

# A cluster investigation method for studying dengue virus genetic diversity, immunological responses and entomological dynamics

<b>Submission date</b>	<b>Recruitment status</b>	<input checked="" type="checkbox"/> Prospectively registered
16/07/2008	Stopped	<input type="checkbox"/> Protocol
<b>Registration date</b>	<b>Overall study status</b>	<input type="checkbox"/> Statistical analysis plan
17/07/2008	Stopped	<input type="checkbox"/> Results
<b>Last Edited</b>	<b>Condition category</b>	<input type="checkbox"/> Individual participant data
24/07/2013	Infections and Infestations	<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Dengue is an infectious disease caused by four types of dengue virus, transmitted by mosquitoes. Dengue can be present with no symptoms at all or as a mild illness with fever, headache and joint aches, but can also be complicated by bleeding and shock. There is no treatment for dengue beyond supportive care and there is no vaccine. The World Health Organization lists dengue fever as one of the most important emerging infectious diseases in the world.

Dengue viruses are highly variable: their genetic material changes slightly each time they replicate within their human or mosquito host. As a result, the millions of individual viruses within a host are all slightly different from each other. We call this the diversity of the virus. The goal of this study is to obtain dengue viruses from patients in hospital with dengue, from the mosquitoes in and around their house and from household members and neighbours that may be infected with or without being sick, and to test if the degree of diversity of the virus in different hosts is related to the severity of illness. The study will also look at the patients immune response in different degrees of dengue severity.

### Who can participate?

This study aims to recruit dengue patients of all ages who have a high fever and test positive for dengue virus. This study will recruit between 18-110 dengue patients per year in Binh Thuan province. The actual number will depend on how many cases occur in the province.

### What does the study involve?

When a dengue case is reported, study staff will take blood samples from the patient. They will take blood when the patient first arrives, and once per day until his/her fever is gone. These samples will be used for testing of the type of dengue virus, the number of viruses and their diversity, and of the patients immune response. Study staff will also draw blood from household members and neighbours of the patient. This study estimates there will be about 5-10 people

who live close to the patient. Mosquito traps will be placed around houses with a dengue patient. A large black plastic container will also be used to collect mosquito larvae, pupae and eggs. These larvae will be bred and stored for future analysis.

**What are the possible benefits and risks of participating?**

Family members and neighbours will be tested for dengue by the study staff and referred to the community health station for clinical assessment and follow-up. Taking blood samples may cause mild discomfort and bruising.

**Where is the study run from?**

The study is run by researchers at the Oxford University Clinical Research Unit (OUCRU) Viet Nam; Binh Thuan Medical College Binh Thuan Province, Viet Nam; and the Academic Medical Center Amsterdam, the Netherlands.

**When is the study starting and how long is it expected to run for?**

The study will run from July 2008 to October 2011 for a total of 3 years and 2 months. After enrolment of 16 index patients and 39 household contacts/neighbours, the study was stopped due to slow enrolment and problems with study staffing.

**Who is funding the study?**

The Wellcome Trust (UK).

**Who is the main contact?**

The Clinical Trials Unit at the Oxford University Clinical Research Unit Viet Nam. +84839241983

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

### Protocol serial number

ctu03dxf08

## Study information

## **Scientific Title**

A community-based study using household sampling around dengue index cases for assessing genetic diversity, immunological responses and entomological transmission dynamics

## **Study objectives**

1. Dengue virus exists as quasi-species in vivo and genetic diversity in mosquitoes is less
2. The genetic diversity of dengue virus in an infected index case is larger than the genetic diversity of the virus in asymptomatic subjects
3. The genetic diversity of dengue virus is less or qualitatively different in asymptomatic subjects, infected household member and cases of different severity
4. The antibody responses, viral load and antigenemia are lower in asymptomatic subjects

## **Ethics approval required**

Old ethics approval format

## **Ethics approval(s)**

Ethics approval received from:

1. Oxford Tropical Medicine Research Ethics Committee (OXTREC) (UK) on the 24th April 2008 (ref: 10/08)
2. Binh Thuan Ethics Committee on the 26th May 2005

## **Study design**

Prospective, observational cohort study

## **Primary study design**

Observational

## **Study type(s)**

Screening

## **Health condition(s) or problem(s) studied**

Dengue fever

## **Interventions**

Patient data and clinical examination will be documented in case record forms (CRF). Blood samples will be collected according to the following schedule:

1. At presentation:
  - 1.1. Blood sample for haematology, biochemistry, serology, NS1 and virology
    - 1.1.1. 2 ml if less than 10 years of age
    - 1.1.2. 5 ml if greater than or equal to 10 years of age
  2. Daily follow up until afebrile: 2 - 5 ml blood sample for haematology, biochemistry, serology, NS1 and virology

Updated 24/07/2013: After enrolment of 16 index patients and 39 household contacts /neighbours, the study was stopped due to slow enrolment and problems with study staffing.

## **Intervention Type**

Other

## **Phase**

Not Specified

## **Primary outcome(s)**

To study dengue pathogenesis by comparing the genetic diversity of virus populations in dengue cases versus infecting mosquitoes and in asymptomatic subjects versus symptomatic cases of different severity

## **Key secondary outcome(s)**

To study dengue pathogenesis by:

1. Studying the evolution of dengue virus quasispecies during the course of illness
2. Studying antibody responses, viral load and antigenemia in asymptomatic and symptomatic dengue virus infections of varying severity

## **Completion date**

01/10/2011

## **Reason abandoned (if study stopped)**

Participant recruitment issue

## **Eligibility**

### **Key inclusion criteria**

Index cases:

1. All ages, either sex
2. Clinical suspicion of dengue:
  - 2.1. Confirmed fever (i.e. an axillary temperature greater than 38°C at presentation)
  - 2.2. Fever less than 72 hours duration
  3. Positive NS1 antigen rapid test (indicative of viraemia)

Sample collection around index case:

All family members and neighbours

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Not Specified

### **Sex**

All

### **Key exclusion criteria**

Does not meet inclusion criteria

### **Date of first enrolment**

20/07/2008

### **Date of final enrolment**

01/10/2011

## Locations

### Countries of recruitment

Viet Nam

### Study participating centre

The Oxford University Clinical Research Unit (OUCRU)

Ho Chi Minh City

Viet Nam

Q5

## Sponsor information

### Organisation

University of Oxford (UK)

### ROR

<https://ror.org/052gg0110>

## Funder(s)

### Funder type

Charity

### Funder Name

The Wellcome Trust (UK) (grant ref: 077078)

## Results and Publications

### Individual participant data (IPD) sharing plan

### IPD sharing plan summary

Not provided at time of registration

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
	Participant information sheet				

