ATOM STUDY: Australian Toxicology Monitoring

Anticoagulation Project Time & Treatment (aPTT)

PROCEDURE

AIM: To investigate the pharmacokinetics and dynamics of warfarin, super-warfarins and newer anticoagulant agents in overdose.

INCLUSION:

1/ Any intentional ingestion of warfarin, dabigatran, bivalirudin, rivaroxaban, apixaban, brodifacoum, other long-acting super warfarins and any heparin overdoses.

EXCLUSION:

Age < 14 years

WHAT IS INVOLVED:

This study involves using serum already collected and obtaining new serum samples, while the patient is in hospital. Patients' should be informed that extra blood samples will be taken. At the most we will collect 4 extra blood samples per 24 hours. The majority of these samples will be taken with the patients routine bloods. Hence there are minimal risks from this study, only that of collecting an extra blood sample. The patient will be de-identified. Samples are tested for drug and clotting factor levels, these include, warfarin (or appropriate ingested drug) and aPTT, PT and factor II, VII, IX and X levels. Once the study is completed the samples are destroyed. As a part of this study we will also be accessing the patient's medical records. This study will allow us to better understand anticoagulants in overdose.

METHOD:

STEP 1 - Obtain **consent** from the patient. Please ask them to sign **page 4** of the **"Subject Information and Consent form"** and then please fax this page to: **(02) 49110501.**

STEP 2 - Complete the patient data form and please fax the completed form to **(02) 49110501**

STEP 3 - Research samples are to be collected in a **serum tube**.

Note on all request forms **"Anticoagulation Project"** – research sample.

Please send the "Laboratory Protocol" to your pathology laboratory with the first serum sample collected.

BLOOD SAMPLE TIMING

Research samples to be collected are 5mL serum samples (SST) and a coagulation/citrate tube correctly filled

SAMPLING TIMES:

Please collect a **serum tube** for research purposes at these times:

a/ **Presentation**; along with coagulation studies (INR/PT, aPTT)

b/ **6-8 hourly;** Along with coagulation studies (and as required to guide treatment)

ANTIDOTE TREATMENT

Please document any treatment given (e.g. Vitamin K, FFP, prothrombin X) and the **time given** on the datasheet attached.

If you have any questions please call Dr Geoff Isbister on 0438466471or 1800 676 944

Please fax all forms to (02) 49110501.

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PATIENT DATA SHEET

PATIENT Sticker/Details:	**Presentation to ED** **DATE:** **TIME:** **CONSENT OBTAINED:** YES / NO
INGESTION details **DATE:** **TIME:**	**Weight (KG):** **Height (CM):**
Study medication ingested (circle): WARFARIN / DABIGATRAN / BIVALIRUDIN / RIVAROXABAN / APIXABAN / BRODIFACOUM OTHER: **DOSE ingested:**	**Usual medication:** YES / NO **Reason for anticoagulation:** DVT / PE / AF / VALVE / OTHER **INTENTION / ACCIDENTAL ingestion (circle)**
CO INGESTIONS : Drugs or EtOH	**CHARCOAL GIVEN:** YES / NO **TIME and DOSE (eg 50g):**

TREATMENT(S) GIVEN:

Vitamin K:

IV / PO:	Dose (mg):	Date:	Time:

FFP (amount/time): _____ **Other:**

Prothrombin X (amount/time):_____

LMWH/Heparin (amount/time):_____

Please fax completed form to (02) 49110501

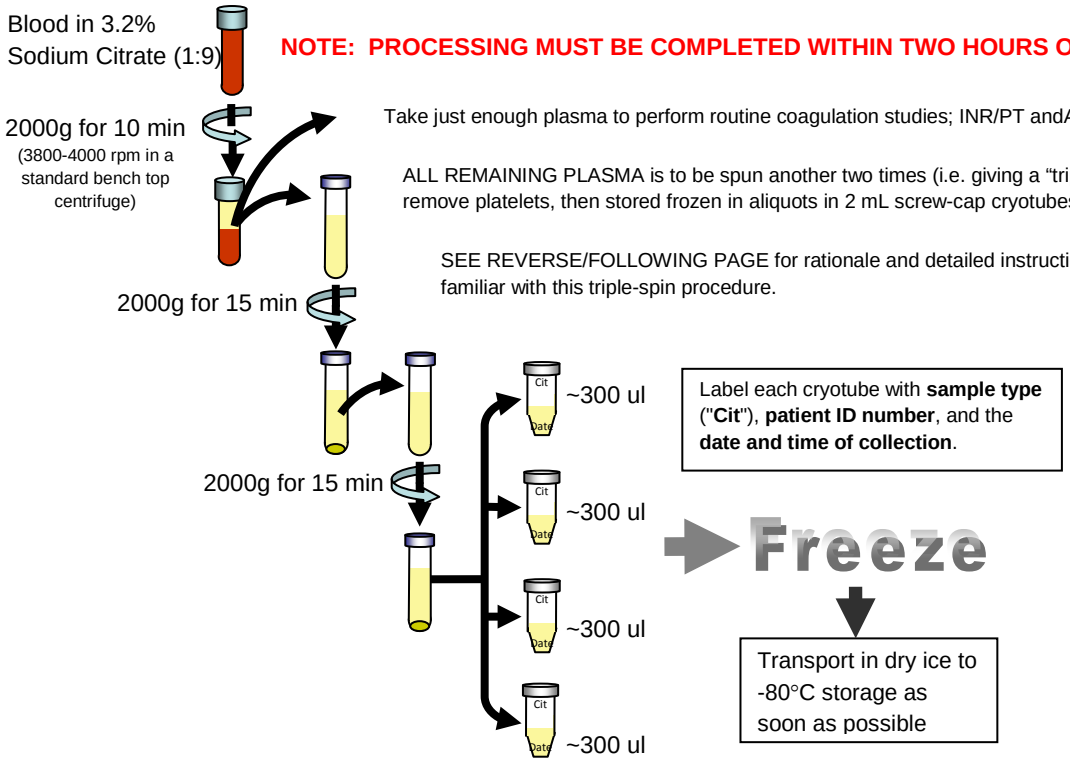
If you have any questions please call Dr Geoff Isbister on 0438466471or 1800676944

ATOM STUDY: Australian Toxicology Monitoring

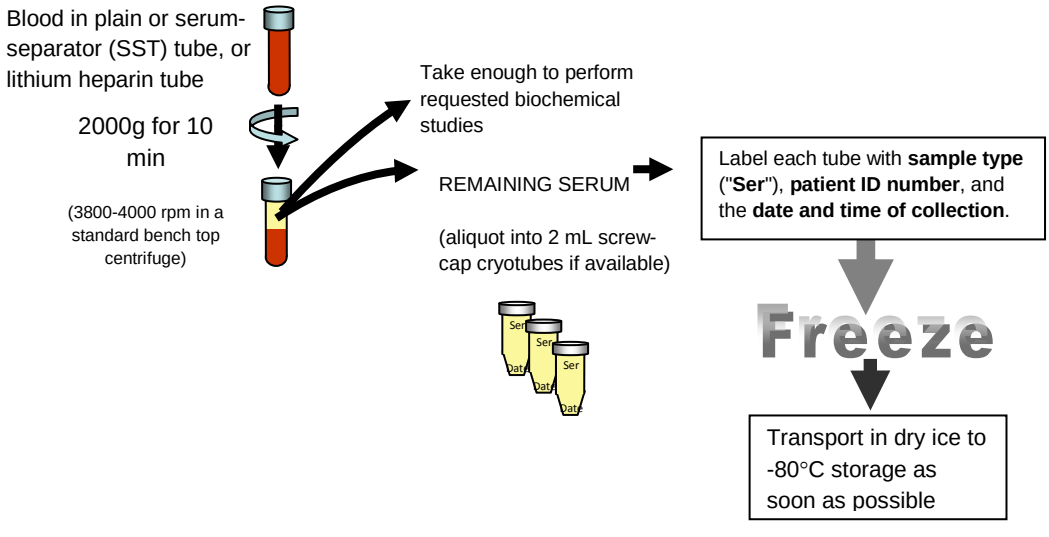
Anticoagulation Project Time & Treatment

