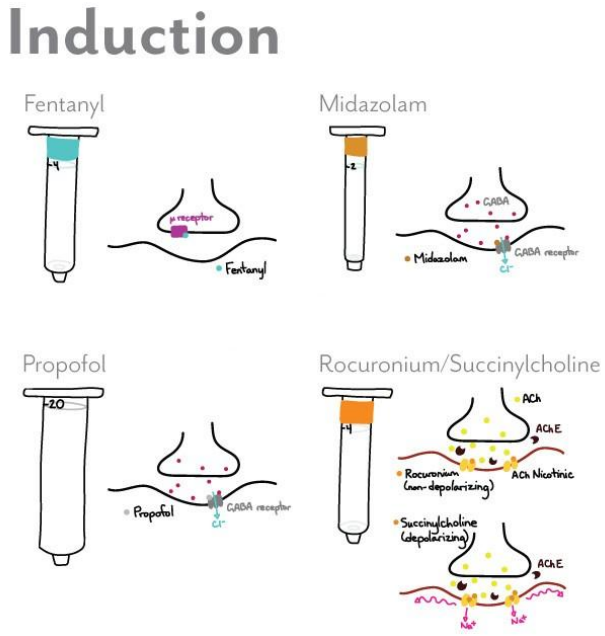

Figure 9. Induction of Anesthesia

When the patient is adequately anesthetized and, therefore, not likely to become hypertensive or significantly increase his heart rate, then he should be intubated. Induction and intubation must be smooth and safe rather than speedy, uncoordinated or disorganized.

Patients with low cardiac output will obviously have a slow circulation time and experience a delay in the onset of action with intravenous drugs. On the other hand, inhalation anesthetics will rapidly come into equilibrium with alveolar gas in patients with a low cardiac output and produce onset of deep anesthesia much faster than normal.

Patients with a cardiac or prepulmonary right-to-left shunt will also experience a slow induction time with inhalation agents, but often a faster induction with intravenous drugs. Many inhalation and intravenous anesthetics reduce systemic vascular resistance. Some also increase venous compliance and pooling. These anesthetics would be dangerous to use in patients with cardiac tamponade who depend on an increased venous pressure for adequate ventricular filling.

The same principles that apply to anesthetic induction agents are also applied to the muscle relaxant used during this period. When tachycardia and hypertension are not desirable, pancuronium bromide should be avoided. On the other hand, when induction produces hypotension or bradycardia, pancuronium is the muscle relaxant of choice.

3.2.4 Maintenance

In general, the patient with cardiac disease should be anesthetized so that this cardiovascular system is neither stimulated nor depressed. The goal is to produce and maintain optimal cardiovascular dynamics at all times. In order to accomplish this objective, it may be necessary to use drugs that produce profound neuromuscular blockade or necessitate reversal or antagonism at the end of the operation. Sometimes the reversal of the actions of those drugs may produce dangerous alterations in circulatory dynamics.

At all times, maintenance of optimal circulatory dynamics is the primary goal both during and following anesthesia. In addition, to provide cardiovascular stability, the anaesthesiologist must be concerned with avoiding agents or techniques that cause atrial or ventricular irritability. Particularly, in patients with ischemic disease, excessive stimulation increases myocardial work requirements and oxygen consumption.

The specific pathology of the patient coupled with the operation to be performed and operative position will often indicate which anesthetic technique will be best. Patients with chronic fibrotic pulmonary changes and a large preoperative pulmonary shunt, undergoing a renal or pulmonary resection in the lateral position, require an anesthetic regimen that uses a high inspired concentration of oxygen, 70% or more.

It has been suggested that patients with coronary artery disease will benefit from anesthetic techniques that produce moderate myocardial depression. There is data that demonstrate, for example, that moderate halothane-induced myocardial depression improves the myocardial blood flow to blood requirement ratio and is, therefore, a good anesthetic to use in patients with coronary artery disease.

In patients who do not have ischemic heart disease, the exact opposite of the ideals for those with coronary artery disease is often most desirable. Patients with cardiomyopathy, cyanotic congenital heart disease and some forms of valvular disease often require stimulation of the heart and circulatory system to maintain adequate myocardial and total body blood flow. Light levels of anesthesia with agents that maintain or increase circulatory levels of epinephrine (see figure 10) and norepinephrine would appear to be most desirable in these patients.

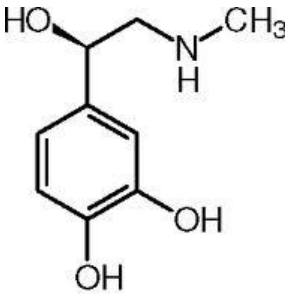

Figure 10. Epinephrine

In considering the properties of the specific anesthetics available to modern anaesthesiologists who have to anesthetize patients with cardiac disease, the old dictum “what you have is not so important, but rather what you do with what you have” is quite appropriate. The skill of the anaesthesiologist plus his knowledge of the cardiac and noncardiac pathology involved and the ideals to be strived for, are far more important in choosing an optimal anesthetic technique than the specific drug or combination of drugs. In the majority of patients, a variety of techniques can work equally well. It is only in patients on the brink of cardiovascular collapse, experiencing severe myocardial ischemia or having no cardiovascular reserve whatsoever that the subtle advantages of one technique will show over another.

The anesthetic techniques for patients with cardiac disease can be divided into three general areas: inhalation techniques, intravenous techniques and various combinations of inhalation and intravenous methods (see figure 11).

Figure 11. Intravenous anesthetics (A) and inhalation anesthetics (B)

The two most popular and important inhalation anesthetics available in 1980 were enflurane and halothane (see figure 12). Although they are two very different compounds, halothane (a halogenated hydrocarbon) and enflurane (a halogenated ether), in many respects, are quite similar. They are both relatively insoluble, potent, volatile, nonexplosive, liquids that are pleasant to inhale and can produce all levels of complete anesthesia in a relatively short period of time with the simultaneous administration of high inspired concentrations of oxygen.

Agents in clinical use	New Agents	Agents of historical interest
Halothane (1956)	Desflurane (1992)	Chloroform (1847)
Isoflurane (1981)	Sevoflurane (1994)	Cyclopropane (1925)
Enflurane (1973)	Xenon (1997)	Diethyl ether (1846)
Methoxyflurane (1960)		Fluroxene (1951)
Nitrous Oxide (1844)		Trichlorethylene (1930)

Figure 12. Inhalation anesthetic agents (Year available for clinical use)

There are some important differences between the two anesthetics that may be concerned in specific patients with cardiac disease. Enflurane is less liable to produce ventricular arrhythmias in the presence of epinephrine and it can produce electroencephalographic patterns consistent with grand mal seizures. Both halothane and enflurane produce significant and probably reasonably comparable levels of myocardial and renal depression. These drugs also depress the central respiratory apparatus, perhaps enflurane to a greater degree than halothane.

The two most important narcotic drugs used for anesthesia of the patient with cardiac disease are morphine and fentanyl. Morphine first became popular after Lowenstein and co-workers demonstrated that 0.5 to 2.0 mg/kg of morphine plus oxygen did not produce changes in any of the cardiovascular variables that they measured in patients without cardiac disease. In patients with aortic valvular disease, this technique decreased systemic valvular resistance and increased cardiac output. In patients with significant impairment of preoperative cardiac output, morphine-oxygen anesthesia maintained or improved total blood flow and did not significantly alter systemic of pulmonary artery blood pressures.

With the beginning of coronary artery surgery in the early 1970s, morphine-oxygen began to be used frequently as an anesthetic technique for these patients. Perhaps the most significant observation was that patients with coronary artery disease were not often nearly as compromised in terms of their cardiac output and anesthetic requirements as patients with severe valvular disease, and therefore often were not adequately anesthetized (frequently aware during operation) with 0.5 to 2.0 mg/kg of morphine. Secondly, the use of very large doses of morphine that were adequate to cause complete anesthesia produced some undesirable side effects including prolonged respiratory depression and increased venous compliance that markedly increased blood requirements.

A third anesthetic technique commonly used in patients with cardiac disease is a combination of intravenous and inhalation anesthetics. The specific effects of most of these techniques on respiratory, cardiovascular, renal and other major organ function have not been studied and are thus unknown. These techniques can produce very adequate levels of anesthesia and desirable cardiovascular and respiratory function. The variety of agents employed, however, often produce undesirable cardiovascular effects that may not be readily apparent to the clinician (see figure 13).

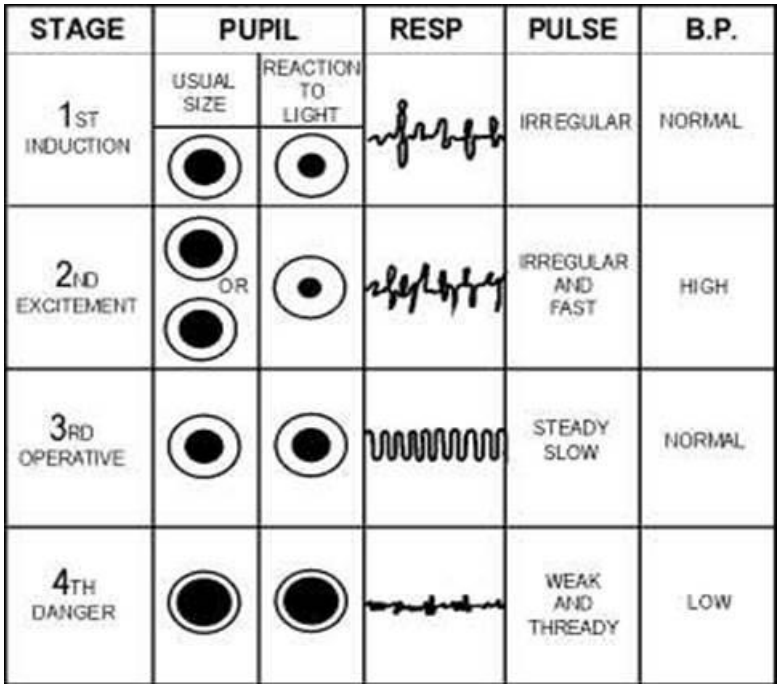

Figure 13. Basic information of every stage of anesthesia

A classic example of this situation is the use of nitrous oxide-narcotic anesthesia with or without a muscle relaxant. It is now known that nitrous oxide-meperidine-oxygen anesthesia produces a minimal amount of blood pressure depression but a significant increase in systemic vascular resistance and decrease in cardiac output. Surgical stimulation in patients anesthetized with this technique results in a return in blood pressure to preanesthetic values, a further increase in systemic vascular resistance and no additional change in cardiac output. While a reduced cardiac output may be well tolerated by most patients with nitrous oxide-meperidine or nitrous oxide plus any other narcotic, some patients with cardiac disease and a severely impaired cardiac output will not tolerate such decreases.

Another misconception among anaesthesiologist is that except for dosages, most narcotics produce similar organ system alterations. This is probably true when the narcotics are used in combination with nitrous oxide and many other anesthetic, sedative and amnesic compounds. But this is not true when the opiates are employed alone in analgesic or anesthetic doses.

The principles governing the use of muscle relaxants during anesthesia in patients with cardiac disease do not differ from those governing usage in patients without cardiac disease. But patients with cardiac disease are more likely to be taking additional drugs that could alter the effects of the neuromuscular blockers.

Many clinicians believe that the high-risk cardiac patient will be anesthetized best by employing, when appropriate, regional or local anesthesia (see figure 14). The rationale is that local or regional anesthesia causes a minimum of circulating myocardial or peripheral vascular depressant compounds and thus cardiac and circulatory dynamics should be least altered with these techniques. On the other hand, it is probably entirely incorrect in patients with ischemic myocardial disease. As has been mentioned previously, these patients do poorly when cardiovascular dynamics, particularly heart rate, myocardial contractility, preload and afterload are increased. In addition, patients with ischemic myocardial disease are frequently extremely apprehensive even when well premedicated, and thus often experience changes in cardiovascular dynamics during regional or local anesthesia. It may be more beneficial to use general anesthesia than regional or local anesthetic techniques in patients with ischemic heart disease.

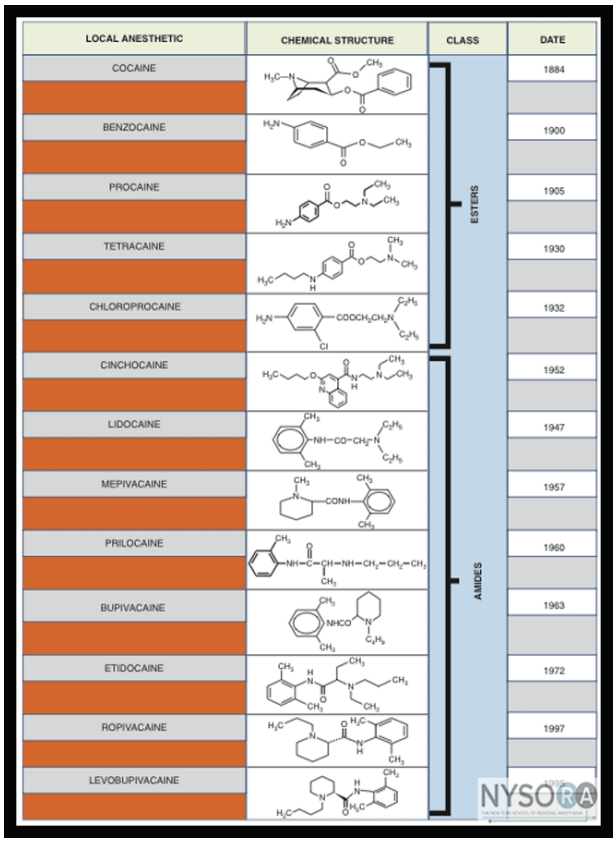

Figure 14. Examples of local anesthetics

The key to a successful anesthesia in all patients, but even more so in patients with cardiac disease, is an understanding of the pathologic physiology and *simplicity*. The importance of simplicity of anesthetic technique, avoiding pharmacologic interactions and increased chance of toxicity secondary to the simultaneous use of a multiplicity of compounds can never be over emphasized. If an anesthetic can be equally well administered using fewer drugs and less mechanical intervention, that is the technique of choice.

It is obvious that many patients with cardiac disease will have marked alterations in absolute or relative circulating blood volume. This may vary from a very low blood volume in patients with severe hypertension to significant increases in volume in patients in congestive heart failure.

Positive pressure ventilation during anesthesia in the cardiac patient can exert a major influence on cardiovascular dynamics. The benefits of positive pressure ventilation for patients with congestive heart failure in keeping alveoli open and thus improving arterial oxygen tensions and saturations is well established. Less well known but equally important is the fact that positive pressure ventilation may actually improve cardiac output by reducing left ventricular-end diastolic pressure in the failing ventricle and permitting the most effective ventricular pressure. On the other hand, positive pressure ventilation can, in the patient with a reduced circulating blood volume, produce a significant decrease in cardiac output and arterial blood pressure by impeding venous return.

