



RCT Adult that Regains Capacity Information Sheet

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DexEnceph: A study of dexamethasone in adults with Herpes Simplex Virus (HSV) encephalitis
Brain Infections Group, University of Liverpool

We understand this is a difficult time for you, so we firstly want to thank you for taking the time to read this leaflet.

You are taking part in a research study on HSV encephalitis. This condition is extremely rare. We want to ask you if you want to continue taking part. A team member will go through this leaflet with you, explaining what taking part in the study would involve and answering any questions.

Important things you need to know

- When you were unwell your friend or relative agreed you take part in this research study. At the time you were too unwell to make this decision for yourself.
- Now that you are better it is for you to decide whether you wish to continue taking part
- Before you decide it is important for you to know why the research is done and what it will involve.
- You can discuss with friends, family and clinical staff before making a decision.
- You are free to decide whether you would like to continue taking part. If you decide not to continue this will not affect the care you receive from your doctors.
- One of our team members will go through this information sheet with you. Please let us know if would like more information.

Important things about the study

- This is a study for patients with encephalitis (swelling of the brain) caused by a virus called herpes simplex virus (HSV)
- We want to find out if reducing the swelling with a drug called dexamethasone is of benefit to patient's memory in the longer term.
- In the study there are two groups of patients, one that received dexamethasone in hospital and one that did not.
- Both groups are having the same investigations to see if dexamethasone has been of benefit.
- Dexamethasone is a commonly used drug in brain swelling and many other conditions.

HSV encephalitis

1. What is HSV encephalitis?

Encephalitis means swelling of the brain and has many different causes. It is often caused by a virus. Herpes Simplex Virus (HSV) is the most common virus that causes encephalitis in the UK.

HSV encephalitis is very rare. It is diagnosed by finding the virus in fluid around the brain and spinal cord. This fluid is called CSF (cerebrospinal fluid). The CSF is obtained by the doctor who performs a lumbar puncture (LP).

HSV encephalitis is treated with the drug aciclovir. Despite treatment, some people are left with significant loss of memory. About 2 out of every 3 people will have memory difficulties long term.

The study

2. Why are we doing this study?

We know dexamethasone can reduce swelling. Reduction in swelling of the brain may improve the recovery of patients with HSV encephalitis.

This study, called DexEnceph, will allow us to compare the recovery of patients that received dexamethasone and those that did not.

3. Why was I been invited to take part?

You were invited to take part because your doctors diagnosed you with having HSV encephalitis when you were in hospital.

4. What will happen to me during the study?

All patients in the study received aciclovir in hospital. This is standard treatment for HSV encephalitis.

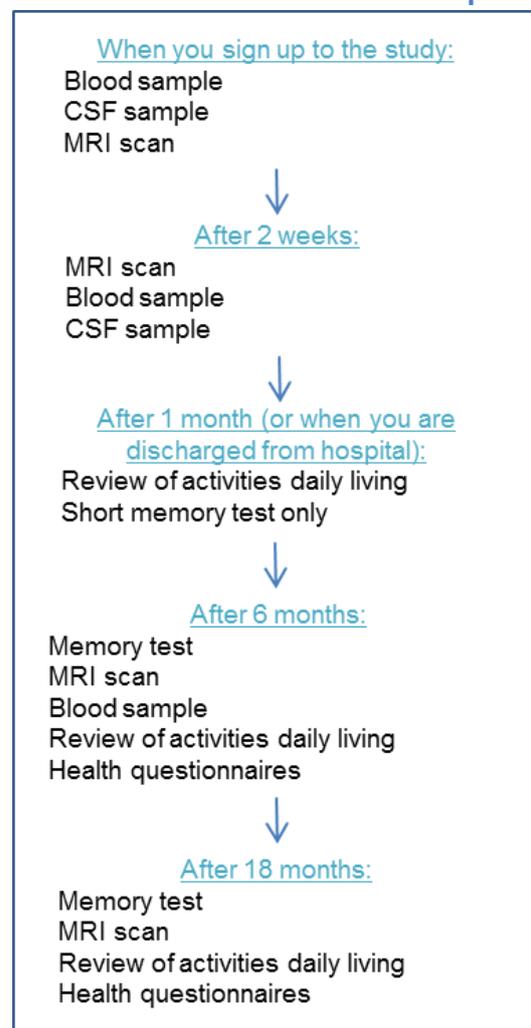
In addition, you may have been offered a short course of dexamethasone. This was decided at random by a computer. This is to be fair, so neither you, your relative, your doctor, nor the research

team, could choose whether you received dexamethasone or not. Half of the people in the study receive dexamethasone and half do not. If you received dexamethasone this will have been for 4 days when you were in hospital.

Your hospital doctors and nurses as well as your close family or friends will know if you received dexamethasone when you were in hospital.

What taking part involves

5. What tests are done if I take part?



All the tests done when you signed up to the study and the CSF tests after 2 weeks were done as part of your care whether you took part in the study or not.