Laboratory Protocol

CITRATE PLASMA PROCESSING PROTOCOL



SERUM PROCESSING PROTOCOL



Please send this information sheet to your pathology laboratory with the first serum research sample collected

ATOM STUDY: Australian Toxicology Monitoring

Anticoagulation Project Time & Treatment

Laboratory Protocol

PLASMA PROCESSING RATIONALE AND DETAILED INSTRUCTIONS:

Overview

The plasma collected for this study is used for functional antigen studies using platelet free plasma.

Processing must be completed within 2 hours of collection

Triple spinning is employed to remove all platelets. This platelet-free plasma is then aliquoted into small tubes which must be frozen within 2 hours of collection and moved in dry ice to a -80C freezer as soon as possible.

It is very important that the plasma is processed and frozen as quickly as possible in order to maintain activity of the various factors that we will be assaying.

Collection

5-10 ml of venous blood is collected into tubes containing 3.2% sodium citrate (standard coag collection tubes) at a ratio of 1:9 and mixed well

Processing

1. Centrifuge the citrate tubes at 2000g (3800-4000 rpm in a standard bench top centrifuge) for 10 minutes to separate the plasma from the red and white cells.
2. Take just enough plasma to perform routine coagulation studies: i.e. INR/PT, APTT
3. Carefully removed all remaining upper plasma fraction from the bottom layer of cells using a transfer pipette and transfer the plasma into a fresh sterile 15ml tube.
4. Centrifuge the plasma at 2000g for 10 min.
5. Remove the upper plasma from any pelleted debris and transfer the plasma to a fresh sterile 15 ml tube.
6. Centrifuge the plasma again at 2000g for 10 min.
7. Remove the upper plasma and aliquot it into 2 ml screw cap Eppendorf/Sarsdedt or equivalent cryotubes in ~ 0.3ml aliquots (4 – 10 tubes in total, depending on amount of plasma available). **If you do not have screw-top cryotubes**, then use the smallest tubes available to you.
8. Label each tube with the **patient ID number**, "**Cit**" (indicating that this is a citrate sample) and **date and time of collection** on the side of the tube, and the **patient ID number on the cap**.
9. **Freeze** tubes in an **upright position** (preferably in boxes) and move to –80C storage as soon as possible. TRANSPORT MUST ALWAYS BE IN DRY ICE.

ATOM STUDY: Australian Toxicology Monitoring

Anticoagulation Project Time & Treatment

Laboratory Protocol

Left over serum/ plasma from earlier time points

The most important samples are the first ones taken, when the patient and doctor may not be aware of the study. Even if these samples have not been processed according to the procedures above, we can obtain important information from them. Therefore, please ensure that samples from this patient are **not discarded** without first discussing with a study coordinator (contact details at the bottom of this page).

Results from your lab

If time permits we would appreciate copies of all results (biochemistry, haematology and coagulation). Please either fax to **(02) 49110501**

OR : Post to Dr Dr Geoff Isbister, Calvery Mater Newcastle, Edith Street, Waratah, NSW, 2298

Sample Transport

Please label these samples as:

"**Anticoagulation Project; Study Hold for Dr Isbister"**

These samples are to be sent to:

For Dr Geoff Isbister

Specimen Reception,
Hunter Area Pathology Service,
John Hunter Hospital,
Lookout Road, New Lambton Heights
NSW 2305
PLACE IMMEDIATELY IN -80 FREEZER

Background information about this study:

The Anticoagulation Project Time & Treatment (aPTT) aims to investigate the pharmacokinetics and dynamics of anticoagulants in overdose. If you have any questions or queries please do not hesitate to contact us on the numbers provided below.

If you have any questions please call Dr Geoff Isbister on 0438 466 471. IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 4911 0501

PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Australian TOxicology Monitoring (ATOM) Study

Study Information Sheet

Invitation

You are invited to take part in a study into drugs in overdose (Australian TOxicology Monitoring (ATOM) Study). The study is being conducted by the Department of Clinical Toxicology at the Calvary Mater Newcastle.