3.2.5 Recovery

Termination of anesthesia in the patient with cardiac disease requires knowledge of the ideal method by which anesthesia should be discontinued with minimal influence on cardiovascular dynamics. The postanesthetic recovery period (see figure 15) is of no less importance than the period of induction of anesthesia. Similar principles of reversal of anesthetic and nondepolarizing muscle relaxant apply during this period: reversal of all pharmacologic effects should be accomplished with a minimal effect on cardiovascular and myocardial dynamics.

Figure 15. Recovery room

Patients should be carefully monitored and well oxygenated during transfer from the operating room to the recovery room or ICU[4].

The anaesthesiologist should not abandon his patient until he is satisfied that all organ systems are functioning at optimal capacity considering the stresses of the situation.

[4] **ICU:** Intensive Care Unit

4. Pediatric Anesthesia

4.1 Preanesthetic Visit

The preoperative visit is essential; it should include explanation at the child's level of comprehension of what can be anticipated regarding hospital routine and the pre- and postoperative hospital course. This explanation should be amplified for the parents. Much fear is caused by apprehension of the unknown and a kind empathetic explanation does much to relieve anxiety. It should be simple and honest, in carefully chosen words that the patient can understand. In addition to the routine evaluation, the physician should obtain a family history for any major problems associated with anesthesia such as temperature elevation (malignant hyperthermia) or a relatively prolonged apnea[5].

One should avoid withholding liquids from small children for an extended period of time. The average daily intake and output of water in the infant is approximately one-tenth of his total body water while in the adult, it is only one-twenty fifth. Thus, infants and small children left without fluids for an extended period of time will become dehydrated before the operation. A useful guide in ordering preoperative food restriction is:

NPO[6] of solids from midnight:	
Newborn to six months	Clear liquids with glucose up to four hours before induction of anesthesia
Six months to two years	Clear liquids with glucose up to six hours before induction of anesthesia
Older than two years	Clear liquids with glucose up to eight hours before induction of anesthesia

4.2 Temperature Regulation

The temperature loss occurs in four ways:

- By radiation, a function of the temperature of the solid object surrounding the subject.
- By conduction, a function of the temperature of the surface on which the patient is resting.
- By evaporating from the lungs, a function of ventilation and evaporation from body surfaces.
- By convection, a function of surrounding air temperature and air flow.

[5] **apnea:** a temporary inability to breathe; cessation of breathing
[6] **NPO:** nothing by mouth

The oxidation of the nonesterified fatty acids and other chemical reactions occurring in the brown fat, causes an exothermic reaction that produces heat but also requires significant metabolic expenditure. Intraoperatively, heat loss can be reduced by the use of a warm room, warm prep solutions, warm irrigation for fluids, warm water mattresses, overhead heating units, wrapped extremities and heated anesthetic gases.

4.3 Nervous System

Because of an incomplete differentiation of the cortex and dominance of subcortical centers, it is postulated that an infant may perceive less pain than an adult. On the other hand, Gregory, Eger and Munson have determined that the MAC (minimum alveolar concentration of an anesthetic at which half the patients will not move upon skin incision) is 40% higher for infants than adults.

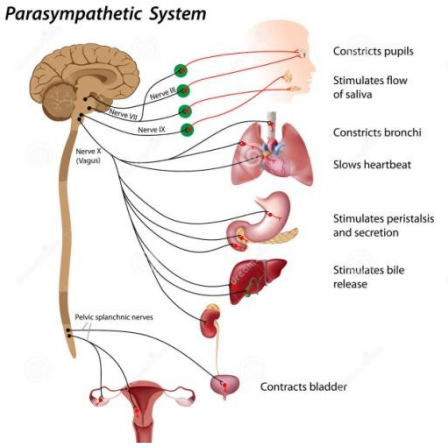

Figure 16. Parasympathetic System

The autonomic nervous system of the infant or young child differs from that of the adult in that the vagus [7] or parasympathetic system predominates (see figure 16). Bradycardia, therefore, is common.

4.4 Respiratory System

The airway of the infant and small child differs from the adult in the following ways.

- *Small nostrils*[8]. Most infants are obligate nasal breathers and do not mouth-breathe. The disproportionally large tongue relative to the size of the infant's mouth also contributes to the difficulty of mouth breathing. Under anesthesia, upper airway obstruction may occur, which can be cleared by opening the mouth and displacing the tongue.
- *High anterior glottis*. The glottis of the infant is located opposite the cervical vertebrae 3-4, as contrasted with the adult glottis, which is opposite to the cervical vertebrae 4-5. This may make endotracheal intubation of the child more difficult than in the adult.
- *Slanting vocal cords.* The anterior limits of the vocal cords slant in the posterior superior direction.
- *A large, U-shaped epiglottis*.

[7] **vagus:** the tenth cranial nerve, which supplies the heart, lungs and viscera
[8] **nostril:** either of the two outer openings of the nose

- *Narrow cricoid ring*. The adult larynx is cylindrical, so that, if the endotracheal tube fits between the vocal cords, it will easily pass into the trachea. A child's larynx is conical, however, with the narrowest portion at the cricoid (see figure 17). Thus, if an endotracheal tube passes between the vocal cords, it still might not pass the area of the cricoid and into the trachea.

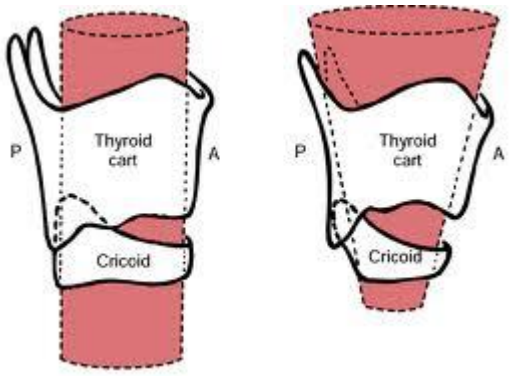

Figure 17. The adult larynx is cylindrical and the child's larynx is conical

- *Pliable sternum*. The infant has a sternum that retracts easily and so the chest wall is extremely compliant.
- *Horizontal ribs*. The child's breathing, therefore, is primarily diaphragmatic.
- *High negative pressure to initiate lung expansion*. The lung, collapsed in utero, may require a high negative intrapleural pressure to initiate expansion.
- *Lower resting $PaCO_2$.* The infant normally has a slightly lower $PaCO_2$.
- *High oxygen consumption.* In relation to weight, however, oxygen consumption and alveolar ventilation of the infant are twice that of the adults.
- *High airway resistance.* Airway resistance is higher in infants than in adults.

4.5 Cardiovascular System

The cardiac output of infants, which is twice that of the adult relative to body surface area, depends on a fast cardiac rate because of small stroke volume. A fall in blood volume is reflected by a decrease in arterial blood pressure.

With a rapid decrease in blood volume, the baroreceptors, active to some degree in the infant, will initially cause tachycardia. This response, however, is less well developed in the infant than in the adult. The infant's heart responds to hypoxia with bradycardia, unlike the heart of the adult, which initially responds to hypoxia with tachycardia.

4.6 Monitoring

The development of better monitoring systems, to more accurately measure physiologic parameters, has made pediatric anesthesia safer. The shibboleth of monitoring is careful and continuous sensory evaluation of the patient by the anaesthesiologist. Specific monitors are listed below.

- The precordial stethoscope of esophageal stethoscope should be used continuously to monitor the heart and breath sounds.
- The electrocardiogram should be monitored for electrical activity. While the electrocardiogram tells nothing about cardiac output, it can alert the anaesthesiologist to the presence of dangerous dysrhythmias.
- Arterial blood pressure of the neonate and child must be monitored and is a valuable tool to asses cardiac output. The Doppler ultrasounds (see figure 18) apparatus can accurately determine blood pressure of the smallest neonate, even in the presence of vasoconstriction, decreased peripheral perfusion or decreased cardiac output.

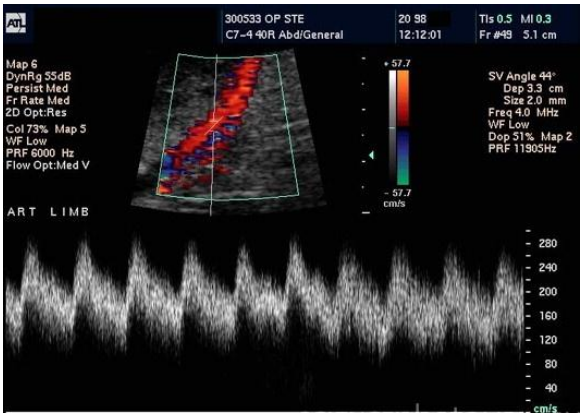

Figure 18. Doppler ultrasounds

- The temperature should be monitored routinely, since the infant undergoing an operation is particularly prone to develop hypothermia. With any temperature rise, the physician must be attuned to the possibility of malignant hyperthermia.

Monitoring physiologic parameters other than with stethoscope, EGB, blood pressure cuff and temperature probe, will depend on the condition of the patient as well as the operative procedure. In the infant, particularly the premature one, arterial oxygen tension should be monitored, as high PaO_2 [9] will cause vasoconstriction of the retinal artery. This represents a factor incriminated in the development of retrolental fibroplasia. Certain procedures and conditions will require an arterial line, pulmonary artery catheter, central venous pressure catheter o electroencephalogram.

[9] **PaO_2:** Oxygen Partial pressure

4.7 Induction of Anesthesia

The method of anesthesia induction depends on the physician's experience with anesthetizing children and on the age of the child. The most frequent approach for newborn infants, particularly those less than 10 days old, is intubation while the patient is awake. For the child less than 6 years old, an inhalation gas induction with contoured face mask is the most frequent approach (see figure 19). The most commonly used inhalational agents are halothane and enflurane; nitrous oxide is usually added. Intravenous induction is acceptable. If the patient has a full stomach, rapid sequence intravenous induction with cricoids pressure or awake intubation are the preferred methods. The most commonly used agent for intravenous induction is thiopental sodium.

Figure 19. Endotracheal intubation

The indications for endotracheal intubation of a child are similar to those in the adult. Procedures about the head and neck, with a few exceptions such as myringotomy or eye exam, require endotracheal intubation. Since the narrowest part of the child's airways is the cricoids, the proper size tube will seal this area. One method of estimating the size of the tube that will be needed is:

$$(Internal\ diameter\ of\ tube) = \frac{Age\ of\ patient}{4} + 4.5$$

Once the endotracheal tube has been placed, the anaesthesiologist must carefully check for bilateral breath sounds and equal symmetric expansion of the chest to be sure the tube has no passed into a mainstem bronchus.

4.7.1 Humidification

The administration of dry anesthetic gases causes damage to the tracheal mucosa as well as impairing the function of the cilia. Procedures lasting longer than one hour, therefore, require humidification of the dry gases. Furthermore, in the infant, dry cold gases significantly increase the loss of heat and the infant may become hypothermic. Thus, the anesthetic gases, should be heated and humidified to ensure stability of the patient's temperature as well as to preserve the tracheal mucosa and cilia.

5. Anesthesia for the Asthmatic Patient

5.1 Clinical Features of Asthma

Asthma involves episodes of bronchospasm associated with wheezing[10] and dyspnea[11], alternating with asymptomatic periods. The nature and extent of the infectious element in true allergic asthma is unknown, but many asthmatic patients have a chronic productive cough, periods of purulent sputum or x-ray evidence of lung infiltration (see figure 20).

The patient with only a yearly asthmatic attack may show normal lungs. An asthmatic person who has attacks more frequently, however, will demonstrate pathology including atelectasis[12] and plugging of airways with tenacious mucus-containing cellular spirals, eosinophils[13] and detached respiratory bronchiolar epithelium with a thickened basement membrane. The lungs of a patient who dies in status asthmaticus are voluminous, but this is considered to be hyperinflation and should not to be confused with severe emphysema, where destruction of tissue and loss of elasticity has occurred.

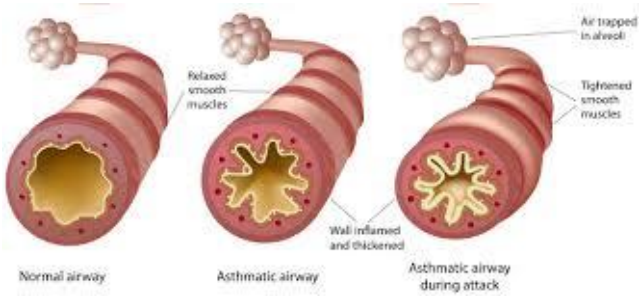

Figure 20. Differences between normal and asthmatic airway

5.2 Pathogenesis of an Asthmatic Attack

The possible pathogenesis of an asthmatic attack maybe appreciated if one realizes that the tracheobronchial tree employs two primary mechanisms for ridding itself of particulate matter and mucus: coughing and functional ciliary activity. The cilia acts only when covered with a blanket of thin watery mucus. When mucus thickens, ciliary rhythm is impaired and whatever mucus is now produced, becomes inspissated in the periphery of the tracheobronchial tree. As desiccation occurs, so does plugging of bronchioles. The only remaining mechanism for clearing the airways at this point is a cough.

[10] **wheeze:** breathe with a whistling or rattling sound in the chest, as a result of obstruction in the air passages.
[11] **dyspnea:** difficult or laboured breathing.
[12] **atelectasis:** partial or complete collapse of the lung.
[13] **eosinophils:** a White blood cell containing granules that are readily stained by eosin.

As attacks progress, so does bacterial infection that can lead to bronchitis. As time passes, the condition may become irreversible with destruction of alveoli, periods of intense asthmatic attacks marked by chronic elevation of frictional airway resistance and the inability to respond to bronchodilators.

5.3 Preanesthetic Management of the Asthmatic Patient

5.3.1 Evaluation

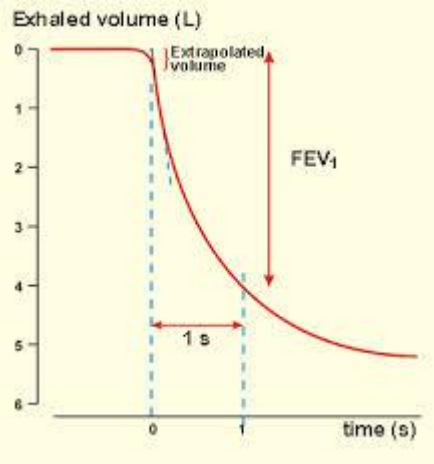

Figure 21. $FEV_{1.0}$

There is a wide spectrum of pathology, symptoms, signs and complications in patients who have been labelled asthmatic because of wheezing and dyspnea. All such patients should have vital capacity and timed vital capacity tests in order to differentiate obstructive from nonobstructive airway disease. If the $FEV_{1.0}$[14] is between 70 and 80 percent of normal, the patient has a modest chronic airway obstruction. An $FEV_{1.0}$ less than 70 percent of predicted in the presence of wheezing and as asthmatic history indicates that the patient is probably asthmatic (see figure 21).

