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OXFORD VACCINE GROUP

Research to find a better anti-rabies treatment

(A randomised comparative study of the immunogenicity of modified intradermal post-exposure rabies vaccine regimens)

We invite you to take part in a research study comparing different ways of giving vaccines to prevent rabies after exposure to an animal bite. We hope the following information will help you decide whether or not to take part. A summary of the major points of the study is in the box below:

• Rabies virus infection is usually transmitted to humans by the bite of a rabid dog. There is no treatment and it is always fatal. Most deaths occur in Asia and Africa, but rabies viruses are found in most parts of the world, and were recently found in bats in the UK.
• Immediately after contact with a rabid animal, treatment with a course of rabies vaccine injections can prevent the disease.
• The vaccines are too expensive for general use in those countries where it is needed most. This study will find a better way of giving vaccine in smaller amounts and will check that it works as well as the standard treatments.
• All participants will receive a course of rabies vaccine injections, equivalent to that given for vaccination before travel. Blood samples will be taken to measure the response to the different treatments.
If volunteers are ever in contact with a rabid animal in the future their treatment will be easier, cheaper and safer.

What is Rabies?

Rabies is a viral infection of animals that is occasionally transmitted to humans, usually from a dog bite. The virus enters nerves in the wound and travels up the nerves to the brain. The incubation period is variable, usually a few months, rarely over a year. The infection causes characteristic spasms and fits which occur on trying to drink water (hydrophobia), but sometimes it appears as paralysis. Once the disease appears, there is no treatment and death follows rapidly. Rabies is found in a variety of animal species in most parts of the world, but most human deaths occur after contact with dogs in Asia and Africa. Bats in the UK have been found recently to be infected with a rabies-like virus.

Can rabies be prevented?

Yes, immediate preventive treatment can be very effective. After contact with a rabid animal it is urgent to clean the wound with soap and water and have a course of vaccine injections. As this takes a little while to work, an injection of rabies immunoglobulin (antibody) is given for rapid temporary protection. Having initial treatment after a bite is not guaranteed to prevent death. It is better to have vaccine treatment before exposure to the virus, as with pre-travel inoculations.

What is the purpose of this study?

This is a continuation of 20 years' research on rabies vaccines. The economical methods of vaccine treatment currently used in Asia are complicated, inconvenient and may not be adequate in all cases. The aim now is to find the most effective, easiest and least expensive way of using modern rabies vaccines. The new method will be compared with the routine expensive vaccine treatment.

What is the vaccine that is being used in this study?

An inactivated (killed) rabies vaccine, purified vero cell rabies vaccine (PVRV) manufactured in France will be used. Experience over 15 years has proved this vaccine to be safe and effective.

Who are we asking to take part?
You can take part if you are between the ages of 18 and 50 years and:

1. You have never had any rabies treatment before.
2. To your knowledge you have a normal immune system and are not on steroid drug therapy.
3. You are not taking chloroquine based antimalarial treatment.
4. You are available to attend appointments over a period of 3 months and would be willing to have a final blood test after a year.

What happens in the study?
You would be given a course of rabies vaccine and to assess your immune response to this, we would take four blood samples over a three-month period and then a final sample after one year. 220 people will be taking part. At the first visit we explain what it involves and ask questions about your general health. If you agree to take part, we will take 10 mls (two teaspoons) of blood. You will be allocated by random chance to one of four groups. You will receive an injection of vaccine either into the skin at one or more sites, or into a muscle, on four or five occasions over a period of three months. After each injection we ask you to keep a health record for a week. As we prefer not to give vaccines during pregnancy, we ask females to give a urine sample for pregnancy testing before the vaccine is given. In this study all volunteers will receive a course of rabies vaccine equivalent to that given for vaccination before travel.

What are the possible side effects of the vaccine?
The vaccine has been used widely for many years, and has been free of significant complications. Mild symptoms of soreness, redness, irritation or swelling at the site of the intradermal injection may occur. More general symptoms such as headache, fever and a 'flu-like' illness have been reported by 3% to 14% of those vaccinated. Occasionally transient rashes are seen.

What are the possible benefits of taking part?
After the study you will have antibody indicating you have some immunity to rabies. If you were ever bitten by a rabid dog you would need to wash the wound immediately with soap and water and have two injections of vaccine to boost your protection. However you would not need the full course of vaccine or a rabies immunoglobulin injection.

What happens if I say no?
Participation in the study is totally voluntary. If you decide to say no, this will not change your normal health care in any way. If you agree to take part you can opt out of the study at any point without giving a reason and without it affecting your normal care. We will make sure that you are kept informed of any new information that may influence your decision to continue.

What else do I need to know?
The rabies study team will keep confidential records of your involvement. This research has the approval of the Oxfordshire Clinical Research Ethics Committee. If you did have cause to complain about any aspect of the way in which you have been approached or treated during the course of the study, the normal National Health Service complaints mechanisms apply and you are not compromised because you have taken part in a research study. Alternatively if you have any complaints or concerns, you may also contact: Dr Peter Sullivan, Consultant Paediatric Gastroenterologist. Department of Paediatrics, John Radcliffe Hospital, Oxford, OX3 9DU.

What do I do now?
If you would like to discuss the study further or think you would provisionally like to take part, you can contact the rabies study team by telephoning:

Telephone & Fax: 01865 857420

Alternatively you can complete the reply slip below and return it to us in the attached reply-paid envelope to:

The Oxford Vaccine Group
Centre for Clinical Vaccinology & Tropical Medicine
Churchill Hospital
Old Rd, Headington
Oxford OX3 7LJ

Thank you for taking the time to consider participating in this study.

Yours sincerely,

Prof. Richard Moxon	***Prof David Warrell***	***Dr Mary Warrell***
Professor of Paediatrics	***Professor of Tropical Medicine***	***Research Fellow***

Reply Slip

Please complete this section and return in the enclosed pre-paid envelope or e-mail us at: mary.warrell@ndm.ox.ac.uk

Name: ______________________________

Address: ______________________________

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Postcode: ______________

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☐ I would like to know more about the study. I realise that this does not commit me to taking part.

Please contact me. My telephone number is ______________________