St George's Healthcare NHS
NHS Trust
Investigator: Maurizio Cecconi

Patient Information Sheet

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish.
The first part tells you the purpose of this study and what will happen to you if you take part. The second part gives you more detailed information about the conduct of the study. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

What is the purpose of the study?
We are investigating treatments for septic shock. This is the low blood pressure that can occur when the body has an overwhelming infection. The low pressure can reduce the blood flow and delivery of oxygen to important organs in the body. This is a medical emergency that requires urgent treatment with fluids and other drugs to help raise blood pressure. The body normally produces stress hormones to help raise blood pressure but in overwhelming infections these mechanisms can fail. Treatment of septic shock includes giving patients additional amounts of these hormones via drips into a large vein and these drugs include adrenaline-type drugs, steroids and other stress hormones. Although all these drugs are routinely used to raise blood pressure we do not know what is the best combination of drugs to use. We are studying the timing and how these drugs work in combination.

Why have I been chosen?
You have been asked to take part in this study as your blood pressure has been low due to a severe infection. We are planning to study 412 patients in total, admitted to different hospitals within the UK.

Do I have to take part?
It is up to you to decide whether or not to take part. As many patients who have septic shock can initially be too ill to make decisions about participation, and treatment is an emergency, we have already spoken to your relatives / close friends / doctors about your participation and begun treatment as part of the study. If you do decide to continue in the study you will be given this information sheet to keep and be asked to sign a consent form. If you decide to continue you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time will not affect the standard of care you receive.

What will happen to me if I take part?
This is a randomised study. Sometimes because we do not know which way of treating patients is best, we need to make comparisons. People are put into groups and then compared. The groups are selected by a computer which has no information about the individual – i.e. by chance. Subjects in each group then have a different treatment and these are compared.

You were assigned to one of four possible treatment groups that varied according to the combination and timing of the routinely used hormone drugs. The combination of drugs may have included a hormone drug (vasopressin) commonly used to treat the low pressure due to infection, an adrenaline-type hormone and steroid hormones. The combination might have included a placebo / dummy hormone instead of the steroid hormones. A placebo is a dummy treatment which looks like the real thing but is not. It contains no active ingredient.

This is a double-blind study. In a blind trial the patient does not know which treatment group they are in. In a double-blind trial, neither the patient nor the doctor knows which treatment group the patient is in (although, if the doctor needs to find out he/she can do so). A double-blind study helps make sure the results of the trial are not affected by doctors' or patients' personal preferences.

In some hospitals we are also collecting blood samples (five teaspoons on each of four occasions) and urine during your first week in the Intensive Care Unit. These samples will normally be collected from drips, lines and catheters already in place as part of your normal care. These samples will be used to measure levels of the hormones, and other chemical messengers that we believe are important in severe infections. We will also collect the blood samples to examine DNA as we believe that normal variations in our genes that control these chemical messengers make individual people respond differently to infection and its treatment. All samples will be coded and not contain any personal identifying information. These samples will be initially stored at this hospital and then be sent to Imperial College for storage and analysis. Samples will be stored beyond the end of this study in accordance with the Human Tissue Act.

What do I have to do?
You will not have to do anything different if you decide to continue in the study. The study drug will be stopped before you leave ICU. The study will not continue once you have left ICU other than to collect information about when you leave hospital or at 4 weeks should you leave hospital before then.