A second group of asthmatic patients are true victims with wheezing, dyspnea, orthopnea[15] and history of a number of such attacks each year. In addition to a thorough physical examination and chest x-ray, these patients should be assessed preoperatively by an $FEV_{1.0}$ test before and after isoproterenol. If the $FEV_{1.0}$ improves, the obstruction is “reversible”.

5.3.2 Premedication

Patients benefit from a good night’s sleep, provided by flurazepam hydrochloride, pentobarbital sodium or secobarbital. Barbiturates may be given orally or parenterally as premedication in a dose of 0.5 mg/kg of body weight. In addition, one may decrease airway resistance, decrease vagal activity and dry secretions with atropine, scopolamine or glycopyrrolate.

An antihistamine with both sedative and drying properties may also be useful. Administration of narcotic drugs preoperatively to the asthmatic patient is controversial since narcotics may cause respiratory depression that persists into the recovery period. On the other hand, narcotics depress the cough reflex, relieve pain and create a general feeling of well-being.

[14] **$FEV_{1.0}$:** volume that has been exhaled at the end of the first second of forced expiration.
[15] **orthopnea:** the inability to breathe easily except when sitting up straight or standing erect.

Steroids have been recommended for improvising pulmonary function and for the prevention of respiratory complications during and after anesthesia. In order to prevent anesthetic and postanesthetic complications for asthmatic patients already taking steroids, additional steroid medication at a full therapeutic dose level is indicated during the perioperative period.

5.3.3 Anesthetic drugs

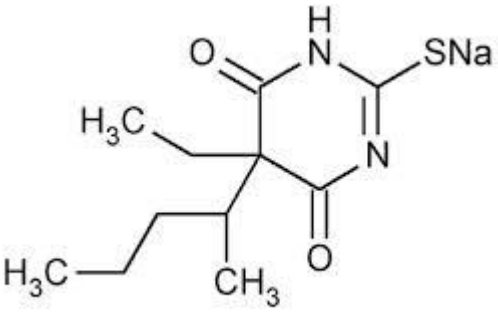

Figure 22. Thiopental sodium

There is virtually no objective information concerning the relationship between anesthetic drugs and complications during or after anesthesia in the asthmatic patients. Thiopental sodium (see figure 22) and other barbiturates have been criticized as induction agents in these patients because clinical evidence indicates that they may cause coughing, which has been related to initiation of bronchospasm.

In order to examine the lower extremity, perineum and inguinal region, low spinal or epidural anesthesia is the technique of choice in the asthmatic patient. Conduction anesthesia does have certain limitations. If the operation lasts longer than anticipated or the surgery becomes more extensive, a general anesthetic must be superimposed. This may be difficult and in instances in which the spinal anesthetic has been used for a specific purpose, such as in the patient with a full stomach, the most feared complication may be created.

Certain general anesthetic agents have been associated with clinical success in the management of asthmatic patients during surgery. In two large series of patients, halothane was considered the most successful inhalation agent; fewer complications occurred with halothane than with thiopental, nitrous oxide, cyclopropane or diethyl ether.

The possibility of cardiac arrhythmias during halothane anesthesia must be considered, since it does sensitize the myocardium to the arrhythmic effects of catecholamines, especially in the presence of hypercabria, hypoxemia or bronchospasm.

Diethyl ether, which for years had been the anesthetic of choice for the management of the asthmatic individual, has three major disadvantages: delayed onset of action, the tendency to stimulate secretions and flammability. Ether is no longer used clinically.

5.4 Bronchospasm

When bronchoconstriction occurs during anesthesia, it is vital to determine whether the patient is actually in an asthmatic attack or if the difficulty breathing and increased impedance are simply due to light anesthesia. Since asthmatic individuals have a sensitive tracheobronchial tree, they may buck, stain or cough on the endotracheal tube (see figure 23). This may progress to wheezing, a severe asthmatic attack and complete bronchospasm. When an endotracheal tube is indicated, the patient anesthetized with a topical anesthetic before the endotracheal tube is inserted. In other words, if it is possible, the patient should inhale halothane or enflurane for 10 to 15 minutes before endotracheal intubation.

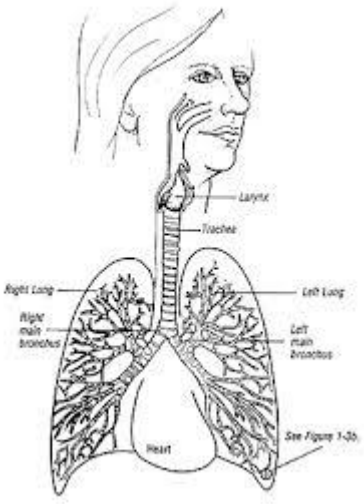

Figure 23. Tracheobronchial tree

Despite clinical and experimental evidence that an endotracheal tube may initiate wheezing, a tube should be inserted to decrease when bronchospasm occurs in the absence of a tube. Nebulized isoproterenol, deep halothane anesthesia, aminophylline or steroids may be used at this time.

5.5 Recovery Room Care

The asthmatic patient should inhale a high oxygen-high humidity mixture in the immediate postoperative period. Pharyngeal and tracheal suction may be necessary because of abundant secretions. To prevent an asthmatic attack in the recovery room, intermittent positive pressure breathing (IPPB) with nebulized isoproterenol may be of prophylactic value, as many other bronchodilator drugs. Assisted ventilation with bag and mask, guided by auscultation, may be useful to improve tidal volume and to avert atelectasis[16]. Daily chest x-rays should be obtained to watch for signs of pneumonia.

A gradually decreasing PaO_2 with a relatively normal $PaCO_2$ probably represents a “shuntlike effect” due to perfusion of atelectatic areas. Should $PaCO_2$ rise, the dead space-tidal volume ratio is probably increasing, overventilation to perfusion may be occurring and the patient may be heading towards an asthmatic attack.

[16] **atelectasis:** collapse or closure of the lung resulting in reduced or absent gas exchange.

5.6 IPPB for the Treatment of Asthmatic Attacks

Intermittent Positive Pressure Breathing (IPPB, see figure 24) should be considered in two types of asthmatic situations. First, consider the administration of IPPB therapy to patients who are not in acute status asthmaticus but who are wheezing or appear clinically to be entering an attack.

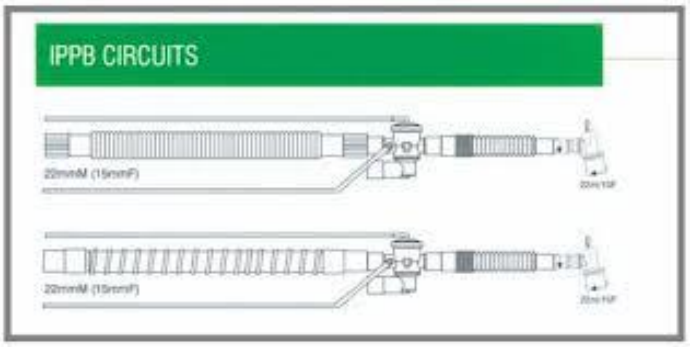

Figure 24. IPPB circuits

The second situation involves the patient with frequent status asthmaticus, in whom long-term mechanical ventilation therapy plus changes in concentration of inhaled atmosphere have been reported. Mechanical ventilation in the severe asthmatic is more dangerous and difficult than ventilating most other patients in respiratory failure and should be considered only when the asthmatic patient has failed to respond the other treatment and is working extremely hard to breathe without improvement.

Additionally, asthmatic persons seem to have a strongly preserved respiratory drive, tend to cough with an endotracheal tube in place and synchronize their breathing with a ventilator. Controlled ventilation, therefore, may be preferred to assisted ventilation. Intermittent mandatory ventilation should be tried before resorting to either heavy sedation with narcotics to depress the cough reflex or paralysis with a nondepolarizing muscle relaxant.

6. Differential Diagnosis of Apnea - Causes

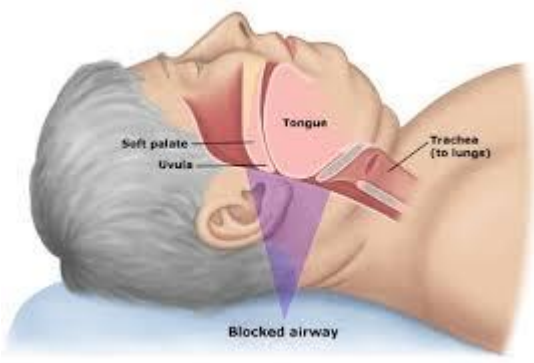

Figure 25. Apnea is a term for suspension of external breathing

Apnea is a term for suspension of external breathing (see figure 25). During apnea, there is no movement of the muscles of inhalation and the volume of the lungs initially remains unchanged. Depending on the patency of the airways, there may or may not be a flow of gas between the lungs and the environment; gas exchange within the lungs and cellular respiration are not affected.

6.1 Premedication Overdose

The action of parenteral drugs is based on the relationship between the concentration of the drug at the receptor site and the sensitivity of the receptor site to that drug. Concentration at the receptor site is directly related to the concentration of drug that reaches the receptor, which depends on many factors, including the route of administration, the degree of ionization of the drug, the amount of drug bound to protein and the relative rates of redistribution, metabolism and excretion of the drug.

6.1.1 Morphine sulphate

A reasonable dose for morphine premedication is 1mb morphine per 10 pounds of body weight, not to exceed 10 mg. As the therapeutic dose of morphine is exceeded, the disadvantages of profound respiratory depression, nausea, miosis and decreased peristalsis outweigh the benefits of euphoria, decreased MAC[17] value and relatively pain-free emergence from anesthesia.

The time interval between administration of the premedicant and induction of anesthesia is of critical importance. Ideally, intramuscular premedicants should be administered 1 to $1\frac{1}{2}$ hour before the induction of anesthesia. It is induced during the denouement of the effect of the premedication. Administration of an inhalation anesthetic at the zenith of the effect of premedication forces the patient to run the risk of cardiorespiratory depression from the additive effects of premedication plus anesthetic drugs.

[17] **MAC:** minimum alveolar concentration

How can the anesthetist decide whether the apnea in a patient is due to the action of morphine or to some other cause? The diagnosis of narcotic overdose is based on clinical intuition and a trial use of a narcotic antagonist, which mechanism action is competitive inhibition. Because of similarity in chemical structure, the receptor site is unable to differentiate between the narcotic and the narcotic antagonist. Ideally, a narcotic antagonist would be able to competitively inhibit the actions of a narcotic on those receptor sites responsible for respiratory depression, without inhibiting the effect of the narcotic on the receptor sites responsible for analgesia.

6.1.2 Secobarbital

Secobarbital, when used as a premedicant, should be administered in a dose of 1.0 mg per pound of body weight, total dose not to exceed 100 mg. Barbiturates can potentiate the respiratory depressing effects of narcotics. Particularly, barbiturates should be used with extreme care in dehydrated, cachectic[18], protein-depleted patients.

6.2 Influence of Protein Binding on Drug Action

Those molecules of a drug that are bound to protein are essentially pharmacologically inactive molecules because they are not available to act at the receptor site. Drug activity depends, therefore, on the nonprotein-bound portion of the drug. If a patient has a low level of circulating protein, then a given dose of a drug that is normally partially protein-bound would have a greater effect on him or her than in an individual who had normal protein content (see figure 26).

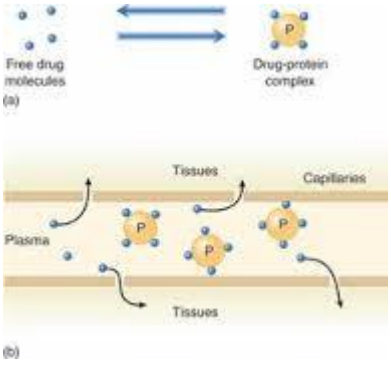

Figure 26. Protein binding on drug action

On the other hand, protein-bound drugs have limited access to the liver and are therefore not deactivated by microsomal liver enzymes. Protein-bound drugs are absorbed by the distal tubule and are slowly excreted. These drugs can become a serum reservoir to maintain serum concentration of the active moiety of the drug.

Several factors influence the extent of protein binding. In the debilitated patient or in the patient suffering from liver disease, less protein will be produced and therefore less protein will be available to bind drugs. Rapid intravenous administration of a drug or rapid absorption from intramuscular sites may exceed the ability of protein to bind that drug. As the drug concentration increases, the number of protein-binding sites decreases.

[18] **cachetic:** relating to or having the symptoms of cachexia, weakness and wasting of the body due to severe chronic illness.

It is also known that protein binding decreases with patient age. It is a common observation that elderly people require fewer drugs than younger people of the same size in order to obtain the same effect.

6.2.1 Thiopental sodium

Thiopental sodium for injection is a short-acting thiobarbiturate that possesses the miraculous property of crossing the blood brain barrier during its first passage through the brain. This allows for an extremely rapid, smooth induction of anesthesia. When administered in therapeutic doses, the drug's activity is dissipated rapidly: within 4 or 5 minutes, a single intravenous bolus of thiopental is cleared from the brain.

6.3 Hyperventilation

One of the most common causes for postoperative apnea is the elimination of the chemical stimulus of respiration through hyperventilation (see figure 27). It is a common misconception that the carbon dioxide tension of the blood is the direct prime chemical respiratory drive.

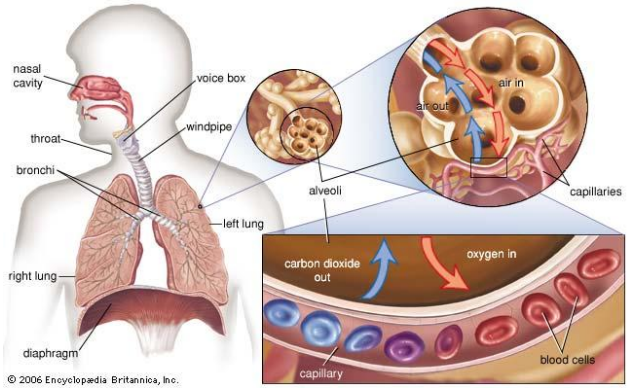

Figure 27. Hyperventilation

Many anaesthesiologists believe that modern anesthetic practice dictates mild hyperventilation during surgery. If carried to excess, the end of the surgical procedure will find the patient in a state of modest respiratory alkalosis[19] and consequently unable to initiate spontaneous ventilation.

To what level must the $PaCO_2$ be lowered before spontaneous ventilation is abolished in the anesthetized patient? Dr. B. R. Fink answered this question in an experiment. He studied a group of healthy volunteers who had a control $PaCO_2$ of 42 torr. These subjects were able to hyperventilate to a $PaCO_2$ in the high teens while maintaining consciousness.

