KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY

COLLEGE OF ENGINEERING

DEPARTMENT OF COMPUTER ENGINEERING

BIOMEDICAL ENGINEERING

AUTOMATED NEONATAL EXCHANGE TRANSFUSION (ANET 4.0)

AMEYAW ARTHUR SAMUEL

BANDOMA GIDEON

CANN JOSEPHINE ESI

SUPERVISED BY: MR. PRINCE ODAME

APRIL, 2023

DECLARATION

We declare that this project is our own work as a requirement for the award of a Bsc. Biomedical Engineering degree, under the supervision of Mr. Prince Odame. We also declare that except where references were made and credit duly given, the project is a result of our collective effort, ingenuity, research and skills.

NAME	SIGNATURE	DATE
AMEYAW ARTHUR SAMUEL	……..	
BANDOMA GIDEON	……	
CANN JOSEPHINE ESI	…….	

SUPERVISOR

Mr. PRINCE ODAME …….

ACKNOWLEDGEMENT

We give God the glory for His faithfulness to us throughout our journey.

Our heartfelt gratitude also goes out to our parents for their unflinching continuous support in all aspects.

We also acknowledge our supervisor, Mr. Prince Odame for his advice, corrections, and the time he invested in us for this project.

We also express our sincerest appreciation to Apedele Bede Abisba, a member of the group that worked on ANET 3.0 for his valuable contributions and suggestions.

Last but not least, we are grateful to all teaching assistants, colleagues and friends for their support.

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND

During pregnancy, the placenta excretes bilirubin. According to recent statistics, 80% of preterm and 60% of term neonates develop jaundice, which can be attributed to the underdevelopment of organs like the liver leading to the build-up of bilirubin(unconjugated bilirubin) in the blood, other tissues, and fluids of the body of neonates. This condition is termed hyperbilirubinemia. Hyperbilirubinemia is a leading cause of long-term neurodevelopmental impairment such as kernicterus and bilirubin-induced neurologic dysfunction (BIND)(Michael et al., 2020). In Sub-Saharan Africa, long-term impairment following kernicterus is eight times more common than in high-income countries.

Diagnostic methods of hyperbilirubinemia include direct and indirect bilirubin levels, red blood cell (RBC) counts, blood type, and testing for Rh compatibility. Neonates whose mothers are diabetic and have Rh disease are more prone. The condition may disappear on its own after birth, usually for a period of 2 to 4 days. But for most neonates, this usually does not happen.

Treatment methods include phototherapy, fiberoptic blanket, exchange transfusion, and ceasing breastfeeding for one or two days. Globally, the most predominant modality is phototherapy especially when there is early detection of hyperbilirubinemia. However, in severe cases of hyperbilirubinemia, usually as a result of late detection, phototherapy becomes a less effective treatment method, and considering the cost of phototherapy units, exchange transfusion becomes a more preferred approach in our part of the world. Exchange transfusion is an allogenic procedure where the neonate's blood which is contaminated with very high levels of bilirubin, is replaced with fresh blood from a donor. Exchange transfusion is a procedure that involves alternating giving and withdrawing blood in small amounts through a vein or artery. If bilirubin levels remain high, the procedure may need to be repeated.

The aim of the project is to design a cost-effective, time-saving workable device to make the procedure of exchange a smooth one with less human intervention for use in our part of the world.

1.2 PROBLEM STATEMENT

A neonatal exchange transfusion is a critical procedure that is performed on newborn infants suffering from severe medical conditions, such as hemolytic disease (HDN), which is caused by incompatibility between the mother's and baby's blood types, jaundice, anemia, or metabolic disorders.

Although the procedure replaces a large volume of the baby's blood and is life-saving, it poses several challenges that threaten the infant's well-being and survival. Other complications can arise during or after the procedure, including bleeding, transfusion reactions, infections, and, most importantly, iron overload, which damages the infant's heart, liver, and lungs. It is crucial to control the transfusion rate carefully to prevent overloading the infant's circulatory system. The transfusion should also be performed slowly to reduce the risk of adverse reactions and complications, such as transfusion reactions, bleeding, and infections.

It is very important that the procedure be performed accurately and consistently in order to ensure the best outcomes for the newborn, but since it takes such a long time, it is tedious and prone to human error.