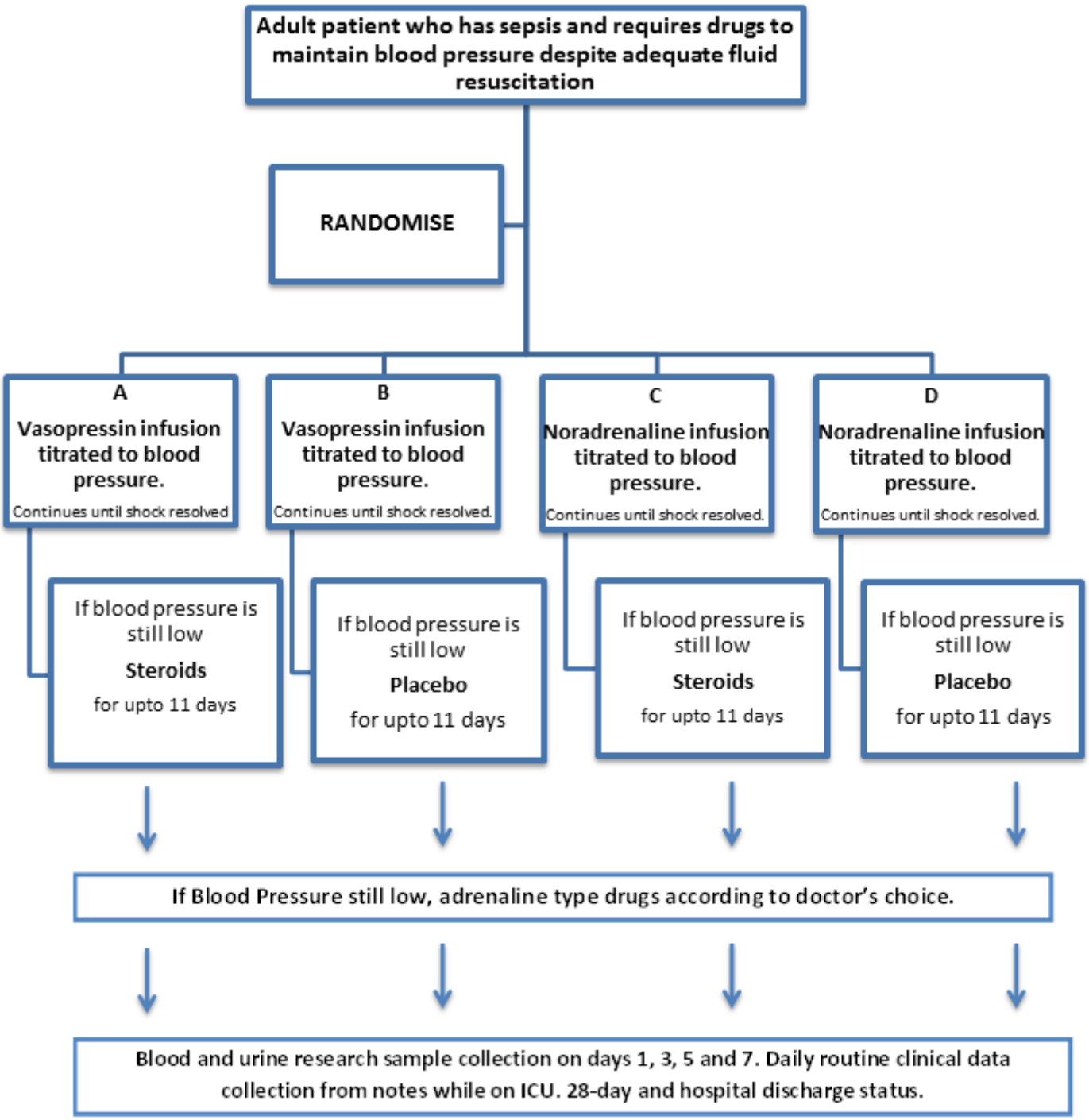
Septic shock is a medical emergency and appropriate treatment needs to start as soon as possible to help patients make the best recovery. Therefore your doctors have already treated you with the study drugs in order not to delay your treatment. If you do not wish to be part of this study, no further information will be collected about you for the trial and the doctors will continue to provide you with whatever medical treatment is needed.

What is the drug or intervention that is being tested?
The first stress hormone being studied is called vasopressin. It is a naturally produced hormone from the pituitary gland in the brain. We know that levels of this hormone can be low in severe infection. Vasopressin has been used in several previous studies and is routinely used in the treatment of low blood pressure due to infection. It causes constriction of the blood vessels and then raises blood pressure.

The second stress hormone being studied is call noradrenaline. It is a naturally produced hormone from the adrenal glands and is very similar to adrenaline. It causes constriction of the blood vessels and raises blood pressure but has less effect on the heart than adrenaline. It is the most commonly used drug to treat low blood pressure due to infection.