[19] **alkalosis:** an excessively alkaline condition of the body fluid or tissues that may cause weakness of cramps

Later, the subjects received inhalation anesthesia. But then, spontaneous ventilation was abolished when the $PaCO_2$ was lowered by approximately 5 torr. Elimination of spontaneous ventilation was determined by electromyography of the diaphragm. If the subject was further hyperventilated to a lower $PaCO_2$, spontaneous ventilation would return when the $PaCO_2$ had risen to 37 torr.

The experiment demonstrates that anesthesia interferes with the normal response of the respiratory centre to decreased $PaCO_2$. Fink demonstrated that the wakeful state allows spontaneous ventilation at a $PaCO_2$ more than 20 torr lower than control. In the anesthetized state, however, lowering the $PaCO_2$ by 5 torr eliminates spontaneous ventilation. Another implication of these studies is the importance of knowing the patient's $PaCO_2$ while the patient is breathing spontaneously ambient air before induction of anesthesia.

6.4 Hypoventilation

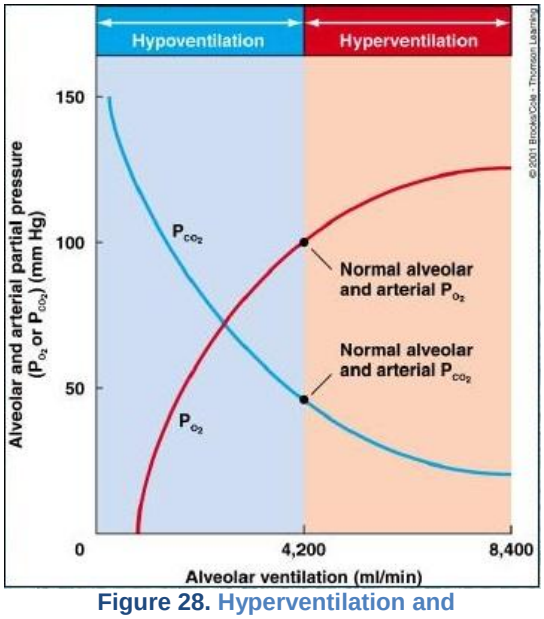

Figure 28. Hyperventilation and hypoventilation

In the patient without respiratory disease, the addition of small amounts of carbon dioxide to the inspired mixture greatly increases minute ventilation. In some patients, however, such as those with advanced emphysema, the $PaCO_2$ can rise so high that the carbon dioxide acts as a narcotic and a respiratory depressant.

During anesthesia, carbon dioxide retention can be caused by sluggishness of the anaesthesiologist. If he fails to maintain constant vigilance and allows the spontaneously breathing patient to continuously hypoventilate (see figure 28), the $PaCO_2$ will increase. More often, elevated carbon dioxide tension during anesthesia results from something as seemingly trivial as exhaustion of the carbon dioxide absorption pellets of from something as catastrophic as the patient becoming disconnected from the anesthesia machine.

Since carbon dioxide retention is a stimulus to catecholamine release, signs of CO_2 retention include hypertension, bounding rapid pulse, warm flushed skin and, occasionally, arrhythmias. The best method of diagnosis is by arterial blood gas analysis. If extreme hypercarbia is discovered, the $PaCO_2$ should be lowered gradually by mild hyperventilation with oxygen. Hyper ventilation that is too rapid can cause increased potassium flux across cell membranes, resulting in arrhythmias. A preoperative blood gas is of inestimable value in determining the level of $PaCO_2$ necessary for postoperative weaning from mechanical ventilation.

6.5 Hypothermia

Body temperature is lowered intentionally in certain situations in order to protect the brain and other tissues from anoxia. If a 1ºC decrease in temperature lowers the cerebral metabolic oxygen consumption by 7 percent, a decrease in body temperature from 37ºC to 30ºC (see figure 29) decreases the cerebral need for oxygen by approximately 50 percent. During operation in which the brain is at risk, such as intracerebral vascular surgery or open heart surgery, it is a common practice to try to decrease body temperature.

Sometimes, however, the lowering of body temperature is unintentional and undesirable. Below 33ºC, many patients suffer respiratory depression or even respiratory arrest.

6.6 Hyperthermia

The syndrome of malignant hyperpyrexia can occur at any age, but it is most common in children. It is characterized by a profound, rapid increase in body temperature that usually occurs shortly after the induction of anesthesia.

One of the earliest diagnostic features is rigidity following the administration of succinylcholine. The patient's temperature can rise as rapidly as 1ºC per minute and as high as 40.5ºC (see figure 29). There is a progressive hypercarbia as well as hypoxemia, which may lead to cardiac and respiratory arrest. Treatment must be instituted immediately with iced lavage of opened pleural or peritoneal cavities, ice applications to the skin, the use of cold IV solutions and cold gastric lavage. The patient must be hyperventilated with 100% oxygen and followed closely for changes in blood gases, serum electrolytes and temperatures.

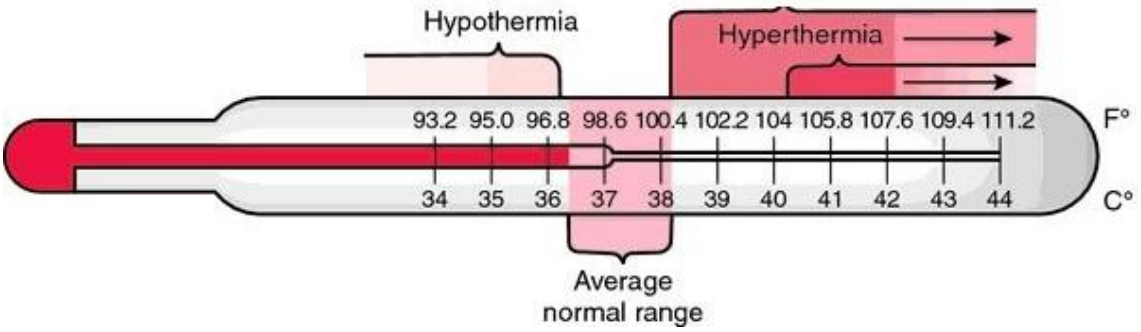

Figure 29. Hypothermia and hyperthermia

6.7 Inhalation Anesthetics

All inhalation anesthetics can depress respiration. Some appear to be respiratory stimulants in the early stages of anesthesia because of their irritant effect on the respiratory mucosa.

When the end of the operation is near, the experienced anaesthesiologist turns off the potent anesthetic and ventilates the patient only with nitrous oxide and oxygen in order to “blow off” the residual anesthetic. Clinical skills involve integrating all factors that concert the uptake and distribution of an anesthetic agent, with the clinical judgment of the appropriate time to turn off the drug so that the patient will awake just as the surgical procedure is completed. Extensive experience is required to correlate all those factors herein described individually, in order to rationalize time the proper moment for discontinuance of the anesthetic agent.

7. Basic information about Anesthesia

The term “anesthesia” comes from the greek for “loss of sensation”, but that is not the only effect it causes in your body. It can also relieve pain, give you amnesia to knock out your memory of the procedure or how it feels, reduce anxiety and paralyze your muscles.

This is usually confused with a similar term: analgesia. Analgesia refers to the reduction or relief of pain and anesthesia refers to lack of sensation. Therefore, analgesia usually accompanies anesthesia. Note that when local anesthetics are used to provide anesthesia, they also frequently cause muscle weakness or muscle relaxation.

7.1 Types of anesthesia

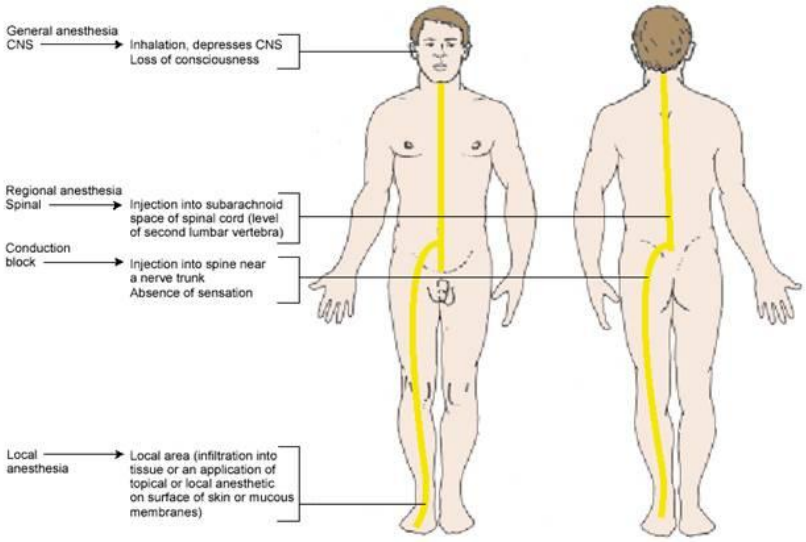

Figure 30. Types of Anesthesia

7.1.1 Procedural sedation

This type of anesthesia is used for short, relatively minor medical procedures and is also known as conscious sedation or twilight anesthesia. In addition to dental work, procedural sedation is used for things like setting broken bones, Lasik[20] and minor cosmetic surgeries.

[20] **Lasik:** (*Laser-Assisted in situ Keratomileusis*), commonly referred to laser eye surgery or laser vision correction.

Under procedural sedation, patients remain fully awake and can respond to questions and instructions. They do not usually remember the procedure or the short period of time following it. Some of the drugs used in procedural sedation can make patients feel giddy or euphoric.

Procedural sedation has a lot in common with general anesthesia. This is because the same types of drugs used in general anesthesia are also administered in this type of anesthesia; they are just given in much smaller amounts.

In high doses, these drugs induce sleep and paralysis and affect the cardiovascular system, but in lower doses, they calm the patient and reduce anxiety. For procedural sedation, one of these types of drugs is used in combination with an analgesic such as fentanyl for pain relief.

Procedural sedation lasts as few as five or ten minutes or as long as an hour. Recovery is speedy and patients will not usually have the side effects associated with general anesthesia, such as vomiting, nausea or dizziness (although they can still occur). Patients under conscious sedation still have to be carefully monitored to ensure that they do not slip into deeper sedation.

7.1.2 Local Anesthesia

Local anesthesia is used to make a very small area of the body, such as a patch of skin, insensitive to pain. It typically provides both analgesia and paralysis by blocking the nerves' impulses so they cannot travel to the brain, but patients may still feel pressure and sensation.

This type of anesthesia can be topical, or isolated just to the surface. These are usually in the form of gels, creams or sprays. They may be applied to the skin before the injection of a local anesthetic that works to numb the area more deeply, in order to avoid the pain or the needle, or the drug itself. The type of local anesthetic patients are injected might be given before procedures like stitches or debridement.

Drugs used in local anesthesia usually end in the suffix "-aine" because they are chemically very similar to cocaine, the first local anesthetic. The problem about using cocaine as an anesthetic is that it is addictive and highly stimulating to the cardiovascular system, so synthetic alternatives were developed. Some of these drugs have negative side effects on their own, such as allergic reactions, and have fallen out of favour.

Local anesthesia usually wears off within four to five hours. The pain relief lasts longer than the actual procedure most of the time. There are usually very few side effects, but patients do have to be careful with the numbed area. In rare cases, injected local anesthetics can cause nerve damage, but they are typically low-risk if they are administered correctly to a healthy person.

7.1.3 Regional Anesthesia

Sometimes, the terms “local anesthesia” and “regional anesthesia” are used interchangeably. Regional anesthesia is used in a wider region of the body. For example, while local anesthesia may be used to numb an area on the leg, regional anesthesia can numb the entire leg. This is known as peripheral regional anesthesia because it blocks a single nerve or specific bundle of nerves. The other type of regional anesthesia is central anesthesia, which usually involves an injection into the cerebrospinal fluid or the epidural space just outside the spinal canal.

Regional anesthesia is also known as a nerve block. Some of the same drugs in the local anesthesia are used in regional anesthesia; they are used in larger dosages and have a stronger effect on the central nervous system. Patients can remain conscious for procedures under regional anesthesia, but they may also be sedated during the administration of the block, during the medical procedure or during both. Sometimes, regional anesthetics are given with a single injection, but they can also be given intravenously or continuously through a catheter.

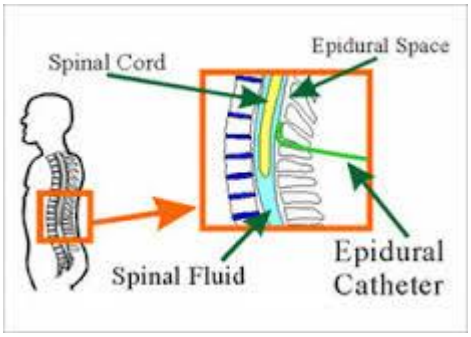

Figure 31. Epidural

Women who have given birth are probably very familiar with the central anesthetic technique known as an epidural. In this procedure, an anesthesiologist inserts a catheter into the epidural space, typically in the lower back area. Spinal blocks, which are injected into the cerebrospinal fluid, are often used for other procedures below the waist, such as caesarean sections of hernia surgery. They tend to paralyze further than epidurals.

Regional anesthesia carries more risks than local anesthesia, such as seizures and heart attacks, because of the increased involvement of the central nervous system. Sometimes regional anesthesia fails to provide enough pain relief or paralysis and switching to general anesthesia is necessary.

7.1.4 General Anesthesia

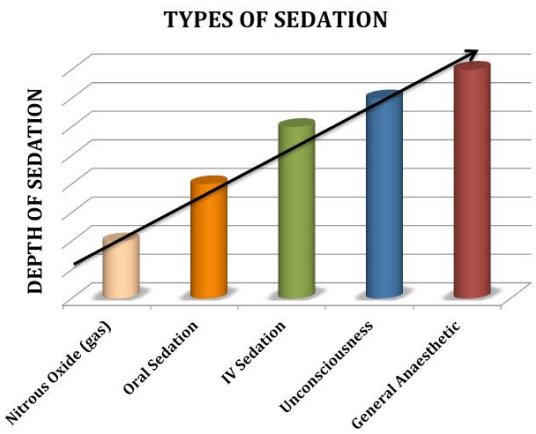

Figure 32. General Anesthesia

When patients get general anesthesia, they are totally unconscious and immobilized. They do not feel, sense or remember anything that happens after the drugs begin to work on your system. It is not completely clear exactly how general anesthetics work, but the current accepted theory is that they affect the spinal cord (which is why patients end up immobile), the brain stem reticular activating system (which explains the unconsciousness) and the cerebral cortex (which results in changes in electrical activity on an electroencephalogram).

Complex surgeries that require a long period of time to perform, typically require general anesthesia. When patients are under this type of anesthesia, they will be wearing a breathing mask or breathing tube, because the muscles become too relaxed to keep your airways open.

There are four stages of general anesthesia:

- During the first stage, induction, the patient is given medication and may start to feel its effects but has not yet fallen unconscious.
- Next, patients go through a stage of excitement. They may twitch and have irregular breathing patterns or heart rates. Patients in this stage do not remember any of this happening because they are unconscious.
- During stage three, the muscles relax, breathing becomes regular and the patient is considered fully anesthetized.
- Stage four is not a part of the regular process. This is when a patient has received an overdose of drugs, which can result in heart or breathing stoppage, brain damage or death, if swift action is not taken.