1.3 OBJECTIVES

This project's main goal is to develop, build, and test the machine on lab subjects that automates the neonatal exchange transfusion procedure. The machine will then be used in clinical settings and intended for commercial purposes as well. All the information utilized in the manual procedure is included in the device's functionality. A motor will be programmed to move the syringe at a constant speed in order to draw and inject blood. Motors will also take the role of the doctor manually switching valves throughout the exchange operation. By doing this, human interference in the process will be eliminated. The automatic shut-off would turn the machine off when the process was complete using the alarm system.

1.3.1 SPECIFIC OBJECTIVES

The following are the project's specific goals:

1. Use programming, classical electronics, and mechanics to virtually automate the exchange transfusion procedure.

2. Include all the information from the manual procedure in our design

3. Create an educational user interface

4. Produce a workable, cost-effective effective and energy-efficient device for the public.

CHAPTER TWO

LITERATURE REVIEW

2.1 HISTORY OF NEONATAL EXCHANGE TRANSFUSION

Neonatal exchange transfusion has become a rare activity in most advanced countries but remains a frequent emergency procedure for severe hyperbilirubinemia in many underdeveloped countries, Ghana inclusive.

Exchange transfusion is a medical procedure that involves the replacement of a patient's blood with a donor or stored blood, or a combination of both.

The procedure involves the removal of neonate's blood containing high amounts of bilirubin and/or antibody-coated red blood cells while simultaneously replacing it with 'fresh' blood which has fresh albumin and binding sites for bilirubin.

The history of NET may be traced to the Talmudic era (1st century C.E.) when the then-Jewish physicians used it as a last option for a number of ailments. A Greek philosopher of the same era Aristotle also mentioned using it to treat jaundice. Because the techniques required to assure the safe transfer of blood between donors and recipients had not yet been invented, exchange transfusions were not often offered until late in the twentieth century. Before the actual exchange transfusion procedure was developed, physicians often used a technique called 'bloodletting' to treat various medical conditions.

The exchange transfusion procedure is usually used to treat anemia, blood disorders, and infections.

This practice involved draining a patient's blood and replacing it with replacement fluids such as wine or animal milk. In 1906, the first successful exchange transfusion was performed by Dr.

George Washington Crile in the United States. Dr. Crile performed the procedure on a patient suffering from jaundice, replacing the patient’s blood with stored blood from a donor.

The patient survived and eventually recovered from jaundice. In the following decades, exchange transfusions were further developed and refined. The approach, interchange even though it was Alexander Weiner who invented and gave the term "transfusion" its initial suggested by Dr. Bruce Robertson, a Canadian physician, in 1921. The technique was applied in the therapy for children with serious burns. In the 1930s, researchers began to use the technique to treat severe anemia in premature babies. A doctor from the hospital in Toronto Dr. Alfred P. Hart was the first to execute an exchange transfusion for sick children in 1925 to treat newborns with hemolytic disease (ref).

It involves drawing blood from the femoral vein to replace the young child's radial artery, longitudinal sinus, or external jugular vein, or it with new donor blood through an ankle cut-down. This was how in the past they used as a process to withdraw blood from the neonate.

Exchange transfusions have saved countless lives over the past century, and continue to be an important medical procedure used to treat a wide range of medical conditions

Recently, technological advancements like the development and use of Rh-immunoglobin, improvements in prenatal ultrasound, intensive phototherapy, and revised American Academy of Pediatrics (AAP) guidelines for hyperbilirubinemia have caused a declined need for blood exchange transfusion in the last 2 or 3 decades. The need for expertise for this procedure in most developed countries has drastically dropped. In developing countries, technological breakthroughs and simulations have evolved to improve the safety of this procedure.

In underdeveloped countries like Ghana however, exchange transfusion remains the most used procedure because of the absence of community-based use of phototherapy, below-standard or ineffective phototherapy devices, and late recognition of high levels of bilirubin.

2.2 THE EXCHANGE TRANSFUSION PROCESS

The process involves taking aliquots of the patient's blood that are considered to be "bad blood" is taken and exchanged with aliquots of the donor's blood that are considered to be "good blood." This is what gives exchange transfusions its name; blood is taken out and replaced; there is an exchange.

