University of Pittsburgh

School of Medicine
Department of Emergency Medicine

230 McKee Place
Suite 400
Pittsburgh, PA 15213

6 June 2003

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
12229 Wilkins Avenue
Rockville, MD 20852

Docket #95S-0158
Dockets Management Branch
Food and Drug Administration
Room 1061, Mail Stop HFA-305
5630 Fishers Lane,
Rockville, MD 20852

RE: IND# 66,463 – Publicly Disclosed Information

Attached to the memo, please find all Publicly Disclosed information related to this Investigational New Drug Application. This IND application is being filed to support a study of the cardiovascular pressor drug Vasopressin Injection during cardiac arrest.

This study involves an Exception from Informed Consent for Emergency Research. Consistent with the Guidance for that process, we must file all publicly disclosed information with the Public Docket.

If there are any questions or problems with this packet, please do not hesitate to contact me.

Sincerely,

Clifton Callaway, MD, PhD
Emergency Medicine
Tel 412-647-9047
Fax 412-647-1111
Email callawaycw@msx.upmc.edu

95S-0158

RPT 10

3 February 2003

Minutes from the community consultation with the Pittsburgh Human Rights Commission

Commissioners asked for justification of a placebo controlled study. We explained that vasopressin had not been tested in a scientific trial in this country and that other studies were equivocal (one study showed equivalence to epinephrine and another showed superiority). We also explained the DSMB plan and assured them the study would be halted early if vasopressin was shown to be better or worse.

Commissioners asked if we would track the ethnic breakdown of subjects enrolled in the study. We agreed to add a field to our data form but explained that the city does not track this data for their patients.

Commissioners asked us to share DSMB findings as the study continued. We agreed.

One of the commissioners express concern there were no minorities on the research team or the IRB. Jeannie Baronne, from the IRB explained the difficulty in finding minority physicians and community members to serve in this capacity.

The Commissioners asked us to consult with the Center for Minority Health before beginning the trial. A meeting has been set with this group to discuss the study.

In attendance from Pitt

Robert Hardesty, MD
Jeannie Baronne
Patricia Erb
Clifton Callaway, MD, PhD
David Hostler, PhD, NREMT-P

Center for Minority Health (CMH)
Community Research Advisory Board (CRAB)

Research Summary Sheet: To be completed by Investigator

(Form must be typed)

Names of Investigator and Co-Investigators (include academic affiliation):

Clifton W. Callaway, MD, PhD; David Hostler, PhD; Ankur Doshi, MD; Jeffery Lubin, MD (Department of Emergency Medicine).

Brian Kuszajewski, NREMT-P (City of Pittsburgh Emergency Medical Services)

Project Director:___Clifton W. Callaway,MD, PhD_____

Due Date of Proposal: _____

Date proposal was/is submitted for funding: ____June 6, 2002_____

Type of Application: _____Local Foundation_____

Sponsoring Agency: _____Pittsburgh Emergency Medical Foundation_____

Requested Level and Duration of Support: _____$1500 / entire project_____

Targeted Population:_____Persons in City of Pittsburgh suffering sudden cardiac death

Method of Recruitment:____All such persons treated by City of Pittsburgh Paramedics

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Comments:_____This study involves Waiver of Informed Consent for Emergency Research. In order to conduct this type of study, we are seeking as much input as possible from the community and its representatives.

Attach <u>one</u> page that includes the following:

1. **Statement of the Problem**
2. **Proposal Abstract**

Statement of Problem:
Cardiac arrest occurs when the heart suddenly stops pumping blood. Survival after cardiac arrest that occurs outside of the hospital using current treatment is estimated to be 7% nationally. Vasopressor medications are a critical component of resuscitation therapy in order to support and elevate coronary perfusion pressure, which is correlated with success of resuscitation. Epinephrine is the sole vasopressor drug available to paramedics.

Recently, vasopressin has been recommended in the American Heart Association guidelines as an agent for use during cardiac arrest resuscitation. Vasopressin is a synthetic form of a hormone produced in the pituitary gland. European and Canadian trials suggest that vasopressin improves survival after out-of-hospital cardiac arrest but not after in-hospital cardiac arrest. Vasopressin is not yet available to paramedics in the United Sates. The efficacy of vasopressin when used by paramedics for cardiac arrest resuscitation has not been determined.

Proposal Abstract:
This protocol proposes a blinded, placebo-controlled, randomized trial of vasopressin use by paramedics during resuscitation from cardiac arrest. All persons treated for cardiac arrest by City of Pittsburgh paramedics will be eligible as subjects. Persons who are <18 years old, have major trauma, are known to be pregnant, or are prisoners will be excluded. This paramedic system serves all 911 calls within the city limits of Pittsburgh.

Vasopressin (40 units) (n=162 subjects) or saline placebo (n=162 subjects) will be administered intravenously in addition to current standard therapy as soon as feasible during the resuscitation. Paramedics will be blinded to which substance they are administering by using a numbered label to cover the drug vial label. Each paramedic unit will carry one numbered study drug vial that has been randomly assigned to contain vasopressin or placebo. The paramedics will use this vial for the next eligible subject. Vials will be replaced after a use.

No subject will have any other therapy withheld or changed as a result of randomization. In other words, all subjects will receive at least standard care. In Pennsylvania, vasopressin is not currently stocked on ground ambulances, and would not be available to subjects outside of this study. Primary outcome measurements will be rate of return of pulses, and survival to hospital arrival. Secondary outcomes will include survival to hospital discharge and neurological status at 6 months.