As the analgesic effect of the anesthetic wears off, patients would also receive some sort of pain relief: an oral medication or even morphine, depending on the surgery. Some people recover within an hour, while others take longer to completely awaken.

After waking up, it is possible that patients will deal with lasting side effects: vomiting, nausea and numbness in the area where surgery was performed. They will probably feel disoriented and they will require assistance to get around. It is also important to mention that there are serious risks associated with general anesthesia, including suffocation, allergic reaction, organ failure, stroke and death.

7.2 History of Anesthesia

By the mid-1840s, the only two anesthetic agents regularly used in industrialized countries were opium and alcohol. Both had many negative side effects, such as addition, and neither could typically dull the pain completely by themselves. Doses that are large enough to provide the desired effect, could just as easily result in death. Sometimes, patients were knocked unconscious by a blow to the head.

Figure 33. Dr. William Morton

Everything changed in 1846. A dentist named Dr. William Morton put on a demonstration at Massachusetts General Hospital when he removed a tumour from the jaw of a patient. Prior to the operation, he used a sponge soaked with ether to render his patient unconscious. Afterwards, the patient claimed that he had no memory of the operation of any pain.

A few years after medical journals published articles about Morton, Dr. Crawford Long stated that he had first used ether in operation in 1841 after observing its effects upon recreational users. In addition, Dr. Charles Jackson claimed that his work had influenced Morton.

The American Medical Association as well as the American Dental Association endorsed Dr. Horace Wells, a dentist, as the first person to use nitrous oxide to pull teeth in 1845. Chloroform was first used as an anesthetic by Dr. James Simpson in the mid-1840s as well.

Anesthesia continues to evolve and become safer, enabling doctors to perform necessary and life-saving operations.

8. Synthesis of Benzocaine

8.1 Objective

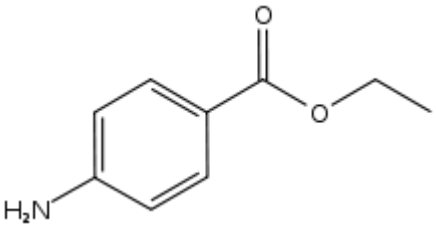

Figure 34. Benzocaine

With experiment, it will be possible to learn how to synthesize Benzocaine, which is a local anesthetic, commonly used as a topical pain reliever or in cough drops. Benzocaine is the ethyl ester of p-aminobenzoic acid (PABA). It can be prepared from PABA and ethanol by Fischer esterification or via the reduction of ethyl p-nitrobenzoate. Benzocaine is barely soluble in water; it is more soluble in dilute acids and very soluble in ethanol, chloroform and ethyl ether. The melting point of benzocaine is 88–90 °C and the boiling point is about 310 °C. The density of benzocaine is 1.17 g/cm^3. Benzocaine was first synthesized in 1890 by the German chemist Eduard Ritsert (1859–1946), in the town of Eberbach and introduced to the market in 1902 under the name "Anästhesin".

8.2 Necessary instruments and materials

- Balance
- Buchner funnel
- Florence flask
- Graduated cylinder
- Pipette
- Iron stage
- Condenser
- pH testers
- Glass rod
- Forceps
- Thermometer
- Rubber connector
- Maria bath
- Capillary tubes
- Wooden pegs

- p-aminobenzoic acid (PABA)
- EtOH
- H_2SO_4
- NaOH
- Distilled water

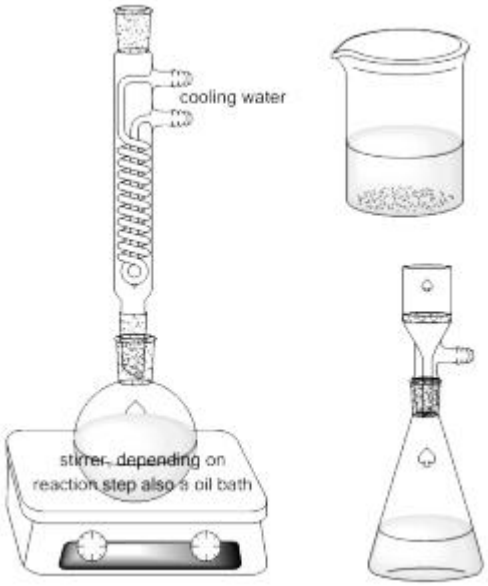

Figure 35. Equipment

8.3 Procedure

First of all, the iron stage was prepared by fixing an utility clamp which held that condenser. Next to the iron stage, a heating mantle was located. Then, 30 ml of ethanol were disposed in a graduated cylinder and 3 ml of H_2SO_4 were fixed in a pipette. At that point, 20 g of NaOH were dissolved in 200 ml of distillate water in order to get a 2,5 M dissolution.

At that time, 3 g of p-aminobenzoic acid (PABA) were weighed with a balance and were placed in a Florence flask with a glass rod to help us. Later, the ethanol was added. When it was dissolved, 3 ml of sulphuric acid were carefully added in ice bath, because this reaction is very exothermic. The Florence flask with the dissolution was joined to the condenser and was put on the heating mantle. The condenser was connected to a tap with a rubber connector. From then on, the mixture was stirred for 82 to 90 minutes at 130 ºC, for maximum yield (see figure 36).

Figure 36. Iron stage, condenser and heating mantle

Next, the solution was cooled down to room temperature and NaOH was added until the pH was approximately above 7. With forceps, the pH testers were placed in the solution to check its pH. Finally, the benzocaine was filtered from the solution using a Buchner funnel and a rubber connector to the tap, in order to make a vacuum drying.

Once the benzocaine was obtained, it was needed to know if it was pure or it had impurities. So, sample's melting point was determined to compare the melting point of pure benzocaine, ranging from 88 ºC to 90 ºC.

Four capillary tubes were filled with a little proportion of the sample, in order to have replicas of the experiment. At that time, the open side of each tube was closed with fire to avoid losses of the sample. Soon after, the capillary tubes were placed in a bain-marie which contained a thermometer to control the temperature. Each capillary tube was disposed with wooden pegs into the water as it heated.

8.4 X-ray diffraction

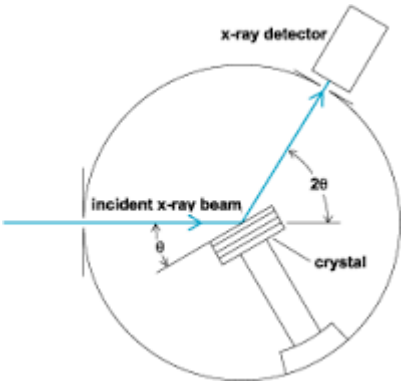

Figure 37. X-ray diffraction

In the autumn of 1912, when he was only 22 years old, William Lawrence Bragg realized that X-rays could be used to detect the arrangements of individual atoms inside solid crystals. With his father's help he created a new science of X-ray crystallography. For his insight, Lawrence Bragg became the youngest ever Nobel Laureate in 1915.

X-ray diffraction relies on the dual wave/particle nature of X-rays to obtain information about the structure of crystalline materials. A primary use of the technique is the identification and characterization of compounds based on their diffraction pattern.

X-ray diffraction is based on constructive interference of monochromatic X-rays and a crystalline sample. These X-rays are generated by a cathode ray tube, filtered to produce monochromatic radiation, collimated to concentrate and directed towards de sample. The interaction of the incident rays with the sample, produces constructive interference and a diffracted ray when conditions satisfy Bragg's Law ($\lambda = 2\,d\,\sin\theta$). This law relates the wavelength of electromagnetic radiation to the diffraction angle and the lattice spacing in the crystalline sample. These diffracted X-rays are then detected, processed and counted.

By scanning the sample through a range of 2θ angles, all possible diffraction directions of the lattice should be attained due to the random orientation of the powdered material. Conversion of the diffraction peaks to d-spacings allows identification of the sample because each substance has a set of unique d-spacings. Typically, this is achieved by comparison of d-spacings with standard reference patterns.

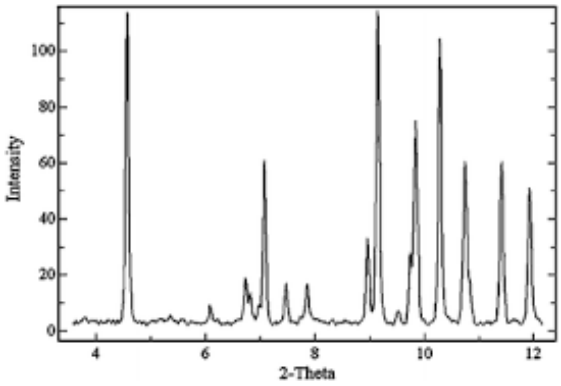

Figure 38. Benzocaine's X-ray diffraction

The sample was exposed to an X-ray diffraction, to verify if it was benzocaine at the Department of Geology of Autonoma University of Barcelona.

It was prepared a slide with benzocaine after grinding it with a mortar and a pestle, because the crystals were too big to use. Then, it was made the diffraction process during approximately 20 minutes.

8.5 Results

While synthesizing the benzocaine, some difficulties were overcome. First of all, when cooling down the solution, it solidified before testing its pH. So, it was necessary to heat it a bit again and test the pH when it became liquid. Then, while neutralizing the pH, it was used too much NaOH and the solution's pH became basic. To counteract the action of NaOH and make the solution's pH neutral, it was HCl. When it has got a solution with a pH above 7, it was kept with the procedure.

However, while making the vacuum drying, it was considered that the sample contained benzocaine and NaCl, as a product of the reaction between NaOH and HCl. For that reason, it had been added a lot of water to dissolve the salt and obtain pure benzocaine.

Figure 39. Melted benzocaine at 89-90 ºC

When the capillary tubes were put in bain-marie, the results showed that it was pure benzocaine. The anesthetic melted between 89 ºC and 90 ºC, because it went from a white solid to a transparent liquid, as it can be seen in figure 39.

Finally, after the X-ray diffraction, the comparison of the d-spacing of the sample with the standard reference pattern of benzocaine was obtained (see figure 40).

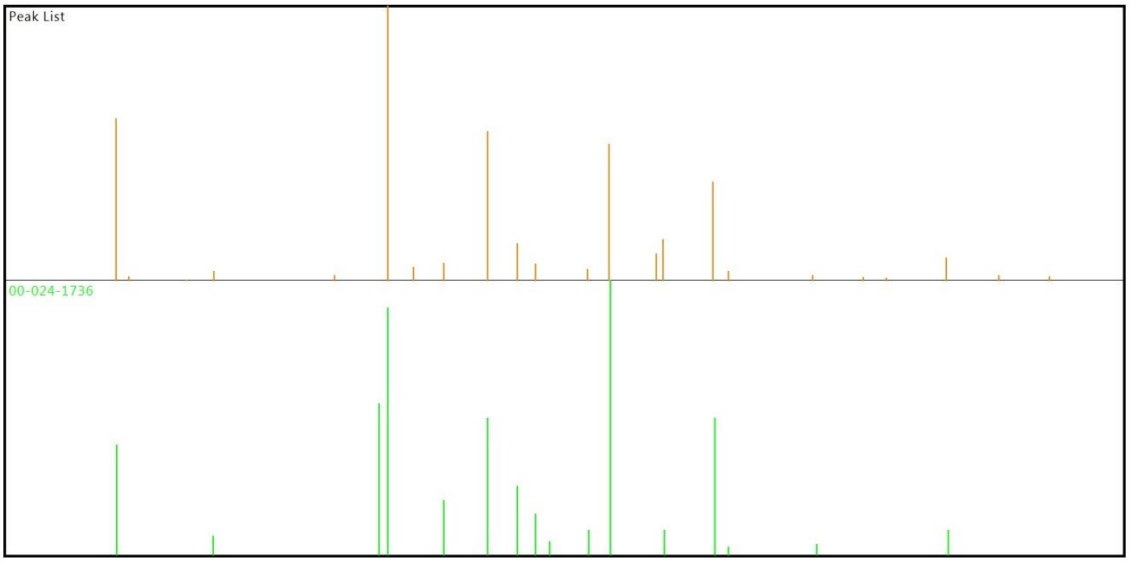

Figure 40. **Comparison of the d-spacing of our sample with benzocaine's standard reference pattern**

The upper graphic shows the d-spacing of the sample and the second one shows the reference pattern of benzocaine. After comparing both of them, it can be seen that most of the peaks are in the same position and only there is a little alteration in the frequency of them.

To sum up, taking into account the melting point of our sample and the X-ray diffraction, we can affirm that we have obtained pure benzocaine. We obtained 2.1 g of the anesthetic and the yield of the reaction is 58%.

9. Study of the X-ray diffraction of benzocaine

In the results of the X-ray diffraction of the sample and after having compared the d-spacing of the benzocaine previously synthesized with the standard reference pattern of this anesthetic, it was realized that the sample's graphic showed peaks that do not appear in the standard reference pattern. It could be because most of the peaks are too small and maybe they were considered as not really important. Then, it was decided to calculate all the theoretical picks that should appear in the graphic by using the Bragg's Law and the Miller Indices with all the possible combinations by doing a permutation with repetition from 0 to 9.

In order to do it faster, software was specially designed for this research project. It calculates the permutation and introduces each combination into

$$d = \frac{1}{\sqrt{\frac{h^2}{a^2} + \frac{k^2}{b^2} + \frac{l^2}{c^2}}} .$$

After having calculated the value of *d*, it is substituted in the Bragg's Law in order to obtain the angle, 2θ. Then, this computer programme shows all the picks that should appear in the d-spacing of benzocaine ordered by the angle. It also has the comparison of the spacing of the sample with the standard reference pattern, so peaks can immediately be located.