6. What do the memory tests involve?

These tests are the most important in this study as they will help us find out if dexamethasone improves memory problems from HSV encephalitis. These tests are sometimes called Neuropsychology tests. They are done 6 and 18 months after the illness.

The key part of this test takes about 35 minutes. If you are not too tired we can continue with further tests that will provide useful information. These can take up to 2 hours.

They are not pass or fail tests. They provide information about your memory and thinking processes.

They can be done in one day or divided over a few short visits. If you have left hospital we can travel to see you in a convenient place for you. The test will be arranged on a day(s) which suits you.

The results can be added to your hospital notes for future reference if you wish or kept confidential within the trial.

7. What does the MRI scan involve?

As part of your care your doctor organised an MRI scan when you were in hospital. If you take part in the study we will ask you to have another 3 scans later on.

MRI scans allow us to assess if the brain has been affected by the infection and, if so, which parts.

Each scan takes about 20 minutes. The scan can be noisy but you will be offered headphones.

The extra 3 scans are planned for:

- 2 weeks after the first one (when you are still in hospital)
- After 6 months
- After 18 months

The scans will be done at a hospital near you. We will reimburse mileage or public transport costs for any research visits.

We will check with you that you are still happy to have the scan each time.

Sometimes scans may find something not related to this illness. If this happens the doctors looking at the scans will tell your own hospital doctors who will look into this further.

None of the research scans are compulsory so if you do not wish to have them you can still be part of the study.

8. Are there risks to having an MRI scan?

There are no known risks from an MRI scan. They do not use radiation. MRI scans are done routinely in patients with HSV encephalitis.

Because MRI scans use strong magnets you will not have the scan if you have any metal implants or fragments in your body.

Where you lie is quite enclosed and some people may find this unsettling. If you have a fear of confined spaces you should discuss this with your doctor before you go for the scan.

If you think you may be pregnant let your local research team know. We will not ask pregnant women to have MRI scans due to possible risks to the foetus.

9. What samples are collected? What does this involve?

We will collect blood and CSF samples during the study.

All patients with HSV encephalitis need a lumbar puncture (LP) when they come to hospital to find out why they are unwell. The doctor uses a small needle to take a sample from the lower part of the back. This is repeated after 2 weeks of treatment to see if all the virus has gone. Both lumbar punctures are part of the standard care in all patients with this condition.

We will take a little extra fluid at this time for the research tests. The amount of fluid we ask for each time is about 1 teaspoon, 5.5mls.

We can also use stored CSF that is leftover for research tests.

Blood tests are done at 3 different times spread over 6 months. We take between 1 to 4 teaspoons of blood, this is 5 to 25mls.

With these blood and CSF tests we will be able to better understand how the infection affects your body and how the body tries to defend itself against it.

10. What will happen to the samples that are collected? Will any genetic tests be done?

All samples will be taken at your hospital and then transported to the University of Liverpool or other laboratories working in the study. The samples will not have any of your personal information written on them. In the University they will be stored in a secure building.

There is an option for the blood and CSF collected to have tests looking at DNA. DNA is found in all cells of the body and contains the genetic information for the working of all human beings. This study collects DNA samples to find out why some people get HSV encephalitis and others do not, and why some people have severe problems due to HSV and others do not. The information we learn from DNA may benefit others with this condition in the future but will not influence your treatment or your future health.

Some of your samples may be left over. We will ask you if they can be used for this and future studies run by the University of Liverpool.

11. How do you review activities of daily living?

We will find out how the illness has affected your day-to-day life.

The research team will look at your hospital notes. They may also talk to you and, if you choose, your relatives. This will happen when you are in hospital and when you have gone home.

We will compare patients who received dexamethasone to those that did not and see if it made a difference.

12. What are the health questionnaires?

Two questionnaires will be sent through the post. They will ask you your views about your health and quality of life. Please send them back in a pre-paid envelope.

Dexamethasone

13. What are the side effects of dexamethasone?

Dexamethasone is used widely in patients and the side-effects are well known as this medicine has been prescribed for a long time. A short course of dexamethasone will be prescribed in this study. Side effects are less common when dexamethasone is given for shorter periods.

The possible side-effects when taking dexamethasone are:

- Stomach pain, indigestion, having more appetite than usual, feeling or being sick.
- Feeling tired or fatigued
- Mood and behaviour changes, especially at the beginning.
- Higher blood sugars.

Other possible risks can include:

- Stomach ulcers and bleeding of ulcers.
- Decreased response to infections.

Dexamethasone is prescribed to women who are pregnant or breast feeding as there are no known risks to the foetus.

Other things to consider

14. Do I have to take part?

No, taking part is voluntary. If you agree to continue taking part, we will ask you to sign a consent form.

If you agree to take part you are free to change your mind at any time, without giving a reason. You may decide to have only some tests in the study without having to drop out of the study altogether. This will not affect the standard of care you receive.