Simple blood transfusions do not include the exchange of blood; blood is only supplied but not taken out. Since some "old" blood and "new" blood are mixed or fused, the procedure is known as a blood transfusion. Exchange transfusions are always allogeneic, meaning that fresh, healthy blood always comes from a donor.

2.2.1 STEPS IN THE EXCHANGE TRANSFUSION PROCESS

1. Without resistance, the catheter can usually be pushed to about 8cm in preterm and 11m in term neonates, with the tip lying in the inferior vena cava. If there is resistance, the catheter can be removed to about 3cm in preterm and 5cm in the term.
2. The neonate is placed on the radiant warmer or flat incubator mattress and there is continuous monitoring of the vital signs of the neonate.
3. Use of anesthesia is not necessary. Soothing techniques, sucrose solutions, and gentle restraints are needed to minimize discomfort and ensure a sterile field.
4. The neonate is not fed and if it has been fed 2-3 hours prior to the procedure, the contents of the stomach are emptied using a gastric tube.
5. Diapers are used to ensure hygiene.
6. The periumbilical region is cleaned using Betadine or Chlorhexidine and covered with sterile surgical drapes.
7. A loose purse string is placed around the base of the cord for hemostasis.
8. An umbilical venous catheter of French size 5 or 8, prefilled with saline and attached to a 10ml syringe is gently inserted into the umbilical vein to the desired location. All the associations ought to be prefilled with saline to avoid air cavitation arriving at the umbilical catheter. The catheter or the associations should never be passed on open to the air to forestall any air embolism. Air embolism is a significant gamble; in this manner, the needle ought to be vertical during the mixture, and air cavitation ought to be kept away from the withdrawal stage. Imbuement of blood with reliable hematocrit requires continuous blending

(delicate shaking or plying) of the giver blood sack each 5-10 cycles. Utilization of citrate anticoagulants in benefactor blood might prompt a diminishing in the newborn child's serum calcium ensuing in changes in calcitonin.

9. The catheter is connected to 2 three-way stopcocks or 1 four-way stopcock.
10. During the procedure, the size of each aliquot should be approximately 5%-8% of the neonate's estimated blood volume. In a term newborn child with a body weight fitting for gestational age, normally 15-to 20-mL aliquots might be removed or imbued at a pace of 5ml/kg/min. For low-birthweight and preterm newborn children, it is a general practice to be careful and withdrawal/imbuement ought to be restricted to roughly 5 mL/kg. Noticing that is significant as the aliquot volume diminishes, the extent of dead space volume would increment making the BET less compelling. Hence, an aliquot of volumes 2 mL is not suggested.

2.3 EXCHANGE TECHNIQUES

The exchange techniques are the procedures or approaches to which the exchange transfusion is done.

- Single catheter pull-push technique: The umbilical vein reaches the inferior vena cava below its junction with the right atrium.
- Double catheter pull-push technique: This process is used with a catheter each in the umbilical vein and umbilical artery.
- Substitute catheter: In the technique, the substitute catheter is placed in either a peripheral artery (usually a radial artery) and/or a large-sized peripheral vein. Usually, a large peripheral or branchial vein is enough. Rarely, one may have to cannulate the jugular or femoral vein if the infant is severely hydrated and peripheral veins are collapsed.

2.3.1 SINGLE CATHETER PULL-PUSH TECHNIQUE

One medical professional often uses this technique in exchange transfusion process without the need for an extra medical professional. It is a conventional technique that uses just one umbilical venous catheter. The end of this series connection is attached to a syringe, and the umbilical vein catheter is connected to two three-way taps or stopcocks that are connected in parallel. Depending on the size of the infant, blood is extracted in aliquots of 5–20 mL, and the correct amount of blood is then restored. This is due to the fact that depending on the baby's weight, if more blood is collected than necessary, the newborn may lose consciousness or have organ failure.

Furthermore, blood is removed at a rate of 1.5–2 mL/kg/min. A nurse keeps track of each cycle's blood amount collected and delivered during the operation. The various vitals of the neonate are also checked periodically.

2.3.2 DOUBLE CATHETER PULL-PUSH TECHNIQUE

Two people are involved in this procedure. Here, many catheters inserted in various blood lines are used to concurrently remove and deliver equal amounts of blood. The utilized blood lines include the umbilical artery and vein. Via the umbilical artery, blood is removed from the infant, while at the same time, blood is fed into the infant through the umbilical vein.

