The Steven and Alexandra Cohen Children's Medical Center of New York (CCMC)
Informed Consent and Child Assent to Participate In Research
Intervention

Protocol Title:	Sodium Bicarbonate to Prevent Acute Kidney Injury in Children Undergoing Cardiac Surgery: A Randomized Control Trial
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Introduction

You are being asked to join a research study. The purpose of a research study is to answer specific questions, sometimes about the safety of a drug or device and how well it works. Being in a research study is different from being a patient. When you are a patient, you and your doctor have freedom in making decisions about your healthcare. When you are in a research study, the researcher will follow the rules of the research study as closely as possible, while monitoring your health.

This consent form will explain:

- the purpose of the study
- what you will be asked to do
- the potential risks and benefits

It will also explain that you do not have to be in this study to receive medical care. You should ask questions before you decide if you want to participate. You can also ask questions at any time during the study.

Why am I being asked to volunteer?

You are being invited to participate in a research study because your child requires surgery to correct a congenital heart lesion (heart problem, such as a hole or abnormally small structures) and will require cardiopulmonary bypass (heart-lung machine) during the procedure.

What is the purpose of this research study?

This study is being done because we are trying to identify a way to prevent injury to the kidney that has been associated with undergoing cardiopulmonary bypass.

The purpose of this study is to evaluate whether giving your child sodium bicarbonate prior to beginning surgery, and then for the first 24 hours after surgery will protect the kidneys from the

effects of cardiopulmonary bypass. Sodium bicarbonate is a common medication used in children who are critically ill, and helps to balance any extra acid in the blood that forms during critical illness. Specifically, we will determine if this study will effect (1) the development and progression of kidney injury, (2) how long children need to be on a ventilator (breathing machine), (3) how long children need to be in the intensive care unit and hospital after surgery and (4) whether there is any ongoing kidney injury after hospital discharge.

Most problems of the heart that children are born with can now be corrected by surgery, with excellent outcomes. Children who require cardiopulmonary bypass during surgery for correction of congenital heart lesions have a higher risk of developing kidney injury. Recently, we have learned that kidney injury can lead to worse patient outcomes, such as requiring longer times on the ventilator (breathing machine) as well as longer times in the intensive care unit and hospital.

We have preliminary information from adult and animal research studies that suggest that when patients receive sodium bicarbonate during the time they are on heart-lung bypass during surgery and then for the first 24 hours after surgery, kidney injury can be prevented. There has not been any study investigating whether this benefit is recognized in pediatric patients.

How long will I be in the study? How many other people will be in the study?
You are being asked to allow your child to participate in this study from the time they are prepared for surgery in the operating room until 48 hours after completion of cardiopulmonary bypass. If your child is still in the hospital 30 days after surgery then we will also assess his/her kidney function as well as height and weight. The purpose of this 30-day review is to check for late occurring problems with kidney function.

We plan to enroll almost 200 children (between birth and 18 years of age) in our pediatric intensive care unit at Cohen Children's Medical Center of New York.

What am I being asked to do?
If you agree to allow your child to participate in the research study, general medical history information as well as height and weight will be collected during the screening visit with the cardiothoracic surgeons.

On the day of surgery, blood and urine samples will be collected at the time the IV line is placed (which is necessary for the surgery to be done). The IV line, or intravenous line, is the small plastic tube placed inside your child's vein with a needle poke in order to provide medication during and after surgery.

The only medical procedures being done for the purposes of this research study are giving you the sodium bicarbonate solution, collecting urine samples more frequently (although the catheter placed in the bladder to collect urine is standard of care for all surgical patients), and, for some patients, 1 extra blood draw (maximum 1-2 milliliters or less than ½ teaspoon) 4-hours after surgery.

If after the first visit, it is determined that your child is eligible for the study, on the day of surgery, your child will be randomly placed into one of two groups: 1) control group or 2)

intervention group. Randomization means that you will be assigned to a group by chance (like flipping a coin) You will have an equal chance of being in either (or any) group. The study is done this way because knowing whether you are in a group can change the results of the study. We will not tell you which group you are in. The research study staff will not know your group either. We can quickly find out which group you are in if we ever need to know for your safety.

