St George's Healthcare NHS
NHS Trust
PI: *Andrew Rhodes*
Blackshaw Road, Tooting
London, SW17 0QT
Reception: 020 8672 1255

PATIENT INFORMATION SHEET AND CONSENT FORM (continue)

1. Study Title:

A randomised blinded placebo controlled trial of hydrocortisone in critically ill patients with septic shock: The ADRENAL Study.

2. Invitation

You are invited to continue to take part in this study for people in intensive care (ICU) with low blood pressure due to a severe infection (septic shock). The investigators want to know if patients with septic shock recover better with or without the addition of low dose steroids (hydrocortisone). Whether hydrocortisone is beneficial in patients with septic shock is not known for certain and as a result some doctors use it and some do not. Either using or not using hydrocortisone is considered to be an equally acceptable standard of treatment.

Before you decide to continue in this study 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. Talk to others about the study if you wish. Please 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 continue to take part.

3. What is the purpose of this study and why have i been chosen?

The purpose of this study is to find out whether adult patients admitted to the intensive care unit (ICU) with septic shock who are given hydrocortisone compared to placebo (a dummy solution) will have an improved rate of survival 90 days later.

Septic shock is the result of an infection, which triggers a complex response by the body (the inflammatory response) that causes a decrease in blood pressure and subsequently one or more organ systems to fail when blood supply to these organs is reduced.

When patients are admitted to ICU with sepsis and/or septic shock there are a number of therapies they may receive. These include fluids given through a drip, antibiotics and drugs to boost the blood pressure and other organ systems.

In addition to these therapies, steroids (hydrocortisone) are sometimes administered. The question of whether steroids are useful or not in the treatment of severe infections has been studied for more than 50 years. Previous research has suggested that the use of low dose steroid may have short-term benefits in improving the circulation. However, there is no agreement amongst doctors around the world about whether treatment with or without low dose steroids improves the overall recovery and survival of patients with septic shock. This study would allow doctors to make informed decisions

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about whether the addition of low dose steroid therapy is better for patients with septic shock in intensive care.
The study will include 3800 intensive care patients who have septic shock.

4. Why have I been chosen?

You have been asked to take part in this study as you are in intensive care with low blood pressure due to a severe infection (septic shock).
Because the usual medical treatment for septic shock may or may not include the use of low dose steroids, we have obtained permission from the Human Research Ethics Committee to seek permission for your continued enrolment in the study either from you or your relative/friend after the study treatment commenced. If you had been well enough at the time, we would have discussed the study with you prior to starting treatment.

5. Do I have to take part?

It is up to you to decide whether or not to continue to take part. The drugs used for this study are routinely administered to treat septic shock. If you do decide to continue to take part in the study, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

6. What are the alternatives for treatment?

If you decide not to continue to participate in this study, you will continue to be provided with the best care for your condition. Usual medical treatment for septic shock may or may not include the use of low dose steroids, according to the medical judgement of your doctors.

7. What will happen to me if i continue to take part?

When you were in ICU with septic shock the independent doctor assess you as eligible for this research study. You were randomly assigned (like flipping a coin) to receive either hydrocortisone or placebo given through a drip for up to 7 days, or until discharge from ICU. You will have had a 50% chance of receiving either the hydrocortisone or placebo. The dummy solution used as a placebo is water for injection. This study is a "blinded" study, which means that neither you nor your doctors and staff in the ICU will know to which treatment you have been allocated.

Study Procedures

If you agree to continue to participate in this study, you will be asked to sign the Participant Consent Form. Participation in this study involves the following:

8. In the Intensive Care Unit

The study medication is given through a small plastic tube inserted in your vein (intravenous catheter), which you would already have had in place and is part of the standard treatment in the ICU. Your ongoing general hospital care has not been affected in any way by the study.

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9. Following Discharge from the Intensive Care Unit

After you are discharged, you will be contacted by telephone to see how you are recovering 90 days and 6 months after you started the study. When you are contacted after6 months, you will be asked to answer some standard questions about your quality of life and this will take about 10 minutes.
Finally, the researchers would like to have access to your medical record to obtain information relevant to this study.

10. Do I have to supply any samples

No additional samples will be collected specifically for the purposes of this study.

11. What do i have to do

You only have to do what has been listed above.

12. Will my taking part in this study be kept confidential?

If you join the study
If you join the study, some parts of your medical records and the data collected for the study will be looked at by authorised persons from the company the company organising the research. They may also be looked at by people from the company, by representatives of regulatory authorities and by authorised people from (the Trust, other NHS bodies) to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and nothing that could reveal your identity will be disclosed outside the research site.
Your medical information will be recorded by the study staff and stored on a secure database. It will not be directly or indirectly identifiable on transfer to the data management centre (The George Institute for Global Health, Australia) for evaluation.
Study data in this de-identified format may be published or given to regulatory authorities if required but individual participants will not be identifiable.