A data safety monitoring board that is separate from the investigators will review progress of the study after every 25 subjects or after any adverse events. This board will have access to the identity of the vials. The data resulting from this study will help guide decisions about whether to add vasopressin to the formulary for paramedics, and will help determine how strongly to emphasize its use in paramedic treatment protocols.

Waiver of informed consent is requested for the emergency portion of this study during which the study drug will be administered, and during which information will be collected from the paramedics. This waiver is necessary because subjects will be unconscious, and vasopressin may be ineffective if administration is delayed by more than 5 minutes. Subjects enrolled without prospective consent will be notified as soon as feasible after enrollment. If subjects are unable to be notified due to death or coma, their family or legal representative will be notified. Informed consent to continue in the study will be obtained from subjects, their family member or other legal representative after initial enrollment. Continuation will consist of medical record review and a follow-up interview after 6 months.

We have presented this study to the Scientific Review Committee of the Department of Emergency Medicine, the Pennsylvania Emergency Health Services Council Medical Advisory Committee (Pennsylvania Department of Health), the Institutional Review Board of the University of Pittsburgh, and the Human Relations Committee of the City of Pittsburgh. An Investigational Drug Application for this use of vasopressin has been filed with the Food and Drug Administration. A press release has been prepared but not sent for distribution to the local media (Post-Gazette and Tribune-Review).

Hostler, David

From: Callaway, Clifton
nt: Tuesday, April 08, 2003 12:24 PM
.o: Hostler, David
Subject: FW: CRAB

-----Original Message-----
From: Callaway, Clifton
Sent: Wednesday, March 19, 2003 2:09 PM
To: 'Angela F. Ford'
Subject: RE: CRAB

Thanks very much for the opportunity to present.

The comments were very helpful. I am immediately planning to incorporate some suggestions into the Data Safety Monitoring Plan, specifically interim assessments of equitable randomization according to demographics.

Two suggestions deserve entirely separate study: assessing disease incidence by zip code, and assessing survival (or failure of survival) by race identified on zip code. I will talk to Mike Robinson and our research group more about the feasibility of that type of query. There will be some new twists to collecting that type of data that are required by the recent implementation of HIPAA. Up until now (April 14, 2003), it would have been a simple retrospective review of charts.

We also will pursue the suggestion to discuss the study in advance with the American Heart Association at an organizational level.

Dr. Thomas said, the group was impressively diverse. I hope we can interact more often in the future.

Clif C.
Clifton Callaway, MD, PhD
Department of Emergency Medicine
University of Pittsburgh
Tel 412-647-9047
Fax 412-647-1111
email callawaycw@msx.upmc.edu

-----Original Message-----
From: Angela F. Ford [mailto:afford@cmh.pitt.edu]
Sent: Monday, March 17, 2003 11:14 AM
To: callawaycw@msx.upmc.edu; garberm@msx.upmc.edu
Subject: Fwd: CRAB

Greetings:
Hope you are both doing well. I need to move the times back to allow for some business to take place
from 11:30am -11:55am, prior (and unrelated) to your presentations. In addition, Dr. Garber has requested that she go 2nd to allow time for her mentor, to arrive, after noon. Would this timeframe work for both of you?

Dr. Callaway: 12 noon -- 12:15 (time includes presentation/questions/feedback)
Dr. Garber: 12:30--12:45 (time includes presenation/questions/feedback)

By the way, the Gold Room is at the top of the stairs (2nd floor) and to the left. Angela

This is confirmation of your attendance at the March 19th CRAB meeting scheduled at the University Club in the Gold Room.

Please plan to present at the time listed below:
Garber -- 11:45
Dr. Callaway -- 12:15

You should be prepared to provide an informal 5 minutes summary/overview of your project and then receive feedback and respond to questions for the next 10 minutes.

Please contact me as soon as possible if you have questions or concerns.
CRAB members received your material in advance and should have reviewed in by the day/time of your presentation.

Looking forward to having you at the meeting.

Angela
****
Be the Change that You Want to See in the World (Ghandi)

Angela F. Ford, MSW, LSW
Associate Director
Center for Minority Health
University of Pittsburgh
Graduate School of Public Health
130 DeSoto Street
125 Parran Hall
Pittsburgh, PA 15261
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www.cmh.pitt.edu

Media Coverage

The following page is a list of Radio and Television coverage of this study.

Station	Medium	Date
WDUQ	Radio	March 6th, 2003
WPXI	Television	March 6th, 2003
		March 7th, 2003
		March 13th, 2003
		March 14th, 2003

University of Pittsburgh
Schools of the Health Sciences
News Bureau

CONTACT: Lisa Rossi
Frank Raczkiewicz
PHONE: (412) 647-3555
FAX: (412) 624-3184
E-MAIL: RossiL@upmc.edu
RaczkiewiczFA@upmc.edu

FOR IMMEDIATE RELEASE

PITT RESEARCHERS TO COLLABORATE WITH PARAMEDICS TO SEE IF THE DRUG VASOPRESSIN CAN IMPROVE OUTCOME OF CARDIAC ARREST

Notice of public disclosure for emergency medicine research, public forum March 13

PITTSBURGH, March 5 – More than 350 people in cardiac arrest are treated by City of Pittsburgh paramedics each year, according to statistics from researchers in the department of emergency medicine at the University of Pittsburgh School of Medicine.