This is also possible with other bloodlines; however arterial lines are often used for withdrawals rather than for giving out donor blood since arterial blood pressure is significantly greater than venous blood pressure. It is also called the Isovolumetric method.

2.4 COMPLICATIONS OF EXCHANGE TRANSFUSION

Exchange Transfusion is regarded as a safe and successful treatment, (1) it is not without risk(refer to Table below) According to a study conducted by (2,6), it was observed that the process can result in the death of neonates as well. The current guidelines for doing an exchange transfusion are based on a balance between the risks of encephalopathy and the problems linked to the treatment. Its death rates range from 0.5% to 3.3% (3). But, if the process is done extremely carefully and bilirubin levels are consistently monitored(5), with the appropriate hygiene, and care, the majority of these issues may be avoided. Typically, pausing or slowing down the trade is the best way to handle these issues (4).

Complications during the procedure	Complications after the procedure
Air Embolus	Infection
Volume Imbalance	Thrombocytopenia
Hyperkalaemia	Hypoglycaemia
Arrhythmias	Blood transmitted infections
Respiratory Distresses	Hypocalcaemia
Anaemia/ Polycythaemia	Anaemia/ Polycythaemia
Acidosis	Hypernatremia

DONOR BLOOD	INFANT COMPLICATION	PREVENTION/TREATMENT
Old blood (high K^+, low platelets)	Hyperkalemia, thrombocytopenia	Use blood less than 5 days old. Monitor ECG during and after procedure. Watch for signs of bleeding
Citrate blood	Hypocalcemia and hypomagnesemia	Consider 1-2 mL kg^{-1} of calcium gluconate after 50-100 mL of blood exchange in sick infants. Monitor serum calcium 2 h after an exchange. In case of unexplained arrhythmia use 2 ml/kg of 10% calcium gluconate infusion
Cold	Hypothermia	Prewarm the blood.
High glucose	Rebound hypoglycemia	Check blood glucose 2 hours after exchange transfusion. Initiate early enteral feeds
Glucose 6-phospho dehydrogenase deficient	Increased hemolysis, rebound hyperbilirubinemia	In endemic areas screen for glucose 6-phospho dehydrogenase status of donor blood

2.5 BLOOD VOLUME CALCULATIONS

The difficulty in calculating the amount of exchange blood needed for newborns is related to how much blood is needed to raise their hemoglobin levels to an acceptable level. Nonetheless, a formula has been developed based on the supposition that the rise in hemoglobin

Throughout the operation, concentration is a linear function of volume exchange (7). The early stages of the blood exchange are when the change in hemoglobin concentration is largest, and it gradually decreases as the blood is exchanged. The total volume of the cells and plasma in the circulatory system is what we refer to as blood volume (8,9). The dilemma of whether or not the techniques for calculating plasma and cell volume include or omit these extravascular components immediately emerges because all components of the blood, including created elements, are to some extent present outside blood arteries. (8,9).

The general exchange volume parameter is given as:

The product of the total volume to be delivered and the weight of the baby which is all divided by 1kg.

Mathematically expressed as:

$$\frac{Total\ Volume\ to\ be\ delivered}{1.0kg}\ x\ weight\ of\ the\ baby$$

	Weight	Exchange Volume	Total Volume of Blood
Preterm	$1kg$	$\frac{200ml}{1.0kg}\ x\ 1.0\ kg$	$200ml$
Term	$2kg$	$\frac{169ml}{1.0\ kg}\ x\ 2.0\ kg$	$320ml$

According to the Table above, during the exchange operation, 200 ml and 320 ml of fluid will be given to preterm and term newborns, respectively. The exchange volume parameter provides the foundation for this computation. To calculate the number of cycles and the duration that the process will last, the formulars below are used:

$$Number\ of\ cycles = \frac{Total\ Exchange\ Volume}{blood\ volume\ per\ cycle}$$

$$Duration = \ Number\ of\ Cycles\ x\ time\ taken\ per\ cycle$$

2.5.1 SINGLE VOLUME

The baby’s blood volume is the same as the amount of the blood volume we estimate.

For instance, just 80ml/kg of blood volume would be needed to do a single-volume transfusion on a term. This method substitutes 60–65% of the baby's red blood volume.

Preterm or term babies mostly in the example table above are given a total of 320ml and 200ml during the exchange procedure.