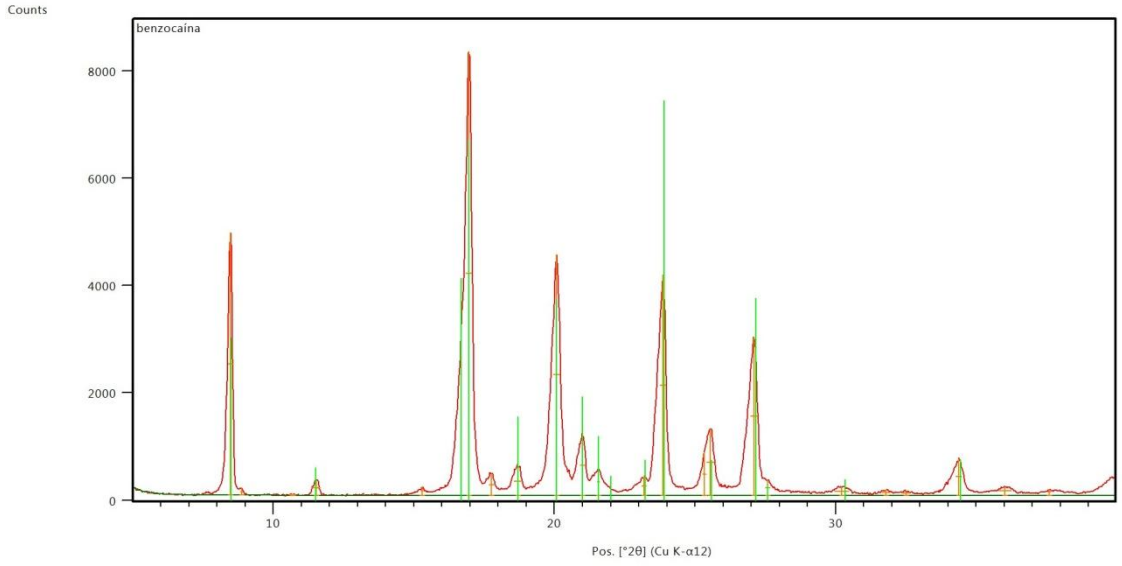

Figure 41. Result of the X-ray diffraction

The red line in figure 41 is the sample's d-spacing and the green one is the standard reference pattern. Taking into account the peak's list obtained by the computer programme, it has been checked how many peaks are missing or how many of them are just represented in the d-spacing of the sample (figure 42).

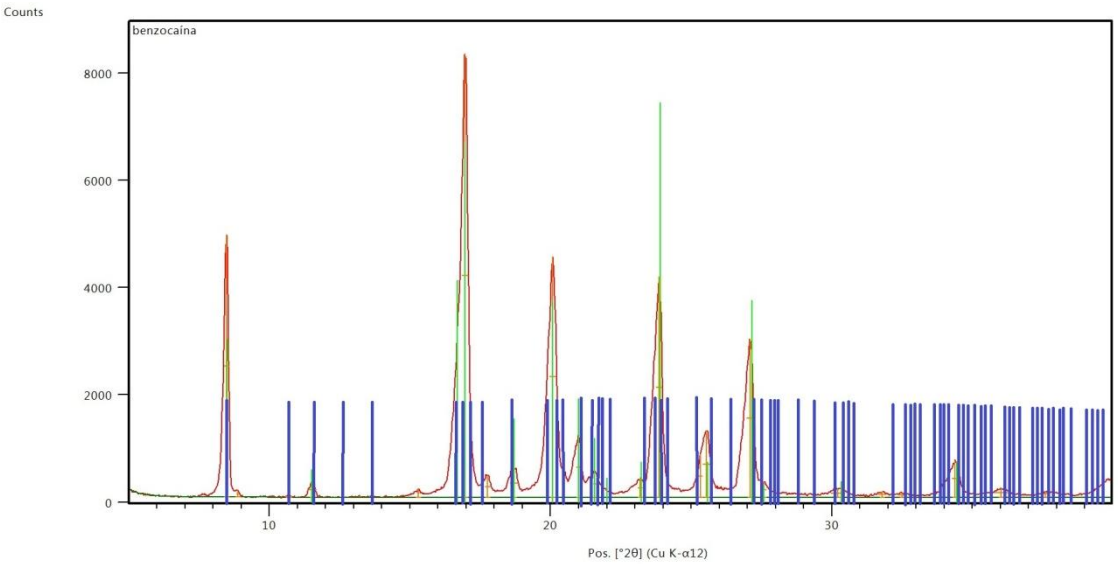

Figure 42. Comparison of the X-ray diffraction's results and software's results

After looking at the figure, the peaks that were detected by using the software, were only represented in the graphic with the red line, the one that represents the sample:

h	k	l	d	2θ
0	0	1	8.18	10.815914586328407
1	1	0	5.144231598904647	17.23813274847233
3	0	2	3.5205475681135057	25.298511097653094
7	0	1	2.786937153693694	32.117775787731084
3	2	0	2.478663175112329	36.242549874497485
1	1	3	2.4091653816744443	37.326054497996175

In conclusion, the d-spacing obtained by the computer programme and the study of the peaks of the X-ray diffraction are congruent with a sample of pure benzocaine origin as it can be seen by simple comparison. Also, the differences observed with the standard reference pattern were not impurities. After analyzing the results, we can conclude that we definitely have obtained pure benzocaine. It has been supported by the result of measuring the melting point of the sample, which leaves no doubt.

10. Induction of anesthesia to microorganisms

10.1 Objective

After having synthesized pure benzocaine, it was necessary to know how effective it was. To prove it, daphnia and paramecium were induced the benzocaine and the thiopental sodium. The main objective was to reduce the heart rate of the microorganisms or to see how their mobility was modified. This experiment was done because it was a way of seeing how anesthesia acts when being introduced to a living being. Then, the problems that anesthesia can cause would be understood better.

Figure 43. Paramecium

Paramecium is a genus of unicellular ciliated protozoa. They are heterotrophs and live in aquatic environments, usually in warm water. They are capable of both sexual and asexual reproduction. This last one is the most common and it is accomplished by the organism dividing transversely. Parameciums only reproduce sexually under stressful conditions.

Species of paramecium (figure 43) range in size is 50 to 300 micrometers in length. Cells are typically ovoid, elongate and are enclosed by a stiff but elastic membrane (pellicle), uniformly covered with simple cilia.

Daphnia is a genus of small, planktonic crustaceans, from one to five millimeters in length (see figure 44). They are members of the order Cladocera and they are one of the several small aquatic crustaceans commonly called “water fleas” because of their saltatory swimming style, resembles the movements of fleas. Daphnia lives in various aquatic environment ranging acidic swamps to freshwater lakes.

Figure 44. Daphnia

In many species, the carapace is translucent or nearly so. Even under a relatively low-powered microscope, the feeding mechanism can be observed. The heart is at the top of the back, just behind the head and the average heart rate is approximately 180 bpm under normal conditions.

10.2 Necessary instruments and materials

- Syringe
- Needle
- Balance
- Spatula
- Beakers of 50 ml
- Concave slides
- Flat slides
- Dropper
- Microscope
- Thiopental sodium
- Benzocaine
- Physiological saline serum
- Paramecium
- Daphnia

10.3 Procedure

10.3.1 Preparation of the diluted solutions

Firstly, the solutions of benzocaine and thiopental sodium should be prepared, very diluted because the microorganisms are too small. One gram of thiopental is added to 10 ml of physiological saline.

$$\frac{1\ g\ thiopental}{10\ ml\ saline} = \frac{0.1\ g\ thiopental}{1\ ml\ solution}$$

Then, 0.1 ml of this solution is taken with a needle and a syringe and it is added to 10 ml of physiological saline, which is disposed in a beaker of 50 ml.

$$\frac{0.1\ g\ thiopental}{1\ ml\ solution} \times \frac{0.1\ ml\ \ solution}{10\ ml\ saline} = \frac{0.001\ g\ thiopental}{1\ ml}$$

This last process was repeated again.

$$\frac{0.001\ g\ thiopental}{1\ ml\ solution} \times \frac{0.1\ ml\ \ solution}{10\ ml\ saline} = \frac{0.00001\ g\ thiopental}{1\ ml}$$

Finally, 1 ml of the resulting solution is added to 10 ml of saline. A solution containing 1 ppm (0.000001 g) of thiopental is got.

$$\frac{0.00001\ g\ thiopental}{1\ ml\ solution} \times \frac{1\ ml\ \ solution}{10\ ml\ saline} = \frac{0.000001\ g\ thiopental}{1\ ml}$$

The same procedure has to be done to prepare the diluted solution of benzocaine. However, at the beginning of the process, 0.1 g of benzocaine is added to 10 ml of ethanol instead of one gram and physiological saline. That is because we have exactly that quantity of thiopental and we are able to reduce the possibility of making a mistake while weighing the anesthetic, but we can do it faster with 0.1 g of benzocaine. What is more, we do not use physiological saline because benzocaine dilutes in ethanol. This leads to a modification at the last stage of the preparation of the diluted solution of benzocaine: at the very end, 0.1 ml of the resulting solution is added to 10 ml of saline, instead of 1 ml taken in the case of thiopental.

10.3.2 Induction of anesthesia to daphnia and paramecium

Parameciums are taken with a dropper and they are put in three concave slides: one for benzocaine, another for thiopental and a group of control, which is going to be administered physiological saline serum. Replicas are not needed because, in each slide, there are some Parameciums and they are replicas to the other ones.

Daphnia are also taken with a dropper and they are put in five flat slides: two for benzocaine, two for thiopental and a group of control, which is also going to be administered physiological saline serum. In this case, we do need replicas, because we are going to work with one daphnia in each slide.

The group of control is put in a microscope that is going to be checked during all the experiment, because we need to be aware of the normal heart rate of the daphnia or the mobility of the paramecium. This group is going to be administered physiological saline serum because it will not disturb them and this, as well as the replicas, will assure that trustful results were obtained.

First, the group of control is put in the microscope and it is administered the physiological saline serum. Then, the group of paramecium that is going to be given the benzocaine is disposed in another microscope, which is connected to a computer and that gives the opportunity of filming the microorganisms. This last group of paramecium is administered 0.1 ml of the diluted solution of benzocaine. Then, it is removed and the group that is going to be given the thiopental sodium is put in the microscope and it is given 0.1 ml of the diluted solution.

After doing that, the group of control of the daphnia is disposed in the microscope that is going to be checked and the saline serum is administered. The same steps of the procedure with the paramecium must be done with the daphnia too. However, in this case, replicas of the experiment are needed and it has to be repeated.

10.4 Results

After having administered the anesthetics and the physiological saline serum to both species of microorganisms, it can be affirmed that both of them had the same impact on paramecium. Benzocaine, as well as thiopental sodium, have reduced the mobility of them and made them move in circles within the first five minutes after the application.

However, daphnia were not disturbed or affected by the anesthetic. It was considered that it could be because they are bigger than paramecium and even they have received 0.9 ml of each anesthetic, the results were the same: the heart rate was between 216 and 228 bpm, the same as the group of control.

11. Conclusions

After having done all this research, it was realized that all the objectives have been achieved.

Regarding to theoretical part it was possible to:

- Know what anesthesia is and how it works into a living being.
- Have learnt about the history, the types of anaesthesia and the difference between them.
- Know that analgesia and anesthesia have different effects when they are administered.
- Be aware of the problems that anesthesia can cause and how it has to be given to people with different diseases or specific problems in health.

Regarding to practical part:

- In the laboratory, it has been synthesized benzocaine, a local anesthetic.
- The sample was induced to paramecium and daphnia and it has been seen how the mobility of paramecium was reduced. However, the heart rate of the daphnia was not disturbed probably because they are bigger than paramecium and it was used a very diluted dose.
- The obtained sample has also been analyzed and studied with an X-ray diffraction and it permitted to assure that benzocaine synthesized is pure.

Then, the hypothesis

> It is possible to synthesize an anesthetic which reduces the heart rate or the mobility of microorganisms.

has been verified, because the anesthetic has reduced the mobility of paramecium, which swam slower and in circles when they were administered benzocaine and thiopental sodium.

However, the heart rate of daphnia has not been reduced. It is easy to suppose that it has been because they are much bigger that paramecium.

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http://www.fcps.edu/islandcreekes/ecology/paramecium.htm

http://www.nytimes.com/2013/12/15/magazine/what-anesthesia-can-teach-us-about-consciousness.html?pagewanted=all&_r=0

http://www-outreach.phy.cam.ac.uk/camphy/xraydiffraction/xraydiffraction_index.htm

http://www.sharecare.com/health/health-care-basics/how-anesthesiologist-how-much-anesthesia

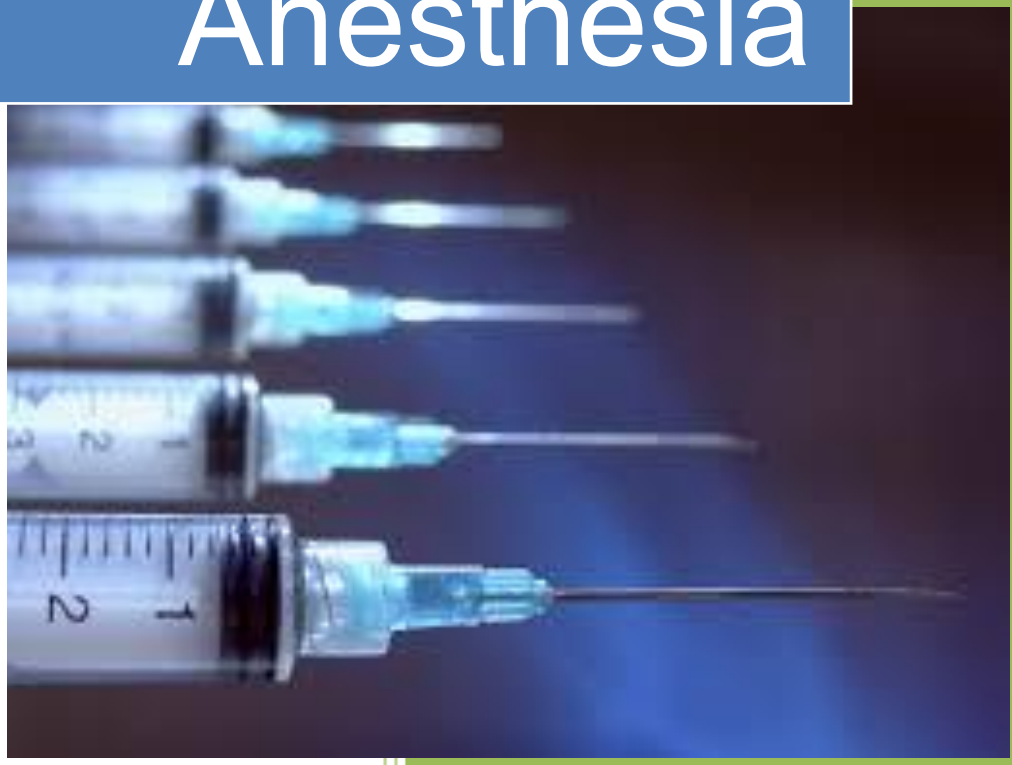
http://www.smc.edu/academicprograms/physicalsciences/pages/equipment.aspx

