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ANYSNAKES: a study to assess different antivenoms for the management of snakebites

Submission date
23/01/2025

Recruitment status
Not yet recruiting

Registration date
03/02/2025

Overall study status
Ongoing

Last Edited
10/12/2025

Condition category
Injury, Occupational Diseases, Poisoning

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Venomous snakes are a leading cause of death in sub-Saharan Africa, as well as causing significant long-term physical damage and psychological problems. The damage is caused by the venom a snake injects into a person through their bite. A major challenge is the lack of effective antivenoms to treat snakebites. Although there is a huge geographical diversity in types of snakes, with up to 130 different species in Africa, three main types of snakes have been identified: snakes whose venom causes problems with blood clotting, those whose venom affects the brain and central nervous system and finally those whose venom leads to cell and tissue dying (known as necrosis). The long-term effects of snakebites can last for life and bring severe disability. Treatment against snake venom ("antivenom") has remained unchanged for over 100 years. Antivenoms are made by injecting a small amount of the snake's poison (or venom) into animals like horses and sheep and then collecting the antibodies that they produce in response. This can be used to treat people who have been bitten by a snake. Unfortunately, the supply of antivenom is often most limited in the countries that are most affected. Treatment is even more challenging as the signs and symptoms resulting from snake bites can be very similar even with different types of snakes; in these cases, it can be hard to treat a patient most effectively. Different doses of antivenom are likely needed and different antivenoms may work better for some types of snakebites. Where resources are limited and not all antivenoms may be available at all times, it is important to understand how the different antivenoms compare with each other, so that physicians can choose the best option that is relevant for an individual patient when they come to the hospital having been bitten. The ANYSNAKES study aims to measure how six different antivenoms may improve the ability of the blood to clot and reduce other signs of severe snakebite, as well as how often they lead to allergic reactions or problems with the brain and central nervous system, to determine the most appropriate dose of each antivenom and work out how they compare with each other. We will also measure the level of antivenoms in each patient's blood and compare this to the venom from the snake bite.

Who can participate?
Patients over the age of 2 years old across several centres in sub-Saharan Africa who have been bitten by a snake

What does the study involve?
Participants will be randomly allocated to receive an antivenom and dose of antivenom from the list of antivenoms that the study doctors have agreed should be good options to use, based on symptoms. These could include EchiTAb Plus ICP, EchiTab G, Fav Afrique, Antivipmyn Africa, PANAF-Premium and Inoserp Pan-Africa. The antivenom will be given as soon as possible after joining the study via an infusion. Some patients may need a second dose of the antivenom if they do not get better. Blood will be collected so doctors can monitor salt levels and kidney function, and to see if the blood is clotting. Additionally, blood samples, samples of the bite wound, photos of the bite wound, and a sample of the blisters will be collected to help work out the type of snake that bit the patient and how much venom the snake injected into them. All patients will be followed up until 42 days after they join the study.

What are the possible benefits and risks of participating?
Participating in this study may not directly benefit the patients taking part, but the information obtained from the study will help us work out the most appropriate dose of each antivenom and work out how they compare with each other. While in the hospital, patients taking part in the study will be reviewed daily by the study team.

Patients may experience pain or discomfort when samples are collected. There may be side effects from the antivenom given to participants, as with any antivenom used routinely to treat snakebite patients.

Where is the study run from?
The Liverpool School of Tropical Medicine, UK

When is the study starting and how long is it expected to run for?
The study will begin recruiting patients in December 2025 and will run for about 4 years.

Who is funding the study?
The Wellcome Trust, UK

Who is the main contact?
The study team can be contacted at mrcctu.anysnakes@ucl.ac.uk.

Contact information

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Advancing management of systemic envenoming by testing multiple antivenoms

Acronym
ANYSNAKES

Study objectives
In individuals presenting to hospital with systemic envenoming following a snakebite:
• Acute effects of systemic envenoming, specifically coagulopathy and shock, can be reduced by choosing a top-ranked antivenom administered at an optimised dose compared with a randomly chosen antivenom from those relevant to the presenting participant.
• Those presenting only with neurotoxicity can be successfully treated with higher doses of antivenom.