Can survival for patients who suffer out-of-hospital cardiac arrest be improved by using a generic drug called vasopressin?

To help answer this question, emergency medicine researchers are participating in a local, one-year research study known as the Vasopressin in Cardiac Arrest Research Project. Researchers will be collaborating with City of Pittsburgh paramedics, who will administer the drug.

Paramedics in Pennsylvania are trained how to use vasopressin for advanced cardiac life support, but most do not carry this drug as part of their treatment regimen.

During this study, each City of Pittsburgh paramedic crew will be asked to carry research vials. Half of the paramedics will receive vials containing vasopressin and half of the paramedics will receive vials containing saline (salt water). None of the paramedics will know whether the vials contain the active drug or the saline.

The paramedics will perform their current standard of care for cardiac arrest, including giving adrenaline (epinephrine), and additionally, will administer the contents of the research vial. It is expected that one-half of patients in cardiac arrest will receive vasopressin in addition to their regular treatment. The researchers hope to give vasopressin to 162 patients in cardiac arrest. A total of 324 people may participate in the study.

- more -

When paramedics are called to the scene of a patient in cardiac arrest, they typically provide advanced tools to help the patient breathe and administer drugs like epinephrine to help promote blood flow to the heart, making it more likely to resume beating. Currently, the only blood flow-promoting drug approved for use by paramedics is epinephrine.

During the vasopressin study, an emergency medicine physician from the University of Pittsburgh will ride with paramedics in the ambulance. It is not unusual for City of Pittsburgh paramedics to have emergency medicine physicians working along side them in the field and is part of the required training for emergency medicine residents at the University of Pittsburgh.

Information gathered during the study will enable researchers to examine whether there is any change in the proportion of victims whose hearts restart after receiving the vasopressin.

"If results of this study show a significant increase in resuscitation from sudden cardiac arrest, vasopressin may eventually win approval for use by all paramedics," says Clifton W. Callaway, M.D., Ph.D., assistant professor of emergency medicine at the University of Pittsburgh School of Medicine and principal investigator of the vasopressin study. "Additionally, it is necessary to conduct this study in the out-of-hospital setting because victims of cardiac arrest often arrive at the hospital too late for the drug to do any good."

Recent studies in Canada and Europe have shown that vasopressin was equivalent or superior to adrenaline when used as a treatment for cardiac arrest. Based on these studies, the American Heart Association recommends vasopressin as the drug to be considered for the treatment of cardiac arrest. However, it is unknown whether vasopressin is helpful when used for victims of cardiac arrest under conditions like those encountered by paramedics in the United States.

Because this study could affect anyone living in Pittsburgh, both the university and the researchers are seeking comments from the public. To explain the research and answer questions, the Pitt researchers are holding a public forum 6:30 – 7:30 p.m., Thursday, March 13 in the Lower Lounge of the William Pitt Union, corner of Fifth Ave. and Bigelow Blvd. in Oakland.

According to federal law and university policy, those who participate in a clinical research study must provide informed consent. Because of the nature of this trial, it is impossible

to obtain consent at the time of cardiac arrest. For this reason, the researchers are notifying the public that informed consent will be waived. Researchers will make every attempt to be in contact with family members and, if possible, the cardiac arrest patient to obtain consent at a later time.

For more information about the public forum, or to make comments or ask questions about the vasopressin study, researchers can be contacted at the following:

By Telephone:	Vasopressin in Cardiac Arrest Research Project (412) 647-2671.
By Mail:	University of Pittsburgh Department of Emergency Medicine 230 McKee Place, Suite 400 Pittsburgh, Pa. 15213 Attention: Clifton Callaway, principal investigator
By E-mail:	callawayCW@upmc.edu

Funding for the Vasopressin in Cardiac Arrest Research Project is supported by the Pittsburgh Emergency Medicine Foundation.

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kr/03-04-03

Pittsburgh, PA
Friday
March 14, 2003

Forum planned on heart drug study

Monday, March 10, 2003

By Anita Srikameswaran, Post-Gazette Staff Writer

It isn't possible to ask someone whose heart has stopped if he wants to participate in a research study, so local researchers who want to test a new drug strategy for treating cardiac arrest will conduct a public forum next week to explain their upcoming study.

Patients normally must sign consent forms before they participate in a research study. But federal research regulations allow informed consent to be waived, according to strict criteria, in cases like this.

The public can learn about the study, ask questions and offer comments during the forum from 6:30 to 7:30 p.m. Thursday in the lower lounge of the William Pitt Union, at Fifth Avenue and Bigelow Boulevard, Oakland.

Cardiac arrest patients will all receive standard medical treatment in the trial. But city of Pittsburgh paramedics also will administer either a vial of the drug vasopressin or harmless saline to patients whose hearts have stopped beating. University of Pittsburgh emergency medicine physicians will ride in ambulances with paramedics during the yearlong project.

Researchers expect that vasopressin will be given to 162 out of a total of 324 patients. The study drug will not be given if family members object.

In addition to performing cardiopulmonary resuscitation, or CPR, and using defibrillators to restart the heart, paramedics can administer epinephrine to cardiac arrest patients.

Vasopressin is similar in action to epinephrine, causing arteries to constrict and boosting blood pressure so that more blood flows to the heart.

"The heart won't start on its own unless you deliver adequate blood flow to it," explained principal investigator Dr. Clifton Callaway. "After a few

minutes of cardiac arrest, the body really needs help with drugs to generate enough pressure to deliver blood to the heart."