The control group will receive a placebo via the IV line in the form of a normal saline solution (sodium chloride) during surgery and in the intensive care unit after surgery. This is considered appropriate care according to the anesthesia team, cardiothoracic surgery team, as well as the intensive care unit team who will care for your child. The placebo is a liquid solution that looks like the study drug but has no real medicine in it. A placebo is often used in research studies so that the doctor and you do not know your study group. The study is done this way because knowing whether you are getting the study drug can change the results of the study.

The intervention group will receive sodium bicarbonate continuously through the IV at the beginning of anesthesia, which will continue for the first 24 hours after surgery. After 24 hours of receiving the sodium bicarbonate continuously, the IV fluids will be changed to the standard solutions used in the Pediatric Intensive Care Unit at CCMC.

This is a double-blinded study. Double blinding is when neither the researcher nor the people in the study know which study group a person is in. It is used to make sure the study data will not be biased. The physicians and nurses caring for your child in the operating room and the PICU will not be aware of which solution your child will be receiving during the first 24 hours after surgery. In case of an emergency, we can find out if you are getting the placebo or the medication.

Standard of care will be maintained regarding checking for abnormal blood tests and will be treated according to standard practice.

What are the possible risks or discomforts?

Potential short-term risks or discomforts linked to the use of sodium bicarbonate in children undergoing open heart surgery are:

- Hypokalemia (low blood potassium). In severe cases, this could lead to heart rhythm abnormalities, and in turn could affect blood pressure.
- Hypernatremia (high blood sodium). In severe case, this can lead to fluid retention. You might notice a swollen appearance.
- Alkalemia (blood pH >7.40): severe alkalemia can cause heart rhythm abnormalities, neurologic changes such as an alteration in the level of consciousness, and the blood calcium level to decrease, which can lead to a rare condition known as tetany (rigid muscles).
- Leaking out of sodium bicarbonate solution from the IV line into the body tissue at high concentrations can lead to tissue injury, although this is extremely unlikely because the type of bicarbonate fluid used in this study is not strong enough to cause this complication.

The group that does not receive the sodium bicarbonate may have more side effects than the other group.

We will try to decrease these potential risks by closely monitoring for clinical adverse events throughout the study according to standard blood laboratory tests and treating abnormal blood tests according to standard practice.

Any time confidential information is collected, there is a risk that information will be unintentionally released. Any information about you or your child obtained from this research will be kept as confidential (private) as possible.

All paper records related to your/your child's involvement in this research study will be stored in locked file cabinets. Computerized records are password protected. Your/your child's identity on these records will be indicated by a case number rather than by name, and the information linking these case numbers with your/your child's identity will be kept separate from the research records.

What if new information becomes available about the study?
During the course of this study, we may find more information that could be important to you and/or your child. This includes information that, once learned, might cause you to change your mind about your child being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?
We cannot and do not guarantee or promise that you or your child will receive any benefits from this study. Possible benefits of study participation include shorter time on the ventilator, less need for dialysis (kidney replacement therapy), and shorter time in the intensive care unit and hospital, related to the decreased development of acute kidney injury.

Future children who require cardiopulmonary bypass (heart-lung machine) for open-heart surgery and their families may benefit from this study, which will provide a better understanding of how to limit the risk of developing kidney injury during and after open-heart surgery.

What other choices do I have if I do not participate?
If you choose not to participate, your child's care team will still do what they think is best for your child, but they will not follow the fluid management guideline. Your child's information will not be collected.

Will I be paid for being in this study?
Neither you nor your child will be paid for being in this study.

Will I have to pay for anything?
There will be no cost to you for your child to be in this research study. Care that would be given if your child was not in this research study, such as the surgery and routine tests post-operatively, will be charged under your usual payment method. There will be no charge to you or your insurance company for any of the costs directly related to this study.

What are your rights as a research participant?
Your participation in this project is voluntary. The quality of your medical care will be the same, whether you join, refuse to join, or decide to leave the study.

If you do not join the study you will not be penalized or lose benefits to which you are entitled. If you join the study you may withdraw at any time without prejudice to your future care at the North Shore-LIJ Health System. Follow-up examinations may be needed to assure your well-being.