2.5.2 DOUBLE VOLUME

Double Volume Exchange Transfusion involves repeating the single volume exchange transfusion. The blood to drawn from the neonate is estimated to be twice the baby's blood volume in circulation.

The blood to drawn from the neonate Between 85-88% of the baby's red blood cells or blood volume are replaced.

The end part of this process is most popular and mostly used to treat newborns with chronic jaundice (hyperbilirubinemia)

The efficiency of the double volume exchange transfusion should have been twice as high as the single volume exchange transfusion, one may have predicted.

Yet this is not the case. Just a 25% average gain in efficiency is observed (i.e. from 80 to 85).

Nearly all of the baby's blood's circulation cannot be exchanged. This occurs as a result of circulation mixing the baby's blood with the blood flowing in. The double volume exchange transfusion is best when efficiency is compared to the total amount of blood that is circulated since it minimizes waste by using less time, energy, and resources while maintaining high efficiency.

The amount of blood exchanged as an aliquot depends on the weight of the infant. This is due to the fact that, depending on the weight of the infant, if more blood than a specific quantity is withheld, the child may lose consciousness or have organ failure. As a result, the following criterion is used to determine how much blood should be exchanged during a cycle.

Due to the circumstances surrounding the infant, the doctor may not strictly adhere to this and instead utilize quantities that are lower or higher.

In light of everything that has just been discussed, take into account the following: noting that the infant will get an exchange transfusion:

A premature infant with a mass of around one kilogram.

As the infant is premature, the standard quantity of blood exchange is around 200 ml per kilogram of the infant. By dividing this statistic by the baby's weight, we can determine the total volume of blood that has to be exchanged. $i.e.$ $200mlkg$ ×$1.0kg$ =$200ml$.

This suggests that a total volume exchange of around 200 ml is required. Also, because the infant weighs less than 1.5 kg, it follows that 5 ml-sized blood aliquots should be switched each cycle.

We divide the entire blood volume by the volume per cycle to determine the number of cycles necessary to exchange the complete blood volume. $i.e.$ $\frac{200ml}{5ml} = 40\ cycles$

The process is carried out extremely slowly, taking 4-5 minutes every cycle, as was already said. Taking this instance into consideration, the total time for the exchange transfusion on the newborn will be equal to the time utilized each cycle times the overall number of cycles. $i.e.$ 40 $cycles$ ×$4mins\ cycle$\s=$160mins$ = 2 hrs 40 $min.$

2.6 PREVIOUS PROJECTS ON ANET

2.6.1 ANET 2.0

In order to operate the complete exchange transfusion setup with little to no human involvement, our predecessors did wonderful work by birthing the concept of Automated Neonatal Exchange Transfusion (ANET) 2.0 which combined mechanics, electronics, and programming. This was accomplished using the following methods:

This was accomplished using the following methods: A push and pull segment made up of a bipolar stepper motor, a lead screw, and guiding rods were employed to accomplish this function. The clockwise rotation of the stepper motor. The threaded rod moves in that direction as the motor rotates counterclockwise to provide a sucking action. The physicians' manual blood drawing and delivery procedures were replaced by this system.

This innovative method for switching valves that use motors driven by software that will be built for the microcontroller to replace the manual switching of valves. The project synchronizes the push-pull segment and the valve control segment to carry out the procedures of blood withdrawal and donor blood replacement.

Two unipolar stepper motors, two three-way valves connected in series, and a catheter end attached to the infant, the waste container, and the donor blood bag made up the valve-switching system utilized in ANET 2.0.

The three-way valves that are employed in this system, however, had to be manipulated by human hands, which presented an issue for connecting the motors with them.

2.6.2 ANET 3.0

The work of the automated Neonatal Exchange Transfusion version 3.0 looked at the flaws of the existing ones from ANET 1.0 and 2.0. Their objective was to also pick up from our predecessors and make the Neonatal Exchange Transfusion an automated one as well.

They combined mechanics, electronics, and programming to achieve this. The design of the device was a little bit different because most of the parts were 3D printed and used for the purpose without building it from scratch.

The three-way valve was manipulated by another motor in this case so the physician wouldn't have to control it. The device was further used to test on animal lab subjects on the exchange transfusion.

Aside from these positive breakthroughs that ANET 3.0 was able to make it had some challenges.