Canadian and European studies indicate that vasopressin is as effective or better than epinephrine in cardiac arrest. Some states, including Georgia and North Carolina, already allow paramedics to give vasopressin. The drug has long been used in emergency departments and intensive care settings.

Callaway said that if there are no objections from the public, the study could begin by late April or early May.

For more information about the forum or the study, the researchers can be contacted by e-mail at **callawayCW@ upmc.edu** or by calling 412-647-2671.

Anita Srikameswaran can be reached at **anitas@post-gazette.com** *or 412-263-3858.*

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By Mail: University of Pittsburgh
Department of Emergency Medicine
230 McKee Place, Suite 400
Pittsburgh, PA 15213
Attention: Clifton Callaway, Principal Investigator

By E-mail: vaso@pitt.edu

Funding for the Vasopressin in Cardiac Arrest Research Project is supported by the Pittsburgh Emergency Medicine Foundation.

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PITT RESEARCHERS TO COLLABORATE WITH PARAMEDICS TO SEE IF THE DRUG VASOPRESSIN CAN IMPROVE OUTCOME OF CARDIAC ARREST

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Public Forum

Thursday, 6:30 PM
13 March 2003
Lower Lounge
William Pitt Union
Oakland – across from the Cathedral of Learning

A research study called

"Vasopressin in Cardiac Arrest"

Investigators from the University of Pittsburgh will discuss a proposed research study during which City of Pittsburgh paramedics will administer an experimental drug during treatment of cardiac arrest. Potential subjects will be unconscious, and the investigators are requesting an Exception from the Requirement for Informed Consent to participate.

Community comments and concerns are invited.

Phone number for comments: 412-647-2671

PAD TRIAL PUBLIC FORUM

March 13th, 2003
6:30 p.m.
William Pitt Union

Please record your zip code for purposes of tracking community representation. Thank you.

15237
15238
15232
15232
15239
26505
19355
15213
15213
15213
15213
15068
15211
15085
15206
15238

Public Forum

Tuesday, 1:00 PM
29 April 2003
Classroom A
230 McKee Place – 5th floor
Oakland – next to Wyndham Hotel

A research study called

"Vasopressin in Cardiac Arrest"

Investigators from the University of Pittsburgh will discuss a proposed research study during which City of Pittsburgh paramedics will administer an experimental drug during treatment of cardiac arrest. Potential subjects will be unconscious, and the investigators are requesting an Exception from the Requirement for Informed Consent to participate.

Community comments and concerns are invited.

Phone number for comments: 412-647-2671
Email for comments: Vaso@pitt.edu

Vasopressin Public Disclosure 29Apr03 1300

STUDY QUESTION SESSION

Kristin Olanson 4.29.03

Public Forums

The following Slides were used at all Public Forums

Vasopressin in Cardiac Arrest

Clifton Callaway, MD, PhD
Ankur Doshi, MD
David Hostler, PhD
Brian Kuzajewski,NREMTP
Jeff Lubin, MD
Mark Pinchalk, NREMTP

Cardiac Arrest

- What is Cardiac Arrest?
  - The heart stops beating
    - Heart attack
    - Irregular heartbeat
    - Lung / other reduce oxygen / blood flow
  - Blood stops going to the brain
    - Lose consciousness
    - Collapse

Cardiac Arrest in Pittsburgh

- Who has cardiac arrest?
- How many survive?
- What treatment do they get?

How Many?