Could you be taken off the study before it is over?
It is also possible that your participation in this study may end without your consent. This decision may be made by a researcher, study sponsor, or the Institutional Review Board (IRB- the committee that oversees research at this institution).

Reasons for withdrawal may include:

- failure to follow instructions,
- failure to show up for study visits,
- it is not in your best interest to continue on this study, or
- the study is stopped.

If you withdraw from this study or if you are withdrawn from the study, any data (or samples) already collected will continue to be used. However, no new data will be collected.

For your safety, if you withdraw or are withdrawn from this study, you are urged to return for final testing to evaluate the function of your kidneys.

What happens if I am injured or hurt during the study?
All forms of medical diagnosis and treatment involve some risk of injury. In spite of all precautions, you or your child might develop an injury from participating in this study.

If your child is hurt from being in the study, you will receive medical care and treatment as needed from the Steven and Alexandra Cohen Children's Medical Center of New York (CCMC). However, you will be responsible for the costs of such medical treatment, directly or through your medical insurance and/or other forms of medical coverage. No money will be given to you.

If costs of care related to such an injury are not covered by your insurer, managed care plan or other benefits program, you may be responsible for these costs. If you are unable to pay for such costs, our research staff will assist you in applying for supplemental benefits and explain how to apply for patient financial assistance from the hospital.

Additionally, we are not responsible for research and medical care by other institutions or personnel participating in this study. You do not waive any liability rights for personal injury by signing this form.

When is the study over? Can I leave the study before it ends?
If you decide to participate, you are free to leave the study at anytime. Withdrawal will not interfere with your or your child's future care.

This study is expected to end after all information has been collected and reviewed. This study may also be stopped at any time by your child's doctor or the study Principal Investigators without your consent because it is necessary for your or your child's health or safety. Such an action would not require your or your child's consent, but you will be informed if such a decision is made and the reason for this decision.

Who can see or use my information? How will my personal information be protected? Privacy/Confidentiality (HIPAA Authorization Section)
If you agree to be in this study, we will collect health information that identifies you. We will collect the results of tests, questionnaires and interviews. We will also collect information from your medical record. We will only collect information that is needed for the research. This information has been described in this consent form. If you sign this consent form, you are giving us permission to collect, use and share your health information. This permission is called authorization.

Study records that identify you will be kept private. You will not be identified in study records or publications disclosed outside the North Shore-Long Island Jewish Health System, except as detailed below.

Investigators will share the results of your study tests and procedures with clinical staff not involved in the study who may be involved in your treatment.

In addition, your records may be reviewed in order to meet federal or state research regulations. Reviewers may include representatives from government agencies such as the Food and Drug Administration and representatives from the North Shore-Long Island Jewish Health System Institutional Review Board (IRB – the committee that reviews research at this institution).

If your research record is reviewed by any of these groups, they may also need to see your entire medical record. Please be aware that once private information is disclosed, it is subject to re-disclosure by the recipient and can no longer be considered protected.

If your research records are used for decisions related to your clinical care, then you have the right to review this information and request changes. This is limited to information about your treatment, and does not include information related to procedures or tests that are for research purposes only. You may access this information only after the study analysis is complete. You have the right to know who has and who will see your records. To request this information, or for any questions related to your health information, you may contact the Research Privacy Officer at 516-562-2018.

If you change your mind about being in the study, you may withdraw at any time. If you want us to stop collecting your health information, you need to send a letter to the researcher at the

following address:

James Schneider, MD
Pediatric Critical Care Medicine
Cohen Children's Medical Center of New York
North Shore Long Island Jewish Health System
269-01 76th Avenue
New Hyde Park, NY 11040

Your letter needs to say that you have changed your mind and do not want the researcher to collect and share your health information. You may also need to leave the research study if we cannot collect any more health information. We may still use the information we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it.

The information that is collected for research will be analyzed for many years and it is not possible to know how long this analysis and follow-up will take. Therefore, you are allowing access to this information indefinitely.

Data from this study may be used in medical publications or presentations. The information will be de-identified so that individual subjects cannot be recognized and the information will no longer be considered Protected Health Information (PHI).