The valve was rotating as well as moving the handle as well, the intended purpose was for it to rotate on its own so friction is not generated. As a result of this, excess heat was generated and the device was working after a while.

Also, the push and pull block had a very rigid sense of motion in plunging.

CHAPTER THREE

METHODOLOGY

This chapter discusses into the nitty gritty of the procedures involved in the data acquisition, analysis process, tools, and materials used in the entire course to design the automated neonatal exchange transfusion device.

3.1 DATA COLLECTION

Primary and secondary data were used in the data collection process. Much information was gathered via conversations with ANET 2.0 and ANET 3.0 project developers. The reports of these two generations of ANET were very useful in the data collection process. The school of veterinary medicine was visited, and questions regarding the kinds of animal testing conducted there and how they were carried out were raised.

The pharmacy department's animal house was the next place to go for information on animal experiments, and there we received guidance on how to conduct our animal tests.

On the other side, secondary data came from readings such papers and journals as well as watching YouTube videos with information on the following subjects:

I. Hyperbilirubinemia
II. Hemolytic disease
III. Exchange transfusion.
IV. Anatomy of the neonate
V. RH and ABO incompatibility
VI. Mechanics of motors, nuts, and threaded rods
VII. Valving technology
VIII. Bubble trap technology among others

3.2 DATA COLLECTION

A qualitative approach was mostly used to analyze the data. This involves use of descriptive data and semi-structured observation methods in analysis. The analysis approach was influenced by brainstorming meetings and going through prior material. Our choice of animal subject for tests as well as the procedures to be used was guided by prior research on animal testing carried out on ANET-related devices such as dialysis machines as well as information gathered from officials of the veterinary medicine school and lab technicians of the pharmacy department animal house.

The shortcomings of ANET 2.0 and ANET 3.0 that would present difficulties during animal tests were identified with the help of discussions with the device's creators and bench tests on the apparatus.

3.3 DESIGN PROCESS

This project combines mechanics, electronics, and programming in order to operate the full exchange transfusion setup and run tests on it to demonstrate its usefulness.

To do this, tests will be run on the automation device's existing prototype, ANET 3.0, from which the device's shortcomings and obstacles will be determined to help with future enhancement of the device in ANET 4.0.

The present model is an improvement to one that currently exists (ANET 2.0). Our goal was to strengthen the model's strong features while addressing all of the flaws inherited from the previous models, which had both positive and negative qualities. The device's primary problems and the solutions utilized to fix them are mentioned below.

• Designing a new coupling to transfer the rotational motion of the motor to turn the valves and to rotate only the

handle without rotating the valves.

• Design a power system on its own that will provide enough power for the motors so that the rotations will be done smoothly.

The threaded rod is responsible for converting the rotatory motion of the bipolar stepper motor into a linear motion. To do this, the rod is coupled with the motor using a coupler. The nut moves along the rod when it rotates. From simulations, the threaded rod recorded very large stress values. This was quite understandable, considering the work it does in converting rotatory motion into linear motion. This is also due to the fact that threaded rods are made for fastening purposes and thus the high friction they create

The threaded rod is very stiff and this will be solved using classical electronics to affect the plunging effect. The Clinician does not get a notice when the process is done so as a solution to this a part of the code prompts the clinician when the process is done.

3.3.1 DEVICE TESTING

The goal of the initial test of the existing device is to check the mechanical parts are responding to code performing as planned, check for its clinical effectiveness, check for failures and the risk at hand, and the adverse effects that may arise in its usage. The device will be evaluated using an animal test, which often offers preliminary proof of the devices' safety, their potential performance in a live system, and the biological reaction that a living system may mount to the device.

3.3.2 ANIMAL TESTING

The use of non-human animals in medical experiments is referred to as animal testing or animal experimentation, and in this concept in vivo testing. Major advances in the treatment of to diseases like breast cancer, brain injury, childhood leukemia, cystic fibrosis, multiple sclerosis, tuberculosis, and others have been made with the help of animal research.

Pacemakers, cardiac valve replacements, and anesthetics have also been developed thanks to animal research. The use of animals in testing is heavily controlled because worries about "cruelty" to animals and their humane treatment are legitimate ones.

Permission was obtained on the usage of the lab subject as a means to means of paying heed to the set rules.