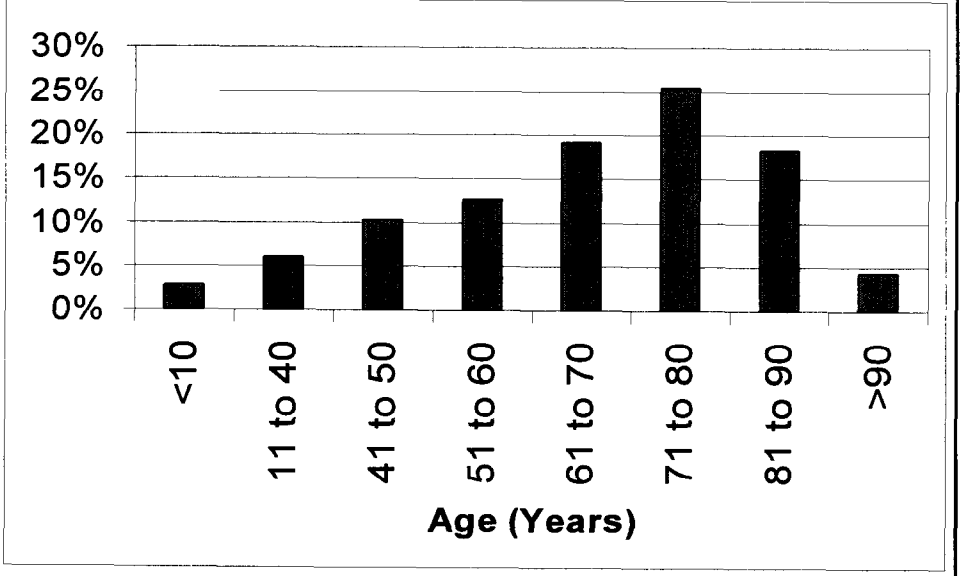
310 – 350 Pittsburghers per year

1 of every 1000 people per year

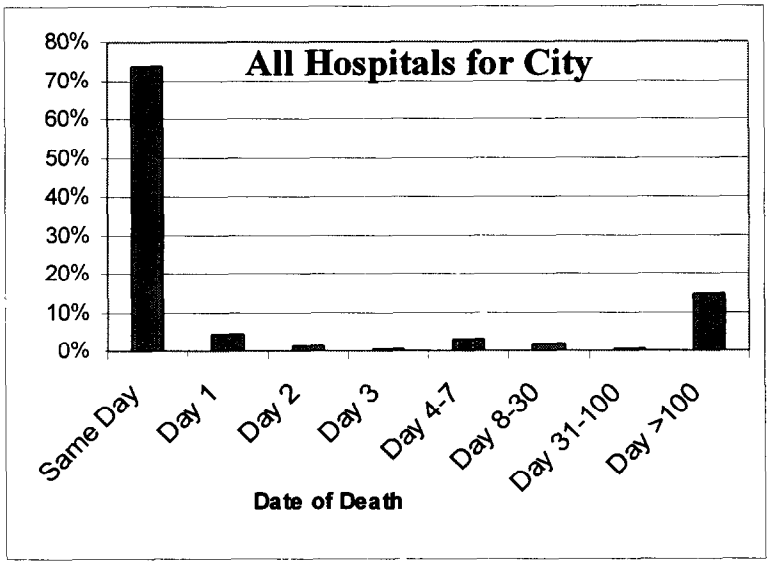
About One Person per Day

Who are they - Sex?

Who are they - Age?

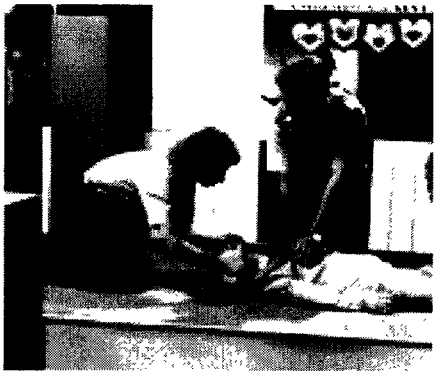


How Many Die? (Death Certificates)



Cardiac Arrest - Treatment

- CPR (Chest Compressions)
  - Provides some blood flow to heart and brain
- Defibrillate
  - Rapid shock with an AED (airport, some buildings) can restart some hearts.
- Call 911
  - Paramedics and Fire Department will bring advanced drugs and equipment

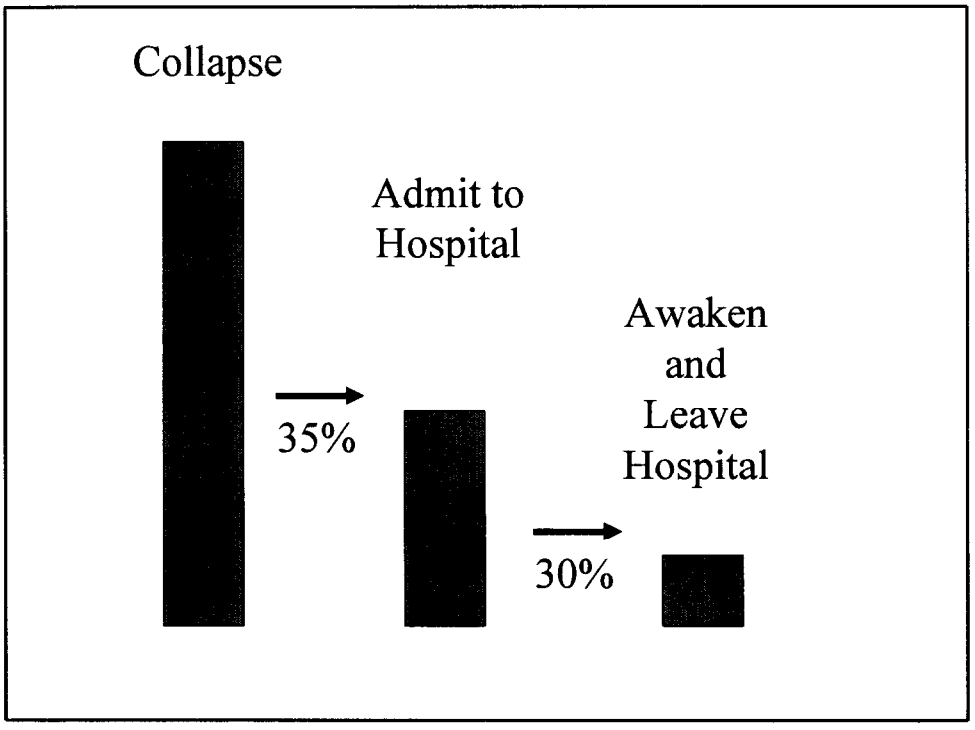


Paramedics will bring drugs that increase the chance of CPR and electricity working.

Treatment?

Restore a heartbeat without any drugs for 5-8%
(CPR and Shocks only)

Remainder require CPR + Drugs
(Advanced Care by Paramedics)



Treatment?

Using their current drugs, paramedics restore a pulse for about 30% of people.

One of their most important drugs is Epinephrine (Adrenaline)

What is to be done?