http://www.xos.com/techniques/xrd/

http://www.youtube.com/watch?v=Vqv1tt4MtYE&hd=1#

http://www.youtube.com/watch?v=ZMxT8ra1hwk&hd=1

Anesthesia



ANNEXES

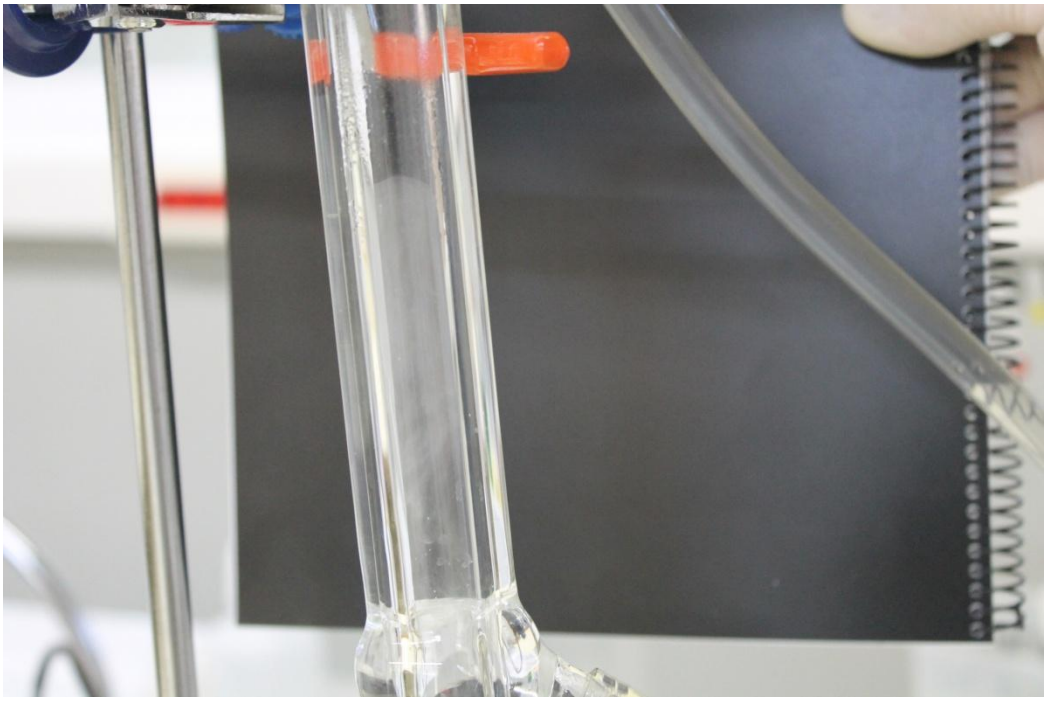
Research Project

INS LAURO

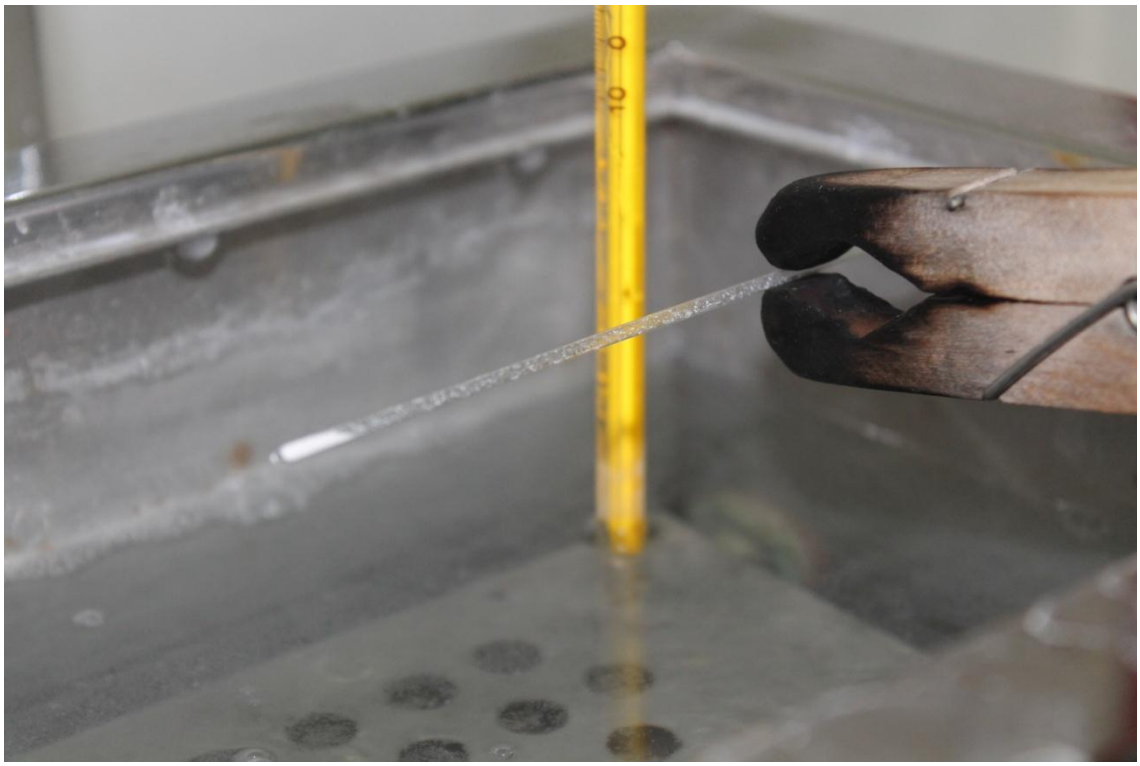
INDEX

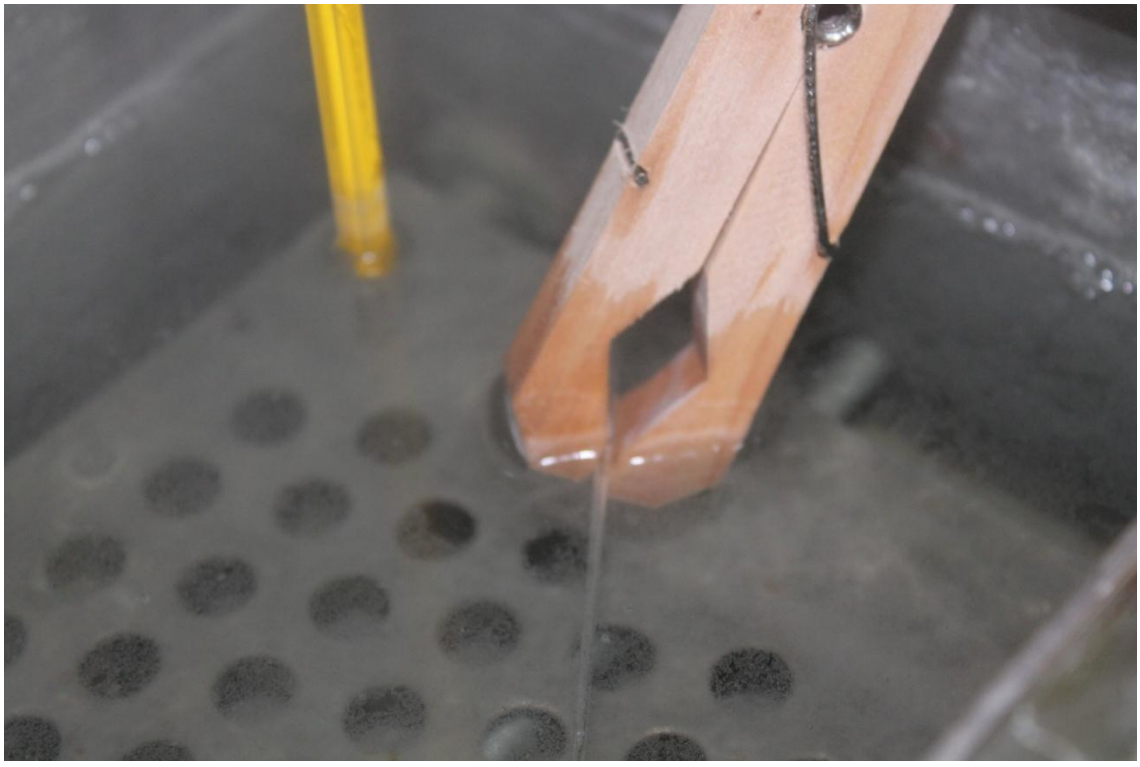
1. Synthesis of benzocaine

In these images, it can be seen how benzocaine was synthesized, especially the process of reflux of the sample. Then, there are some pictures of the procedure involving the melting point. Finally, there are images of the crystals of benzocaine and videos of this experiment are included in a CD.