The other hormone being studied is hydrocortisone. It too is a naturally produced steroid hormone from the adrenal glands. Again we know that levels of this hormone can be low in severe infection. Hydrocortisone has been used in many previous studies and is routinely used in the treatment of low blood pressure due to infection. It makes blood vessels more responsive to adrenaline and thus causes constriction of the blood vessels and then raises blood pressure.

Figure 1: Treatment plan



1 copy for subject; 1 copy for Principal Investigator; 1copy to be kept with hospital notes

What are the side effects of any treatment received when taking part?
All of these hormones are routinely used in treating low pressure due to infection and are generally thought to be as safe as each other and other drugs used to raise blood pressure. They are all short acting drugs and any effects of the drugs will have already worn off. Vasopressin and noradrenaline are powerful constrictors of blood vessels and caution must be used in treating patients who have poor circulation problems. Hydrocortisone may be associated with a slightly increased risk of developing new infections. It can also increase levels of sugar in the blood. The doctors and nurses looking after you will watch careful for these possible side-effects and will treat them as necessary and even stop the drugs if needed.

What are the possible benefits of taking part?
It is possible that one of the combinations of these drugs is better that then the other combinations. At the moment we do not know which combination is best. This study might help improve the treatment of people with septic shock in the future.

What are the possible disadvantages and risks of taking part?
There is little additional risk from taking part in this study as all drugs are already commonly used to treat septic shock. Only very small quantities of extra blood samples have / will be collected, usually from existing lines, but it might be necessary to collect a sample from a new needle which might result in some minor discomfort during collection and possibly a small bruise.

What if something goes wrong?
Imperial College London holds insurance policies which apply to this study. If you experience serious and enduring harm or injury as a result of taking part in this study, you may be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator (Dr……, contact details at end). The normal National Health Service complaints mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial AHSC Joint Research Office.

Will my taking part in this study be kept confidential?
All information, including personal information, which is collected about you during the course of the research will be kept password protected and strictly confidential. Any information about you which leaves the hospital will have your name, and address removed so that you cannot be recognised from it. Other doctors in this hospital treating you will be told of your participation in this study.

What will happen to the results of the research study?
The results of this study will be presented at medical meetings and published in scientific journals. Only group information and no personal information will be presented.

Who is organising and funding the research?
This study is being organised by doctors and scientists in Imperial College, London. It is funded by the National Institute for Health Research.

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people called a Research Ethics Committee. This study has been reviewed and approved by the NRES Committee South Central – Oxford A Research Ethics Committee.

Who can I contact for independent research information?
If you have any questions about being in a research study, you can contact the Trust's Patient Advice Liaison Service (PALS). They will give you advice about who you can talk to for independent advice.

Further information
Thank you in advance for considering participation in this study. If you have any questions about this research, the study staff will be more than happy to answer them.

Study Investigators Contact details

Study Investigator	Maurizio Cecconi (PI), Anthony Gordon (CI)
Study Nurse	Johannes Mellinghoff
Day time Telephone	02087253295
Emergency Telephone	02087253295

VANISH

Vasopressin vs Noradrenaline as Initial therapy in Septic shock

CONSENT FORM FOR PATIENTS ABLE TO GIVE CONSENT

Subject #		**Site #**	*007*
Name of Research Doctor			

Please initial each box if you agree with the following:

☐ I, *(forename and surname)*…… …… freely agree to take part in the study.

☐ I confirm that I have read and understood the patient information sheet dated …30/01/2012……. Version…1.2…… for the above study and have had the opportunity to ask questions which have been answered fully.

☐ I understand that my participation is voluntary and I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

☐ I understand my identity will never be disclosed and any information collected will remain confidential.

☐ I agree that my medical records and other personal data generated during the study may be examined by representatives of the sponsor, by people working on behalf of the sponsor, and by representatives of Regulatory authorities.

☐ I agree that I will not seek to restrict the use to which the results of the study may be put.

☐ I understand that genetic analysis will be carried out on my samples as part of this study.

☐ *Additional* - I agree to the storage and use of my samples for future ethically approved research projects.

Participant	**Person responsible for collecting the informed consent**
Date: *Signature:* *Printed Name:*	*Date:* *Signature:* *Printed Name:*

1 copy for subject; 1 copy for Principal Investigator; 1copy to be kept with hospital notes