- Better and more CPR
- Faster Access to Defibrillators / Lifesaving Equipment.
- Better Tools (Drugs) for Paramedics

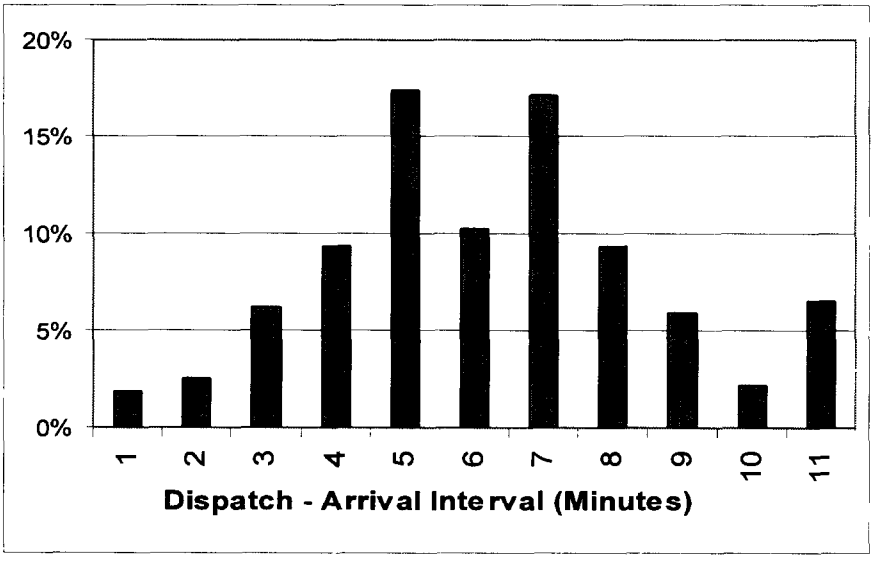
Vasopressin in Cardiac Arrest

- VASOPRESSIN
  - A vasoconstrictor (raises blood pressure)
  - Improves blood flow to the heart during CPR
  - Lasts longer than epinephrine
  - Its effects are additive to those of epinephrine

Vasopressin in Cardiac Arrest

- In Canada, vasopressin = epinephrine when given 3-4 minutes after collapse to patients with cardiac arrest in the hospital.
- In Germany, vasopressin>epinephrine when given 7-9 minutes after collapse to patients with cardiac arrest outside of the hospital

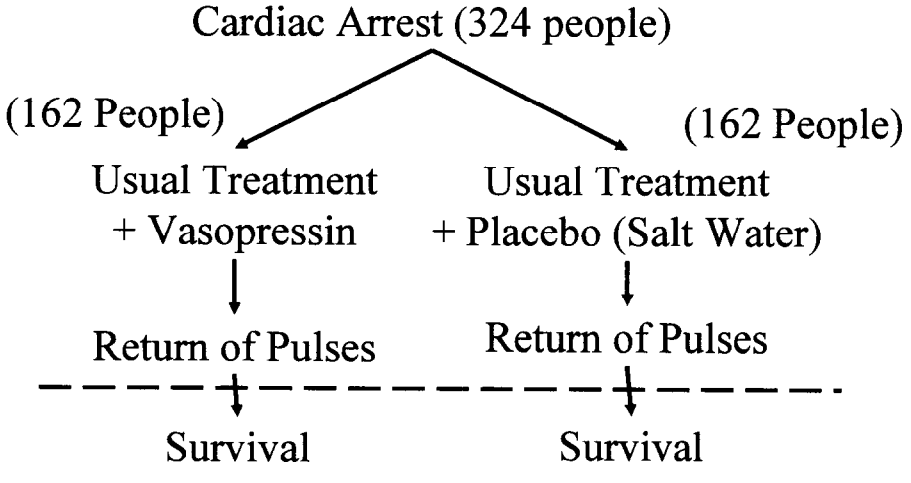
Pittsburgh Paramedic Arrival?



Vasopressin in Cardiac Arrest

- Why not just use it?
  - Not proven under the conditions encountered by US paramedics.
  - Just adding drugs without proven benefit takes time away from other tasks.
  - Unknown whether it will help certain types of patients more than others.

Vasopressin in Cardiac Arrest Study



Risks?

- Severe elevation in blood pressure.
  - Unlikely during cardiac arrest
- Rapid heart rate.
  - Can be treated by paramedics.
- Reduced blood flow to bowels.
  - Not observed during cardiac arrest.
- Rare chance of allergic or unknown reactions

Why a Placebo (Salt water)?

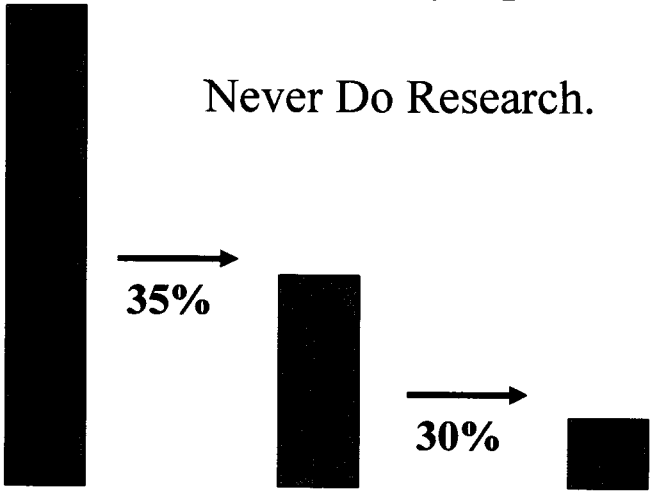
- Need a group for comparison.
- There are constant effort to improve care.
- If we give vasopressin in 2003 and see more survival than in 2002.
  - Maybe due to drug
  - Maybe more CPR training
  - Maybe additional training to Fire Department
  - Etc.