3.3.3 SIGNIFICANCE OF ANIMAL TESTING

Prior to entering the clinical phase, a medical product must be thoroughly examined for safety, efficacy, and efficiency. This helps us decide what modifications need to be done before being put on the market. In order to evaluate these devices, animal experiments are frequently done. These studies usually give preliminary proof of the devices' safety, their potential performance when used in a live system, and the biological reaction that a living system may mount against the device.

The FDA advises that animal studies for medical devices be planned with the goal of analyzing the hazards expected by the device's design, any known dangers associated with the device type, and any new concerns that may have surfaced in earlier investigations.

For instance, several skincare and cosmetic products are tested on animals to guarantee their safety, and many medical professionals and biomedical researchers support the practice since it contributes to the humane treatment of diverse animals and their safety with regard to medical device standards.

3.3.4 MAIN OBJECTIVES OF ANIMAL TESTING

This is to see the operation of the existing device, the advances, drawbacks, and additions that can be added to the device.

3.3.4.1 Identification of loopholes and to improve on them.

This helps to see the flaws of the work that was done by the previous years and to see the additions that can be added to make the device a well-improved and commercial one.

3.3.4.2 Evaluate the efficacy of the device or demonstrate proof of principle.

This would entail confirming the consistency and correctness of cycle length, blood volume (aliquots) every cycle, and the entire treatment. It would also entail monitoring for any symptoms of illness during or after the procedure.

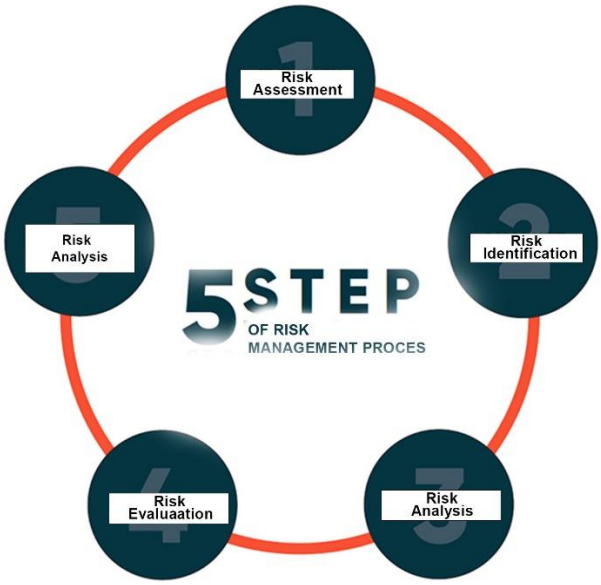
3.3.4.3 Provide evidence of safety

Proof demonstrating the device's safety, including its handling and performance when compared to current automation techniques and practices. Performance and handling, device safety, physiological response, determining whether or not the device can have effects distant from the site of use (mechanical or biologic stresses), unexpected morbidity and mortality, or all observed instances of animal illness and death, and determining whether or not such events are device-related are all recommendations for evaluating safety.

3.3.4.4 Risk assessment for risk management

A risk is a mix of the likelihood that harm will occur and how serious that harm will be. Risk analysis and evaluation are the two steps that makeup risk assessment. The process of identifying risks and estimating the risk is known as risk analysis.

Comparing the projected risk to predetermined risk criteria, on the other hand, is the process of determining if the risk is acceptable.



3.3.5 SELECTING AN ANIMAL FOR THE TEST OF THE AUTOMATED NEONATAL EXCHANGE TRANSFUSION DEVICE

Animal experiments and research are being undertaken on a variety of species. These creatures include fish and birds as well as rats, mice, rabbits, guinea pigs, dogs, primates, chimps, and orangutans. Every one of these creatures has distinctive traits and peculiarities that help researchers get the most useful results from their scientific investigations.

The most productive animals to utilize in the development of cosmetic and skin care products are rats and mice. The greatest choice would be rabbits since they have a physiology that is most similar to that of humans and because their weight is most similar to that of newborns.

The size of the gadget and its components in relation to the test subject is an additional crucial factor. The catheter, for instance, would have to fit into the blood vessels of the test subject

3.3.6 ANIMAL TEST PROCEDURE

3.3.6.1 HOW WILL THE DATA BE COLLECTED

The goal of the animal experiments is to gather information that will be used to evaluate the device and provide proof of concept and design verification. The quantities removed or transfused each cycle, the duration of each cycle, and cumulative volumes will all be recorded in order to calculate the total amount transfused.