If you withdraw from the study we will stop collecting data. We will ask you if we can use the information and samples we have gathered up to the point that you withdraw.

15. What happens if there is a problem?

If you have any concerns about any part of this study, please speak with your hospital doctor (consultant) or one of your research team.

If you remain unhappy and wish to complain formally you can do this using the NHS Complaints Procedure. You can get information on how to do this from the Patients Advice Liaison department (PALS) in your hospital.

If you suffer harm from taking part in this study, there are no special compensation arrangements. If harm occurs to you and it is due to someone's negligence, you may have grounds for legal action for compensation against the NHS hospital where you are being treated but you may have to pay your legal costs.

16. Who will know I have taken part in this study?

Only people in your clinical care team and people involved in the study will have access to personal data.

All information collected about you during this study will be confidential and anonymised. It will be handled, stored and destroyed in accordance with the General Data Protection Regulation.

University of Liverpool is the sponsor for this study based in the United

Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. University of Liverpool will keep identifiable information about you for 15 years after the study has finished

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information <http://www.dexenceph.org.uk/>. Our Data Protection Officer is Victoria Heath and you can contact them at V.Heath@liverpool.ac.uk.

Benefits and risks

17. What are the benefits of taking part?

You may benefit from receiving dexamethasone, however we will not know this until the end of the study. You may also benefit from the increased monitoring of having extra scans and memory tests.

The information we get from this study may benefit patients in the future.

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

The disadvantage in taking part in this study may be the risk of having the side-effects of dexamethasone listed in question 13 (this will not be the case if you were in the group that did not have dexamethasone).

There is the inconvenience of having the dexamethasone through the drip when you are in hospital. Once you leave hospital there is the inconvenience of travelling to hospital for 2 scans, having the memory tests and completing questionnaires.

Our study team includes The Encephalitis Society, a charity that supports patients and families (www.encephalitis.info).

The study has been reviewed for scientific content by expert members of NIHR. The National Research Ethics Service Committee Liverpool Central has reviewed the study and given approval for it to take place.

Contact details

If you have any questions about this study, then please contact the study team members at:

Principal Investigator (Doctor leading this study in your hospital):

Name: _____

Telephone: _____

Research Nurse:

Name: _____

Telephone: _____

Name of your Hospital: _____

Further information

This study is being run at your hospital and many other NHS hospitals throughout the UK. It aims to recruit 90 patients over 4 years.

It is organised by the University of Liverpool and is funded by the National Institute for Health Research (NIHR), the public body in charge of research in the UK.



RCT Adult that Regains Capacity Consent Form

Version 5.0, Dated: 25/May/2018

EudraCT Number: 2015-001609-16

Centre Name:

Centre Code:

Name of Principal Investigator:

Study Number:

Please complete this form. When completed give one copy to the participant to keep, send one copy to CTU [fax/encrypted email/post], and keep one in the participant's medical notes. Please put the original in the site file.

For patient: once you have understood each statement please initial the YES OR NO box

YES

NO

1. I confirm I have read and understand the Information Leaflet (dated DD/MM/YY) for the above study, and have had the opportunity to ask questions and have these answered satisfactorily.	INITIAL IF YES	INITIAL IF NO
2. I agree to continue taking part in this study.	INITIAL IF YES	INITIAL IF NO
3. I understand that my participation is voluntary and that I am free to withdraw from the study at any time without giving a reason and without my care or legal rights being affected.	INITIAL IF YES	INITIAL IF NO
4. I agree for my consent form and contact details to be passed to the University of Liverpool for the administration of the study.	INITIAL IF YES	INITIAL IF NO
5. I understand that relevant sections of my medical notes and any data collected during the study may be looked at by authorised individuals from the research and clinical team and Regulatory Authorities where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	INITIAL IF YES	INITIAL IF NO
6. I agree for genetic tests to be done on blood and CSF collected from now. I understand these genetic tests will not be of any individual significance to me.	INITIAL IF YES	INITIAL IF NO

7. I agree to have MRI scans as part of the trial.	INITIAL IF YES	INITIAL IF NO
8. I agree to gift the remainder of any blood or CSF sample to the University of Liverpool where it will be stored for use in future research. This may include genetic tests.	INITIAL IF YES	INITIAL IF NO
9. I agree to any images or scans that are taken to be used for teaching, education and publication (in scientific journals, books or internet).	INITIAL IF YES	INITIAL IF NO

Name of Participant
(Please print)

Signature

Date (DD/MM/YYYY)

Researcher*

Signature

Date (DD/MM/YYYY)

*** Important:** Prior to signing please ensure local research contact details are complete on page 6.

Information to Research Team:
Once a Consent Form has been signed, please copy three times: One for the participant, one to file in the medical notes and fax/post/encrypted email one to CTU. Please place original in the site file.

Please fax/email/post this consent form to CTU **separately** to other anonymised trial documents (e.g. CRF).