Australian TOxicology Monitoring (ATOM) Study
Digoxin Overdose & Response to Antibodies (DORA)
Procedure

AIMS: to investigate the effects and pharmacokinetics of digoxin and digoxin Fab in acute and chronic toxicity in order to improve the dosing and indications for digifab.

INCLUSION:

1/ Any patient presenting with an acute digoxin poisoning.

2/ Any patients presenting with suspected chronic digoxin poisoning.

EXCLUSION: Age < 14 years

WHAT IS INVOLVED: This study involves a structured audit of the outcomes of standard management - doing ECGs, clinical observation (pulse, BP), taking blood samples and documenting common clinical symptoms. These should be done on admission, 1, 4 hours later and when clinically indicated until discharge. Care should be taken not to take blood out of the cannula used to administer antibodies (an additional cannula may need to be inserted).

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) 80160868 (**or email to **betty.chan@sesiahs.health.nsw.gov.au)**

STEP 2 - For this study extra blood samples will be required to be collected. Consider inserting an extra cannula to collect blood samples to avoid repeated venipuncture.

STEP 3 – Perform ECG at the time when blood samples are taken.

STEP 4 - Complete the patient data form and please fax the completed form to **(02) 80160868** (or email to above address).

STEP 5 – Research samples are to be collected in a **serum tube**. **Note** on all request forms **"DORA study"** – research samples. Please send the "Laboratory Protocol" to your pathology laboratory with the first research serum sample collected.

ECG AND BLOOD SAMPLE TIMES:

Research samples to be collected are 5mL serum samples (SST)

Please collect a serum tube for research purposes at these times: (Please note that potassium levels should be checked after the administration of digoxin Fab at 1 and 4 hrs.)

a) 1 hour following admission or 1 hour after infusion of digoxin Fab

b) 4 hour following admission or 4 hours after infusion of digoxin Fab.

c) Anytime when blood or ECG is taken for clinical monitoring.

AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY

Patient Data Sheet #1 – Digoxin Poisoning

Digoxin Overdose & Response to Antibodies (DORA) study

PATIENT STICKER:	**DATE AND TIME PRESENTED TO ED:**
	CONSENT OBTAINED: YES NO
WEIGHT (KG): **HEIGHT (CM):**	**Please circle:** **ACUTE / CHRONIC DIGOXIN POISONING**
CURRENT MEDICATIONS:	**PAST MEDICAL HISTORY:**
DOSE OF DIGOXIN TAKEN: **TIME OF INGESTION:**	**DOSE OF DIGOXIN TAKEN DAILY:** **TIME OF LAST DOSE DIGOXIN INGESTION:**

SYMPTOMS ON PRESENTATION: (PLEASE CIRCLE)

CVS: Arrhythmias – Atrial fibrillation / Bradycardia /Junctional bradycardia / Complete heart block / Ventricular ectopics / Atrial tachycardia / Ventricular tachycardia / Ventricular fibrillation.

GIT: Nausea / Vomiting / Abdominal pain

CNS: Confusion / Visual disturbances

Others:

CO INGESTION :DRUG	**AMOUNT**	**TIME INGESTED**

Initial Digoxin level: **Time taken:**	**Initial K:** **Cr:** **Time taken:**
CHARCOAL GIVEN: YES NO **TIME AND DOSE:**	**Time & date Digoxin Fab commenced:** **Dose Digoxin Fab:**

AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY

Patient Data Sheet #2 – Digoxin Poisoning

Digoxin Overdose & Response to Antibodies (DORA) study

Time (indicative times given but write actual times)	Blood Sample/ ECG (tick)	HR	BP	Level of Coma (Awake or GCS)	CNS or Abdominal symptoms	Other Comments (Record other treatments given and whether patient has responded)
Baseline *						
0.5 hr						
1hr*						
2hr						
4hr*						
Blood taken						

* do ECG & take blood for EUC, digoxin level plus one gold top tube for research purpose. Please take one extra gold top tube whenever blood is taken from patient for clinical monitoring purpose. (**Note** – Digoxin levels may be misleading after digifab, as they measure digoxin bound to DigiFab as well as 'free' digoxin)

Response to Digoxin Fab: (please circle & provide information)

Time taken for digoxin Fab to work (from the end of infusion): _____ HR _____ BP _____

(1) Resolution of ventricular arrhythmias: _____

(2) Improvement of BP: _____

(3) Resolution of bradycardia (HR<50): _____

(4) Improvement of _____: _____

Thanks very much!

If you would like to receive a copy of the results of this study or the results of the assays for free digoxin levels on your patient put your email address here _____

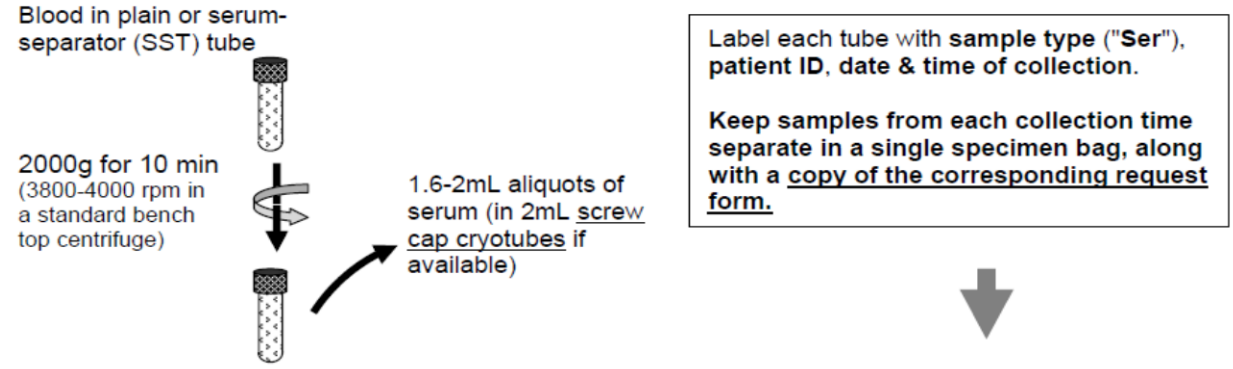
Australian TOxicology Monitoring (ATOM) Study

Digoxin Overdose and Response to Antibody (DORA) Study

Laboratory Protocol

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

1. Serum



Freeze as soon as possible and transport in dry ice (or other suitable frozen transport) to -80°C storage. **NOTE: please freeze all available (earlier) left-over samples, even if they have been left unfrozen for several days, noting the date and time of freezing on the request forms.**

2. 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).

3. Results from your lab

If time permits we would appreciate copies of all results (biochemistry, haematology and coagulation).
Please either fax to **(02) 80160868**

OR:

Post to: Dr Betty Chan
Prince of Wales Hospital
Emergency Department
Barker Street, Randwick NSW 2031

If you have any questions please call Dr Betty Chan (principal investigator) on **0439601068**.
IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160868

4. Sample Transport

Samples should be sent in a single batch on patient discharge.

Please label these samples as:

"**Digoxin Overdose and Response to Antibody (DORA): Study Hold for Dr Isbister"**

These samples are to be sent to:

NSW:

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 Digoxin Overdoes and Response to Antibody (DORA) study aims to investigate the pharmacokinetics and dynamics of digoxin and response to digoxin Fab in acute overdoses and chronic poisonings. 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 Betty Chan (principal investigator) on **0439601068**. IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160868

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.**