Problem

- We do not know who will have a cardiac arrest and collapse.
- Once they collapse, we cannot ask permission to do this research.
- We have seconds – minutes to decide.

Solution 1

Never Do Research.



Solution 2

Protection of Human Subjects; Informed Consent and Waiver of Informed Consent Requirements in Certain Emergency Research; Final Rules, Federal Register (FR), 61 FR 51498, October 2, 1996.

Appropriate Oversight of Our Research

- Institutional Review Board
  - Ethics / Safety / Appropriate Conduct
- Food and Drug Administration
  - Ethics / Safety / Appropriate Conduct
- Department of Health
  - Prehospital Emergency Health Services Council
- Data Safety Monitoring Board
  - Dr. Ronald Roth; Dr. Paul Beck

Notification of the Community

- Press Release on March 5, 2003
- Featured so far in
  - Pittsburgh Post-Gazette
  - WPXI-TV news
  - WDUQ radio
  - Pittsburgh Business Times
- Release is on Web Site
  - www.upmc.edu/NewsBureau/tx/vasopressin_paramedic_study.htm

Consultation with the Community

- University of Pittsburgh Institutional Review Board
  - Includes community members
- City Human Relations Commission
- Center for Minority Health
- This Forum and one every month
- Open Email and Telephone lines.

When will it start?

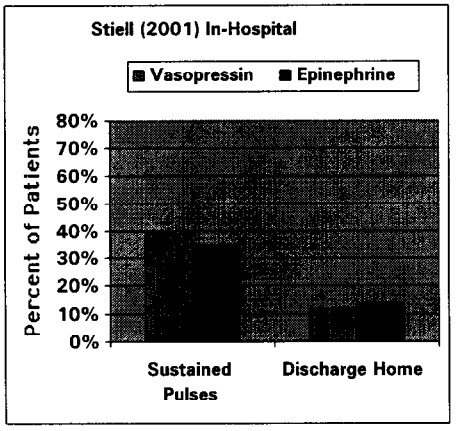
Week of May 5, 2003

Remain Open to Comments.

- Email:
  - –VASO@pitt.edu
- Telephone:
  - –412-647-2671
- Regular Open Meetings

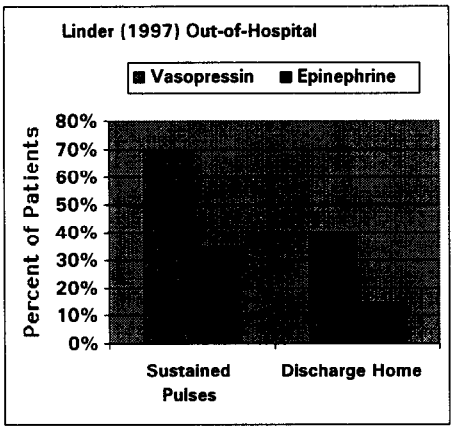
Vasopressin in Cardiac Arrest

- Stiell et al (2001).
  - In-hospital cardiac arrests in Canada
  - Subjects got drug 3-4 minutes after collapse
  - No difference



Vasopressin in Cardiac Arrest

- Linder et al (1997)
  - Out-of-hospital cardiac arrests in Germany
  - Subjects got drug 7-9 minutes after collapse
  - Vasopressin better



DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

INVESTIGATIONAL NEW DRUG APPLICATION (IND)

(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)

Form Approved: OMB No. 0910-0014.
Expiration Date: November 30, 2002
See OMB Statement on Reverse.

NOTE: No drug may be shipped or clinical investigation begun until an IND for that investigation is in effect (21 CFR 312.40).

1. NAME OF SPONSOR	2. DATE OF SUBMISSION
Clifton W. Calllaway, MD, PhD	6 June 2003
3 ADDRESS *(Number, Street, City, State and Zip Code)*	**4. TELEPHONE NUMBER** *(Include Area Code)*
Department of Emergency Medicine, University of PIttsburgh 230 McKee Place, Suite 400 Pittsburgh, PA 15213	412-647-9047
5. NAME(S) OF DRUG *(Include all available names: Trade, Generic, Chemical, Code)*	**6. IND NUMBER** *(If previously assigned)*
Vasopressin Injection, USP	66, 463

7. INDICATION(S) *(Covered by this submission)*
Treatment of cardiac arrest occurring outside of the hospital.

8. PHASE(S) OF CLINICAL INVESTIGATION TO BE CONDUCTED:
☐ PHASE 1 ☐ PHASE 2 ☑ PHASE 3 ☐ OTHER _____ *(Specify)*

9. LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS (21 CFR Part 312), NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, DRUG MASTER FILES *(21 CFR Part 314.420)*, AND PRODUCT LICENSE APPLICATIONS (21 CFR Part 601) REFERRED TO IN THIS APPLICATION.