13. Involvement of the general practitioner/family doctor (GP)

Your GP will not be specifically notified of your participation in this study.

14. Expenses and payments

Participation in this study will not cost you anything, nor will you be paid.

15. What are the other possible disadvantages and risks of taking part?

Being in the study does not pose any extra disadvantage or risk to you, above the risks associated with your usual treatment in the intensive care unit. Both treatments (receiving or not receiving steroids) are accepted treatments for your condition. However, if you feel there is a problem that might be related to your involvement in the study, you should immediately alert the staff caring for you.

16. What happens if there is a problem?

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 can

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receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any UK public NHS hospital.

In addition, 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 sufficiently serious and is caused by unsafe drugs or equipment, or by the negligence of one of the parties involved in the study (for example, the researcher, the hospital, or the treating doctor). You do not give up any legal rights to compensation by participating in this study.

Please contact Patient Advisory Liaison Service (PALS) if you have any concerns regarding the care you have received, or as an initial point of contact if you have a complaint. Please telephone 020 7377 6335, minicom 020 7943 1350, or email pals@bartsandthelondon.nhs.uk, you can also visit PALS by asking at any hospital reception.

17. What if relevant new information becomes available?

Sometimes during the course of a study, new information becomes available about the treatment that is being studied. While you are participating in this study, you will be kept informed of any significant new findings that may affect your willingness to continue in the study.

18. What are the side effects of any treatment received when taking part?

Short-term treatment with steroids, as planned in this study, has been used for many years in conditions like asthma and the treatment is generally well tolerated.

When all previous studies of steroids for septic shock are considered together, the only side effects due to steroids were changes in body salt and water composition and in blood sugar concentration. Other potential side effects of steroids include muscle weakness and an increased risk of subsequent infections, but when previous studies are considered together these have not been observed more frequently in patients with septic shock who were treated with steroids.

Although hydrocortisone has been given to many patients over many years and is in regular current use, there may be additional unforeseen or unknown risks.

As you will be in the intensive care unit when the study medication is given, you will be closely monitored and treated immediately if any side effects were to occur.

If at any point during the study your study doctor feels it is in your best interests to cease the study medication, or if during the study there is evidence to suggest beyond reasonable doubt that one study treatment is more beneficial than the other, then your involvement in the study may be stopped.

19. What are the possible BENEFITS of taking part?

While we intend that this research study furthers medical knowledge and may determine the best treatment of septic shock in the future, it may not be of direct benefit to you.

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20. What happens when the research study stops?

When the results of the study are published, a copy of the publication/summary of the results will be forwarded to you, if you so wish. The results of the study will provide doctors with the best treatment for people in ICU with septic shock.

21. What if there is a problem and contact details for Further Information:

When you have read this information, *Dr A. Rhodes* or one of the other study team members will discuss it with you further and answer any questions you may have. If you would like to know more at any stage, please feel free to contact *Dr. Hollmann D. Aya*, research fellow in Intensive Care Department on 020 8725 0399.

Any person with concerns or complaints about the conduct of a research study should contact the NRES REC Coordinator on 01223 597685 and quote 12/EE/0368.

22. Who is organising and funding the research and where was it reviewed?

The study is being conducted within this institution by Dr Rhodes, Consultant, General ICU, St Georges Healthcare Trust.

The study has been designed by a group of intensive care researchers from around Australia and New Zealand. The study is being co-coordinated by the George Institute for Global Health, a not-for-profit research institute affiliated with the University of Sydney. The hospital is being paid for the work required for this study.

This study was given a favourable ethical opinion for conduct in the NHS by the Ethics Review Committee at NRES Committee East of England-Cambridge Central.

The conduct of this study at the St. Georges Healthcare Trust has been authorised. Any person with concerns or complaints about the conduct of this study may also contact the Research Governance Officer (researchgovernance@sgul.ac.uk).

Thank you for taking the time to consider this study.

A copy of this information sheet and signed consent form will be given to you to keep.

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A randomised blinded placebo controlled trial of hydrocortisone in critically ill patients with septic shock

PARTICIPANT CONSENT FORM TO CONTINUE

I,_____*[name]*of _____*[address]*have read and understood the Information Sheet on the above named research study (Protocol No. GI-CCT372273 v5, 28 April 2014) and have discussed the study with _____*[Investigator]*

- ☐ I have been made aware of the procedures involved in the study, including any known or expected inconvenience, risk, discomfort or potential side effect and of their implications as far as they are currently known by the researchers.
- ☐ I understand that my continued participation in this study will allow the researchers to have access to my medical record, and I agree to this.
- ☐ I freely choose to continue to participate in this study and understand that I can withdraw at any time.
- ☐ I also understand that the research study is strictly confidential.
- ☐ I hereby agree to continue to participate in this research study.

Name of participant (please print)	Participant Signature	Date

Name of person taking consent (please print)	Signature of person taking consent	Date

When completed: 1 copy for subject; 1 copy for Researcher and 1copy (original) to be kept with hospital notes