If the researchers learn about potential serious harm to you or someone else or other public health concerns, it will be shared with the appropriate authorities.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?
If you have questions, concerns or complaints regarding your child's participation in this research study or if you have any questions about your child's rights as a research subject, you should speak with one of the Principal Investigators listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of the Institutional Review Board (the committee that oversees research at this institution) by calling (516) 562-3101.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the Steven and Alexandra Cohen Children's Medical Center of New York (CCMC) to use your child's personal health information collected for research purposes within our institution. You are also allowing the Steven and Alexandra Cohen Children's Medical Center of New York (CCMC) to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this informed consent will be given to you.

SIGNATURE PAGE FOLLOWS

Summation/Signature

You have read the above description of the research study. You have been told of the risks and benefits involved and all your questions have been answered to your satisfaction. A member of the research team will answer any future questions you may have. You voluntarily agree to join this study and know that you can withdraw from the study at any time without penalty. By signing this form, you have not given up any of your legal rights.

_____ _____

Name of Subject (Please Print) Age

_____ _____ _____

Name of Parent/Legal Guardian (Please Print) Signature of Parent/Legal Guardian Date

_____ _____ _____

Witness's Printed Name Witness's Signature Date

(Preferably someone not connected with the research project)

Investigator's Statement

In addition to advising the above subject of other forms of treatment and therapy which are appropriate, I have offered an opportunity for further explanation of the risks and discomforts which are, or may be associated with this study and to answer any further questions relating to it.

_____

Name of Investigator

_____ _____

Investigator's signature Date

North Shore-Long Island Jewish Health System
Campus: Steven and Alexandra Cohen Children's Medical Center of New York
Assent to be in a Research Study (8-17 years)

Title: Sodium Bicarbonate to Prevent Acute Kidney Injury in Children Undergoing Cardiac Surgery

Why are we meeting with you?
We want to tell you about something we are doing called a research study. A research study is when people collect a lot of information to learn more about something. Some of the people who work here are doing a study to learn more about children who have heart surgery and how it may affect the kidneys. After we tell you about it, we will ask if you'd like to be in this study or not.

Why are we doing this study?
Children who need surgery to fix their heart problem need to be placed on a heart-lung machine. This may hurt the kidneys.

We are working in our hospital to see if we can protect the kidneys of children who need heart surgery. We want to find out if a medicine can keep the kidneys safe during surgery.

What will you be asked to do and how long will it take?
Only if you agree, here's what will happen:

1. Before surgery, we will collect some information about you.

2. We will pick one-half of the children who agree to be in the study to be given a medication during surgery. If you are picked, you will be given the medication and we will watch closely to see how your kidneys are working and if any injury occurs.

Will this study hurt?
Sometimes things that don't feel good happen in research studies. Some things that could happen may hurt you, make you feel yucky, or make you feel upset. You might experience things like your heart beating funny, may be extra tired feeling, or may have an area of skin around an IV site hurt. Some of the things might happen to you or they might not. Or things might happen that we don't know about yet.

Will you get better if you are in this study?
Maybe. We hope that giving this medication will keep your kidneys healthy. This study will help us answer that question.

Do you have any questions?
You can ask questions any time. You can ask now. You can ask later. You can talk to me or you can talk to someone else.

Do you have to be in this study?
No, you don't. No one will be mad at you if you don't want to do this. Please talk to your parents about this before you decide whether or not to be in this research study. We will also ask your parents to give their permission for you to be in this study. But even if your parents say "yes," you can still decide not to be in this research study. And, remember, you can say yes now and change your mind later. It's up to you. We will give you a copy of this form to keep.

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Putting your name below means that you have decided to be in this study. You and your parents will be given a copy of this form after you have signed it.

_____
Name of Subject

_____ _____
Sign your name here ↑ Date

_____
Name of Investigator Obtaining Assent

_____ _____
Signature of Investigator Obtaining Assent Date

_____ _____
Signature of Witness Date

By initialing in the following places, the investigator indicates his/her opinion that the child cannot give consent/assent because he/she is:

____Too young at age ____ Initials investigator _____

____Too ill. Explanation below Initials investigator _____