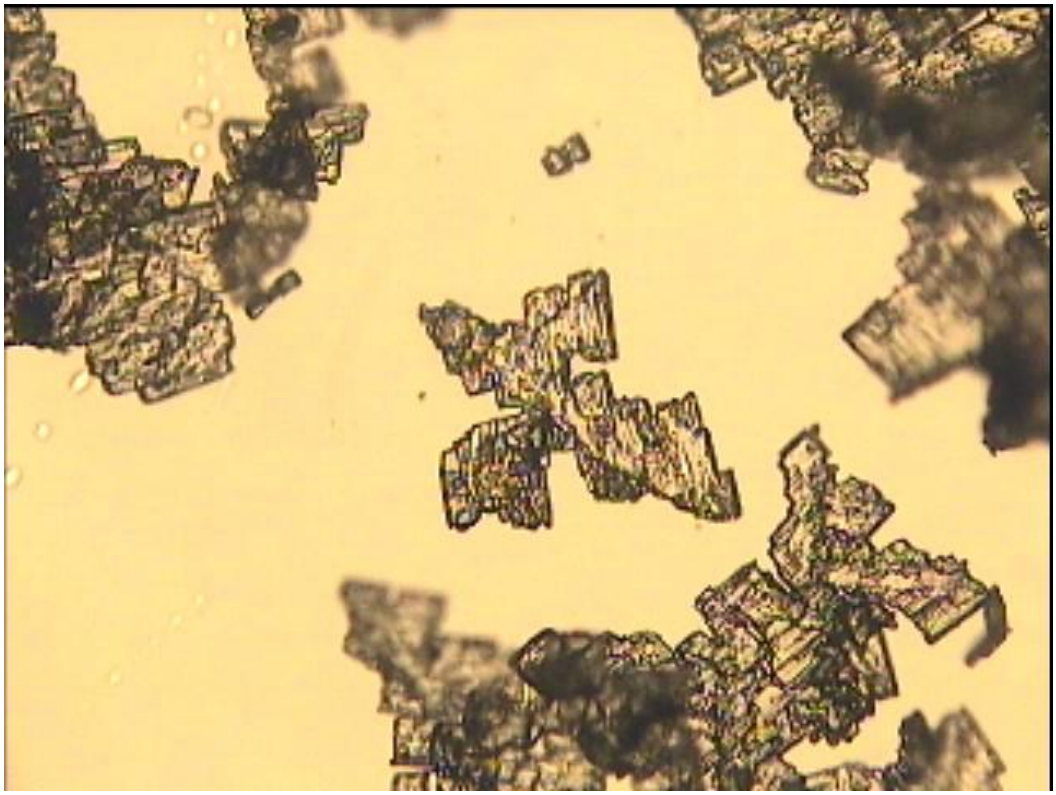


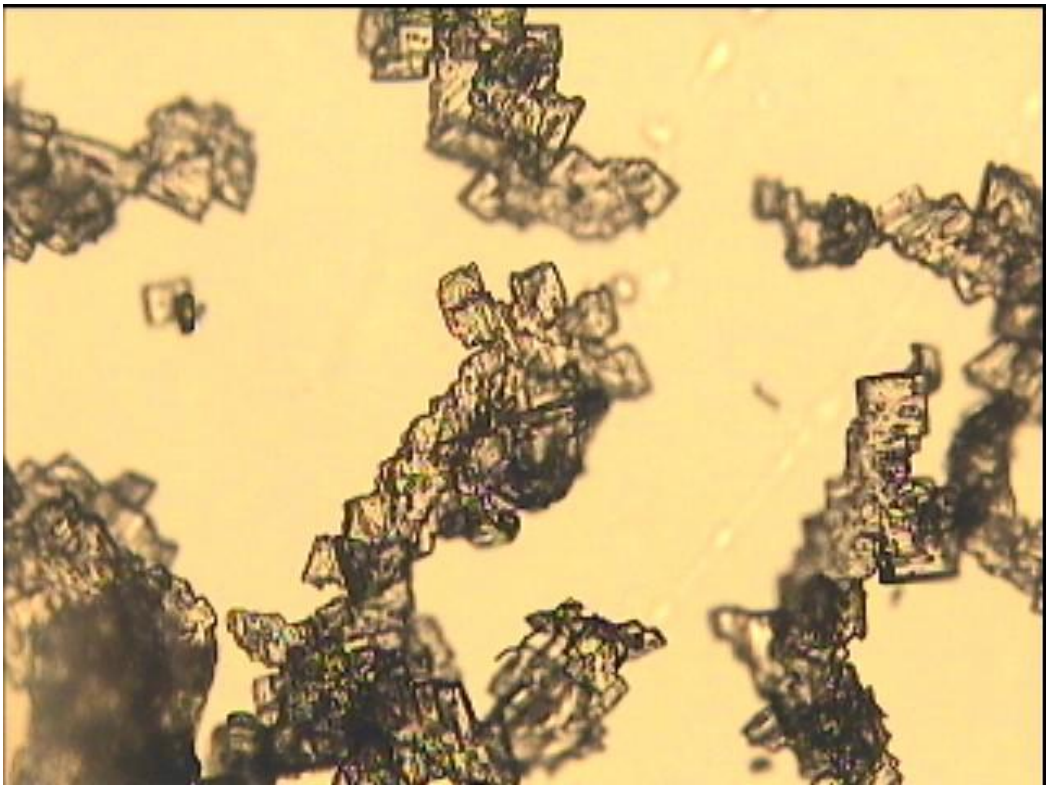
1.1 Melting point





1.2 Crystals of benzocaine

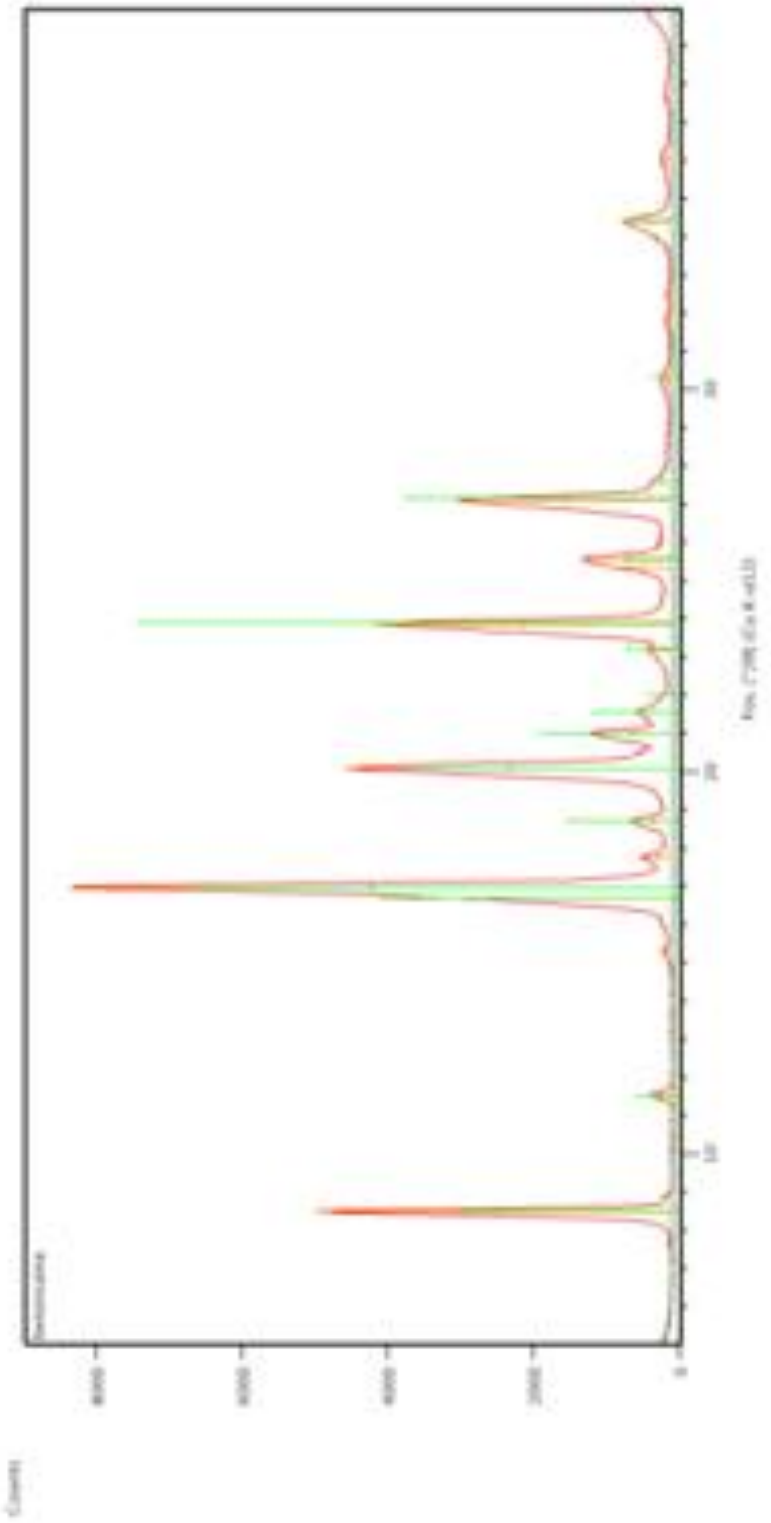


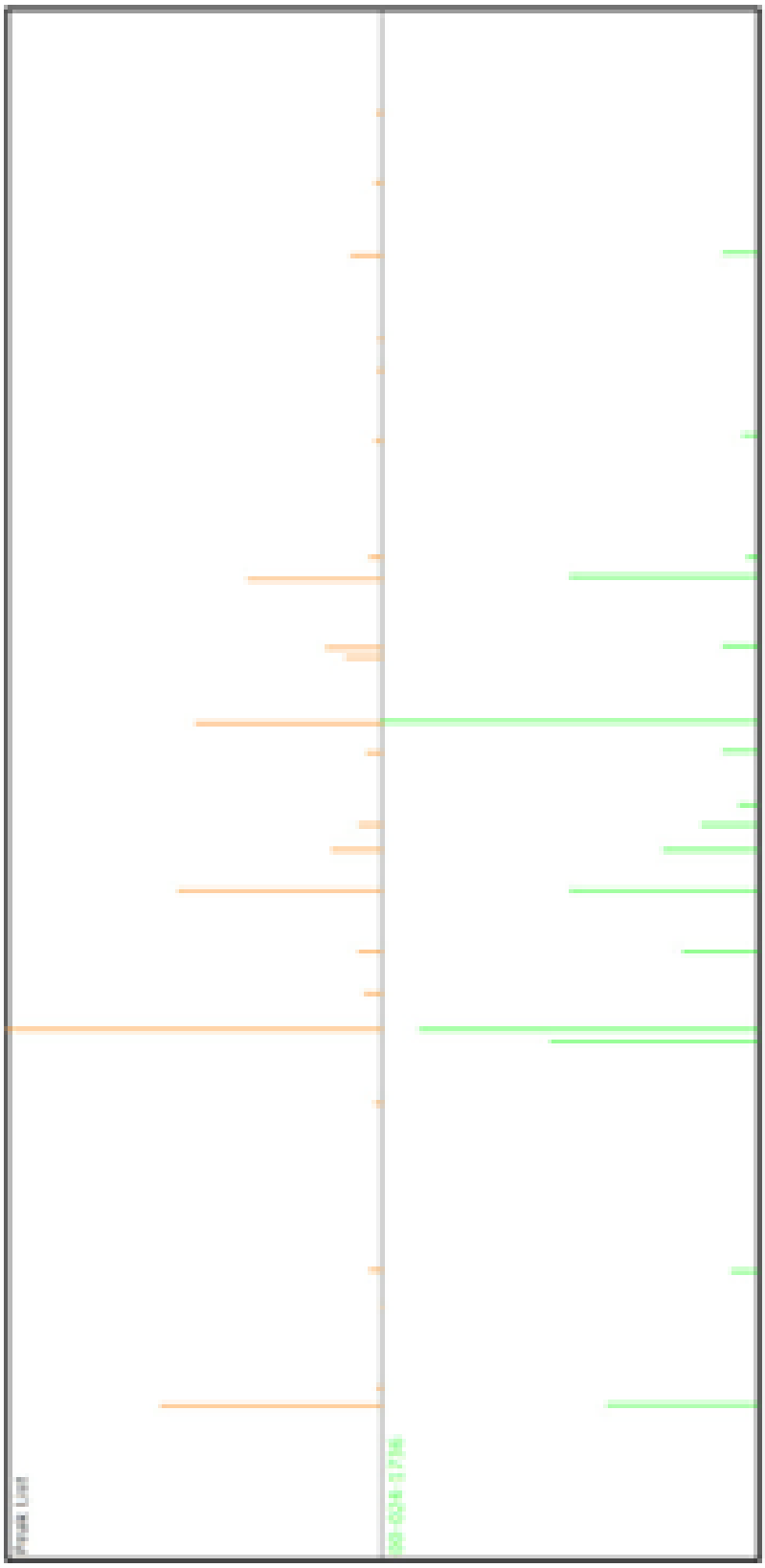


1.3 Videos

2. X-ray diffraction

Here, there are the graphics obtained in the X-ray diffraction. Both of them show the comparison between the d-spacing of the sample and the standard reference pattern.





3. Software

This is the computer programme designed especially for this research project. To use it, it is necessary to open the folder called “Benzocaine” and click on “Benzocaine” directly, without opening the other folders. When it is executed, it takes a few minutes to appear.

Then, the list of peaks calculated by the software is shown, as well as the graphic that compares the results of the X-ray diffraction and the peaks calculated using the Bragg’s Law.

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h = 4 k = 0 l = 3 d = 2.413566320352768 2th = 37.255487005261266
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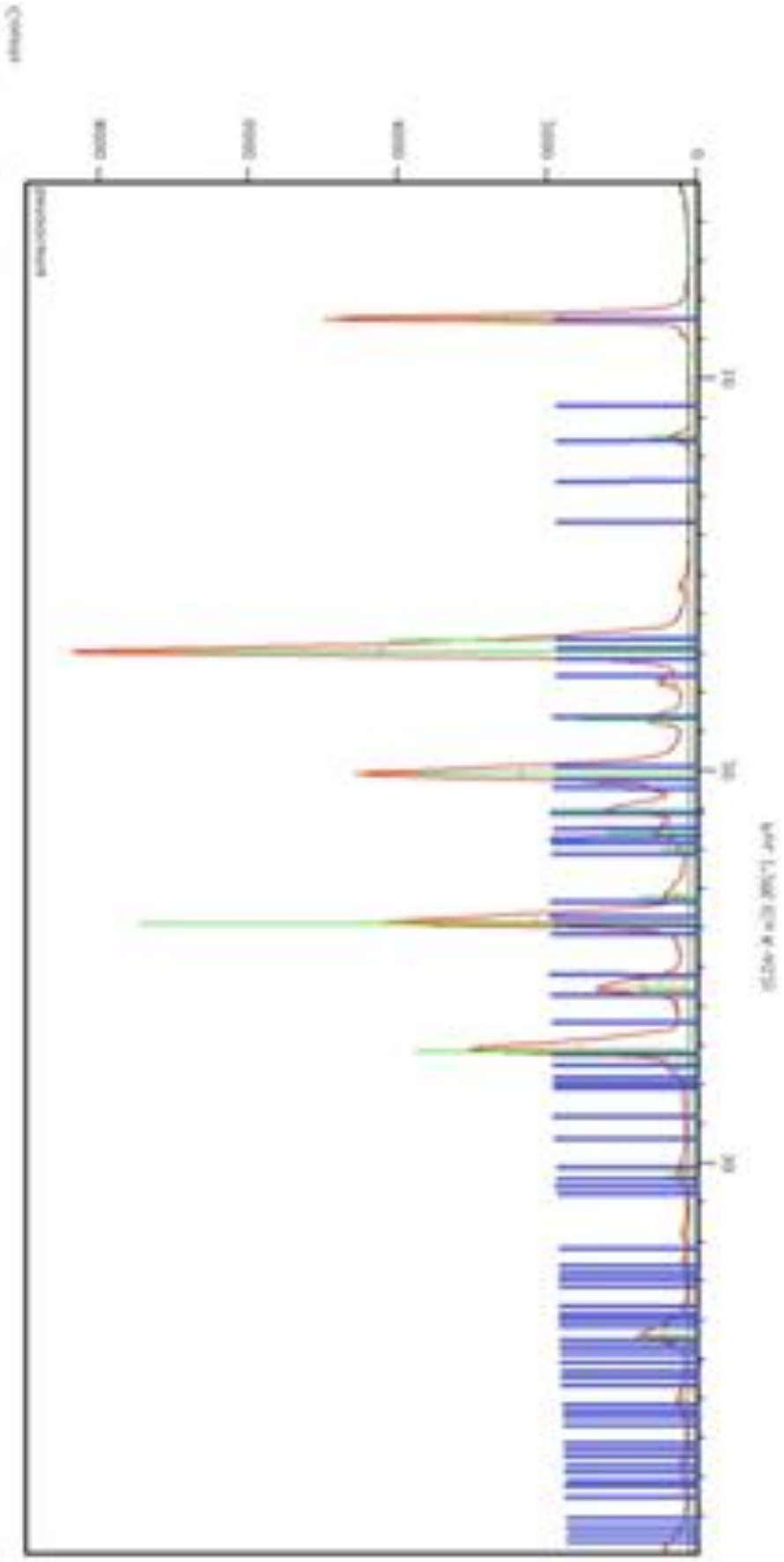
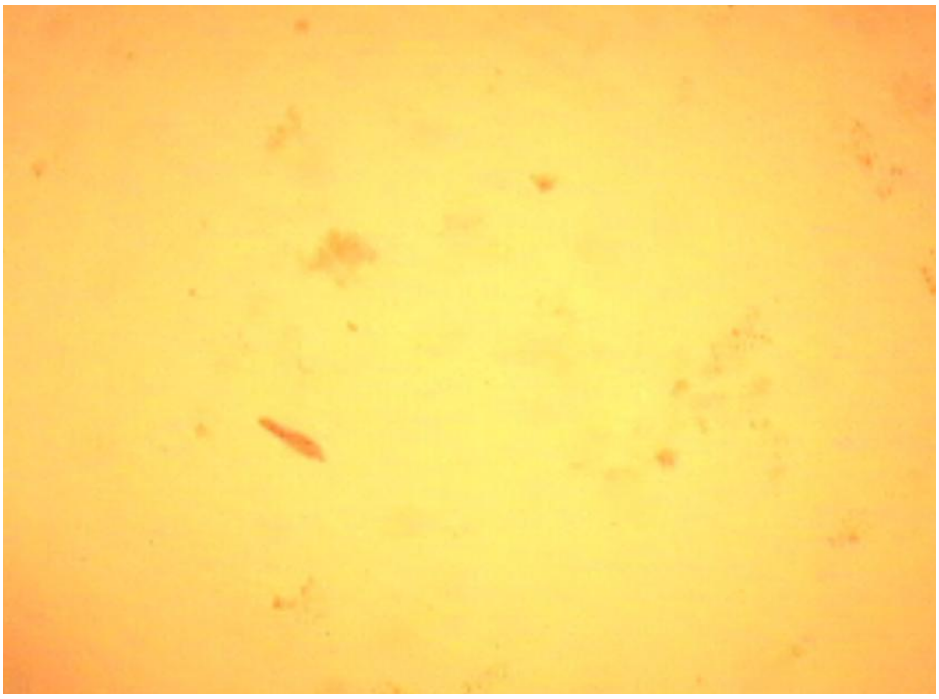
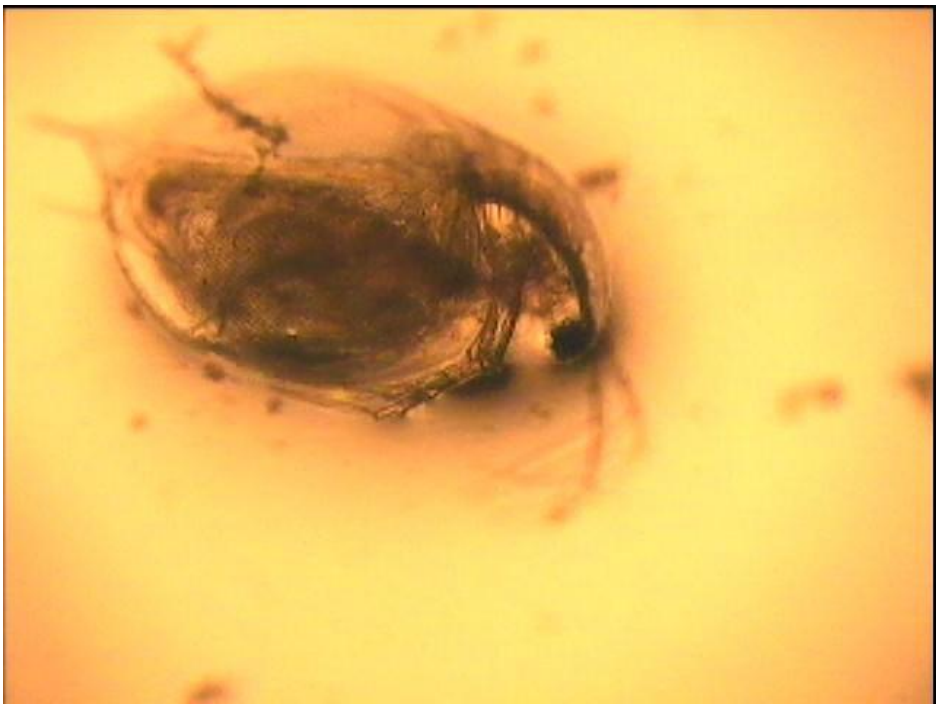


4. Induction of anesthesia to microorganisms

These are paramecium and daphnia, the microorganisms that were administered thiopental sodium, benzocaine and physiological saline serum. Then, there are videos of the experiment in a CD.





4.2 Videos