Before you decide whether or not you wish to participate in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish.

1. 'What is the purpose of this study?'

This study measures drug levels in blood (and sometimes urine) after drug overdoses. By taking several samples, the study aims to find out how long it takes for the body to get rid of the drug. We are also looking at the effect of the drug on the body. This information might be useful to decide how long to keep people in hospital and whether drug levels might be helpful.

2. 'Why have I been invited to participate in this study'

You are eligible to participate in this study because you have ingested a drug that we wish to gain more information about in overdose.

3. 'What if I don't want to take part in this study, or if I want to withdraw later?'

Participation in the study is completely voluntary you will suffer no disadvantage if you elect to not be involved in the study and will continue to receive optimal ongoing care. You may withdraw from the study at any time and have the option of withdrawing all data relating to the study and have any blood samples destroyed.

4. 'What does this study involve?'

If you agree to participate in this study, you will be asked to sign the Participant's Consent Form.

We may collect some extra blood samples while you are in hospital to measure drug levels in the blood. In most cases we will try to use blood samples that are collected as a part of your treatment. This excess blood would have been discarded. For some drugs urine will also be collected. An intravenous cannula, which is a fine plastic tube placed into a vein in the hand or arm, will be used to take the blood samples during the study to minimise discomfort This may be in addition to the intravenous cannula inserted for treatment of the overdose, if required.

In some participants urine will also be collected, and you will be informed of this at the time of consenting. You will be asked to pass urine into a container at specific times for up to 24 hours. In addition the researchers would like to have access to your medical records to obtain relevant information to the study.

5. 'How is this study being paid for?'

This study is being paid for by the Department of Clinical Toxicology Prince of Wales Hospital.

6. 'Are there risks to me in taking part in this study?'

The only risk of being involved in the study is the additional need for an intravenous cannula. This will not be required in all participants and we will aim to use the cannular inserted into your arm as a part of your treatment. This will be inserted by experienced health care staff. There are minimal risks from taking blood, but they include a small risk of bruising at the site, dizziness and fainting, and the small chance of an infection developing from the presence of the cannula. The standard precautions of using a sterile technique to collect blood and insert the cannula will significantly reduce the risk of this and will be adhered during the study. There is no risk from urine collection, which will be collected by nursing staff.

7. 'What happens if I suffer injury or complications as a result of the study?'

If you suffer any injuries or complications as a result of this study, you should contact the study doctor as soon as possible, who will assist you in arranging appropriate medical treatment.

You may have a right to take legal action to obtain compensation for any injuries or complications resulting from the study. Compensation may be available if your injury or complication is caused by the procedures, or by the negligence of any of the parties involved in the study. If you receive compensation that includes an amount for medical expenses, you will be required to pay for your medical treatment from those compensation monies.

If you are not eligible for compensation for your injury or complication under the law, but are eligible for Medicare, then you can receive any medical treatment required for your injury or complication free of charge as a public patient in any Australian public hospital.

8. 'Will I benefit from the study?'

This study aims to further medical knowledge and may improve future treatment of certain drug overdoses, however it may not directly benefit you.

9. 'Will taking part in this study cost me anything and will I be paid?'

Participation in this study will not cost you anything and you will not be paid.

10. 'What will happen to my tissue sample after it has been used?'

The blood or tissue sample/s you provide during the study will be destroyed at the completion of the study.

11. 'How will my confidentiality be protected?'

The samples that are collected in this study will de-identified and stored as a study number. The study mastercode will only be known to the researchers and will be password protected. Only the researchers named above will have access to your details and results that will be held securely at Prince of Wales Hospital.

Any identifiable information that is collected about you in connection with this study will remain confidential and will be disclosed only with your permission, or except as required by law.

12. 'What happens with the results?'

If you give us your permission by signing the consent document, we plan to discuss/publish the results with the HREC for monitoring purposes, peer-reviewed journals and presentation at conferences or other professional forums.