10. ***IND submission should be consecutively numbered. The initial IND should be numbered "Serial number: 000." The next submission (e.g., amendment, report, or correspondence) should be numbered "Serial Number: 001." Subsequent submissions should be numbered consecutively in the order in which they are submitted.***

SERIAL NUMBER: 0 0 2

11. THIS SUBMISSION CONTAINS THE FOLLOWING. *(Check all that apply)*

☐ INITIAL INVESTIGATIONAL NEW DRUG APPLICATION (IND)
☐ RESPONSE TO CLINICAL HOLD

PROTOCOL AMENDMENT(S):
☐ NEW PROTOCOL
☐ CHANGE IN PROTOCOL
☐ NEW INVESTIGATOR

INFORMATION AMENDMENT(S):
☐ CHEMISTRY/MICROBIOLOGY
☐ PHARMACOLOGY/TOXICOLOGY
☐ CLINICAL

IND SAFETY REPORT(S):
☐ INITIAL WRITTEN REPORT
☐ FOLLOW-UP TO A WRITTEN REPORT

☐ RESPONSE TO FDA REQUEST FOR INFORMATION
☐ ANNUAL REPORT
☑ GENERAL CORRESPONDENCE
☐ REQUEST FOR REINSTATEMENT OF IND THAT IS WITHDRAWN, INACTIVATED, TERMINATED OR DISCONTINUED
☐ OTHER _____ *(Specify)*

CHECK ONLY IF APPLICABLE

FOR FDA USE ONLY

CDR/DBIND/DGD RECEIPT STAMP	DDR RECEIPT STAMP	DIVISION ASSIGNMENT: IND NUMBER ASSIGNED:

PSC Media Arts (301) 443-1090 EF

12. **CONTENTS OF APPLICATION**

This application contains the following items: *(Check all that apply)*

- ☐ 1. Form FDA 1571 *[21 CFR 312.23(a)(1)]*
- ☐ 2. Table of Contents *[21 CFR 312.23(a)(2)]*
- ☐ 3. Introductory statement *[21 CFR 312.23(a)(3)]*
- ☐ 4. General Investigational plan *[21 CFR 312.23(a)(3)]*
- ☐ 5. Investigator's brochure *[21 CFR 312.23(a)(5)]*
- ☐ 6. Protocol(s) *[21 CFR 312.23(a)(6)]*
  - ☐ a. Study protocol(s) *[21 CFR 312.23(a)(6)]*
  - ☐ b. Investigator data *[21 CFR 312.23(a)(6)(iii)(b)]* or completed Form(s) FDA 1572
  - ☐ c. Facilities data *[21 CFR 312.23(a)(6)(iii)(b)]* or completed Form(s) FDA 1572
  - ☐ d. Institutional Review Board data *[21 CFR 312.23(a)(6)(iii)(b)]* or completed Form(s) FDA 1572
- ☐ 7. Chemistry, manufacturing, and control data *[21 CFR 312.23(a)(7)]*
  - ☐ Environmental assessment or claim for exclusion *[21 CFR 312.23(a)(7)(iv)(e)]*
- ☐ 8. Pharmacology and toxicology data *[21 CFR 312.23(a)(8)]*
- ☐ 9. Previous human experience *[21 CFR 312.23(a)(9)]*
- ☑ 10. Additional information *[21 CFR 312.23(a)(10)]*

13. IS ANY PART OF THE CLINICAL STUDY TO BE CONDUCTED BY A CONTRACT RESEARCH ORGANIZATION? ☐ YES ☑ NO

IF YES, WILL ANY SPONSOR OBLIGATIONS BE TRANSFERRED TO THE CONTRACT RESEARCH ORGANIZATION? ☐ YES ☑ NO

IF YES, ATTACH A STATEMENT CONTAINING THE NAME AND ADDRESS OF THE CONTRACT RESEARCH ORGANIZATION, IDENTIFICATION OF THE CLINICAL STUDY, AND A LISTING OF THE OBLIGATIONS TRANSFERRED.

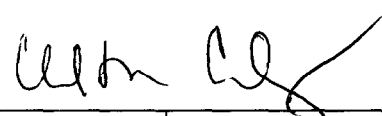
14. NAME AND TITLE OF THE PERSON RESPONSIBLE FOR MONITORING THE CONDUCT AND PROGRESS OF THE CLINICAL INVESTIGATIONS

Clifton W. Callaway,MD,PhD
Assistant Professor of Emergency Medicine
University of Pittsburgh School of Medicine

15. NAME(S) AND TITLE(S) OF THE PERSON(S) RESPONSIBLE FOR REVIEW AND EVALUATION OF INFORMATION RELEVANT TO THE SAFETY OF THE DRUG

Clifton W. Callaway,MD, PhD - Principal Investigator
Ronald N. Roth, MD - Medical Director for City of Pittsburgh Emergtecy Medical Services
Paul Beck, MD - Medical Command Physician for City of Pittsburgh Emergency Medical Services

I agree not to begin clinical investigations until 30 days after FDA's receipt of the IND unless I receive earlier notification by FDA that the studies may begin. I also agree not to begin or continue clinical investigations covered by the IND if those studies are placed on clinical hold. I agree that an Institutional Review Board (IRB) that complies with the requirements set fourth in 21 CFR Part 56 will be responsible for initial and continuing review and approval of each of the studies in the proposed clinical investigation. I agree to conduct the investigation in accordance with all other applicable regulatory requirements.

16. NAME OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE	17. SIGNATURE OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE	
Clifton W. Callaway		
18. ADDRESS *(Number, Street, City, State and Zip Code)*	19. TELEPHONE NUMBER *(Include Area Code)*	20. DATE
Department of Emergency Medicine 230 McKee Place, Suite 400 Pitsburgh, PA 15213	412-647-9047	6 June 2003

(**WARNING**: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)

Public reporting burden for this collection of information is estimated to average 100 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments *regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:*

Food and Drug Administration
CBER (HFM-99)
1401 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER (HFD-94)
12229 Wilkins Avenue
Rockville, MD 20852

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

Please **DO NOT RETURN** this application to this address.