3.3.6.2 COMPLICATIONS OF EXCHANGE TRANSFUSION

There are certain problems with exchange transfusion. Current guidelines for doing an exchange transfusion are based on a balance between the risks of encephalopathy and the problems linked to the treatment. Its death rates range between 0.5% and 3.3%.

But, if the process is done extremely carefully, with the appropriate hygiene, and care, the majority of these issues may be avoided. Typically, slowing down or pausing the trade is the best way to handle these issues.

3.3.7 RISK ANALYSIS AND EVALUATION

The hazards associated with the device are grouped into;

I. Hazards associated with blood related devices and exchange transfusion.

These are hazards that have been identified from literature to be associated to most blood contacting devices and the exchange transfusion process. These hazards include;

- Catheter related complications
- Air emboli
- Thrombosis
- Hypo and hyperthermia
- Hemodynamic (related to excess removal of injection of blood): hypo or
- hypertension
- Hypo or hyperglycemia
- II. Hazards predicted from design and bench testing of device
- These hazards where identified as possible complications that can arise from the device
- design and bench tests performed on the device.
- Coagulation of blood
- Air emboli
- Thrombosis
- Endurance of device
- Ergonomic hazards (repetitive movements, improper set up)

III. General device hazards

These are hazards related to general device use in both normal and fault conditions.

Some examples include;

- Electrical hazards
- Misuse
- Mechanical hazards
- And Unforeseen malfunctions

3.3.7.1 Risk Assessment Table

I. Hazards predicted from design and bench testing

Hazard	**Reasonable foreseeable sequence or combination of events**	**Hazardous Situation**	**Harm**	**Probability of occurrence**	**Severity**
Coagulation of blood	Blood clots after leaving patient body or donor bag	Thrombosis	Pain and swelling Stroke /heart attack Death		
Air emboli	Air bubble or foam trapped in blood line due to line – pump separation	Blood vessels blocked	Heart attack stroke Respiratory failure Death		
Thrombosis	Blood clots get into the blood vessels from the blood line	Blood clots accumulate or block blood vessels	Pain and swelling Stroke /heart attack Death		

Endurance of device	Device ability to perform well for long periods	Device stops before procedure is completed	Shock Inconsistencies in operations Death		
Ergonomic hazards (repetitive movements, improper set up)	Device not setup correctly Blood line separation	Inaccurate measurements Air emboli Pressure altered			

II. Hazards associated with blood related devices and exchange transfusion

Hazard	**Reasonable foreseeable sequence or combination of events**	**Hazardous Situation**	**Harm**	**Probability of occurrence**	**Severity**
Catheter related complications	Allergy, Poor catheterization , Blood line breaks	The wrong type of catheter or catheterization used	Thrombosis Air emboli		
air emboli; thrombosis	Air bubble, foam or clots blocking blood vessel	Blood vessels blocked	Heart attack stroke Respiratory failure Death		
Hypo or hyperthermia	Reactions to blood being exchanged	Temperature rises above normal temperature			
Hemodynamic (related to excess removal of injection of blood): hypo or hypertension	Inaccurate timing of blood pumping, Inaccurate, inconsistent volume drawn and pumped	Too much or too little blood drawn or pumped Blood drawn or pumped too early or too late	Shock Heart rate complications Heart attack Death		
Hypo or hyperglycemia	Inaccurate, inconsistent volume drawn and pumped	Too much or too little blood drawn or pumped	Shock Death		

III. General device hazards

Hazards	**Reasonable foreseeable sequence or combination of events**	**Hazardous Situation**	**Harm**	**Probability of occurrence**	**Severity**
Electrical hazards	User comes into contact with live wire, Fluids come into contact with electrical components	User is exposed to electricity	• Injury • Death		
Mechanical hazards	Improper contact or entanglement to machine parts	Exposure to injurious machine parts	• Injury • Death		
Misuse	Use of device or its parts for wrong purpose				
Unforeseen malfunctions					

REFERENCES

Michael, K., Wong, R. J., Burgis, J. C., Sibley, E., & Stevenson, D. K. (2020). *Fanaroff and Martin's Neonatal-Perinatal Medicine* (Vol. 91).