In any publication, information will be provided in such a way that you cannot be identified. Results of the study will be provided to you, if you wish.

The information collected from this study will be stored in a de-identified fashion. This personal information will be accessed, used and stored in accordance with Commonwealth Privacy Laws and the *NSW Health Records and Information Privacy Act 2002*. It is assured that all records dealing with participation in this study will be kept for five years after completion of the study under secure conditions. Authorised persons within the institution may also inspect records for purposes of data audit only. Individual participants in the study will not be identifiable in any reports of the data from the protocol or any publications resulting from the research.

13. 'What should I do if I want to discuss this study further before I decide?'

When you have read this information, the researcher Dr Angela Chiew or member of the treating team will discuss it with you and any queries you may have. If you would like to know more at any stage, please do not hesitate to contact Dr Angela Chiew on 0412575580.

14. 'Who should I contact if I have concerns about the conduct of this study?'

This study has been approved by the South Eastern Sydney Local Health District – Northern Sector Human Research Ethics Committee. Any person with concerns or complaints about the conduct of this study should contact the Research Support Office which is nominated to receive complaints from research participants. You should contact them on 02 9382 3587, or email ethicsnhn@sesiahs.health.nsw.gov.au and quote ***HREC project number*: 12/067.**

This project has also been authorised to be conducted at The Sydney Children's Hospital Network. If you have any concerns about the conduct of this study, at this site please do not hesitate to contact the Research Governance Officer on (02) 9845 3011.

The conduct of this study at the Calvary Mater Newcastle has been authorised by the Little Company of Mary. Any person with concerns or complaints about the conduct of this study may contact Dr Nicole Gerrand, Manager, Research Governance Officer, Calvary Mater Newcastle, Telephone: 02 4921 4950, Email: hnelhd-hrec@hnehealth.nsw.gov.au

Thank you for taking the time to consider this study.
If you wish to take part in it, please sign the attached consent form.This information sheet is for you to keep. More information, concerns and complaints: If you have any questions at any time please contact Dr Angela Chiew on phone: **0412575580**, she will be happy to answer them.

1. I,.....
of.....
agree to participate in the study described in the participant information statement set out above

2. I acknowledge that I have read the participant information statement, which explains why I have been selected, the aims of the study and the nature and the possible risks of the investigation, and the statement has been explained to me to my satisfaction.

3. Before signing this consent form, I have been given the opportunity of asking any questions relating to any possible physical and mental harm I might suffer as a result of my participation and I have received satisfactory answers.

4. I understand that I can withdraw from the study at any time without prejudice to my relationship to The Sydney Children's Hospital Network

5. I agree that research data gathered from the results of the study may be published, provided that I cannot be identified.

6. I understand that if I have any questions relating to my participation in this research, I may contact Dr Angela Chiew on telephone 0412575580 who will be happy to answer them.

7. I acknowledge receipt of a copy of this Consent Form and the Participant Information Statement.

8. I understand that there may be occasions for the research staff to request copies of information from my medical records that will allow the completion of the study datasheets and associated information for the study. Specifically I consent to the hospital providing the details of this admission after the event when they are contacted by the research staff.

Complaints may be directed to contact Dr Nicole Gerrand, Manager, Research Ethics and Governance, Hunter New England Local Health Network,Telephone: 02 4921 4950, Email: hnehrec@hnehealth.nsw.gov.au

Signature of participant	**Please PRINT name**	**Date**
_____	_____	_____
Signature of witness	**Please PRINT name**	**Date**
_____	_____	_____
Signature of investigator	**Please PRINT name**	**Date**
_____	_____	_____

REVOCATION OF CONSENT

I hereby wish to **WITHDRAW** my consent to participate in the study described above and understand that such withdrawal **WILL NOT** jeopardise any treatment or my relationship with the Prince of Wales Hospital.

Signature of participant	**Please PRINT name**	**Date**
_____	_____	_____

The section for Revocation of Consent should be forwarded to **Dr Angela CHIEW Prince of Wales Hospital, Emergency Department and Clinical Toxicology Unit Barker Street Randwick 2031.**