Ethics approval required
Ethics approval required

Ethics approval(s)
submitted 19/08/2024, Liverpool School of Tropical Medicine Research Ethics Committee (Pembroke Place, Liverpool, L3 5QA, United Kingdom; +44(0)151 705 3100; lstmrec@lstmed.ac.uk), ref: 23-034

Study design
Multicentre personalised randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Snakebite

Interventions
Randomisation and dosing:
Randomisation will use a novel Personalised Randomised Controlled Trial (PRACTical) design, in which each participant is randomised only to pre-defined antivenoms that are agreed upon and clinically acceptable to each specific site for the type of participant. The design will also include a dose optimisation component, separately for participants who have coagulopathy and those who have only shock as signs of systemic envenoming, randomising participants allocated to each antivenom to several vials between a minimum and a maximum inclusive.

The potential randomisation options for the 6 trial antivenoms and doses of each are as follows, based on pre-defined locally relevant antivenoms.

Patients presenting with coagulopathy only:
• EchiTAb Plus ICP, Fav Afrique, Antivipmyn Africa, PANAF-Premium, Inoserp Pan-Africa: 1, 2, or 3 vials
• EchiTab G: 1 or 2 vials

Patients presented with shock, with or without coagulopathy:
• EchiTAb Plus ICP, Fav Afrique, Antivipmyn Africa, PANAF-Premium, Inoserp Pan-Africa: 3, 4, 5, or 6 vials

Patients presenting with neurotoxicity:
• EchiTAb Plus ICP, Fav Afrique, Antivipmyn Africa, PANAF-Premium: 20 vials
• Inoserp Pan-Africa: 10 vials

Treatment: For each antivenom, treatment should be commenced as soon as possible and ideally within 1h after enrolment. Treatment will generally be a single administration; however, repeat administration of the same antivenom at the same dose may be considered at 8h after randomisation (typically ~6-7h after the first administration) if a participant presenting with coagulopathy still shows no evidence of clotting (on 20WBCT) or in any participant whose conditions worsens, including after 8h.

Assessments:
All participants will be clinically reviewed at screening, randomisation, 3h, 8h, 14h, 24h, 48h, daily whilst in hospital, and at discharge or Day 7, whichever is earlier, which will include evaluation for AEs and SAEs.

Lab tests, samples and assessments will be collected/completed as follows:
• Whole blood clotting test (at screening, 8h, 14h, 24h, 48h) and clotting panel (at randomisation, 8h, 14h, 24h, 48h)
• Haemoglobin (at randomisation, 24h, 48h)
• Sodium, Potassium Creatinine (at randomisation, 24h, 48h, and at discharge or Day 7

(whichever is earlier))
• Serum to assay venom/antivenom (at randomisation 3h, 8h, 24h)
• Bite site swab (at randomisation) and blister fluid sample collection if applicable (at randomisation, and/or if later developed)
• Urine pregnancy test in women of childbearing potential (48h)
• Economic evaluation (EQ-5D-5L) (at randomisation, 48h, at discharge or Day 7 (whichever is earlier), and on Day 14 and Day 42)
• Participant-specific functional scale (Day 14 and Day 42)
• Disability assessment (at randomisation, Day 42)

Additionally, ancillary sub-studies will be conducted in participants aged 18 years and older, who are not pregnant or breast-feeding, and will be conducted in specific sites only with a limited number of participants with specific syndromes:
1. Detailed serum samples to assay venom/antivenom (Syndrome independent): In 50 patients, 3 blood samples will be collected at 1h,3h, and 48h, in addition to the 4 being collected in the trial, to create a more complete profile of venom/antivenom concentration.
2. Longitudinal coagulation parameters (Coagulopathy only): In 50 patients, blood samples will be collected at 14h, 48h, daily whilst in hospital, and at discharge or Day 7 (whichever is earlier), in addition to the 4 being collected in the trial. This will allow for a comparison of characteristics of coagulation parameters to identify the most accurate parameter to detect and monitor venom-induced coagulopathy.
3. Local tissue damage assessment (Coagulopathy or shock): This substudy will assess the utility of imaging (thermal imaging, infrared, digital photography) techniques and limb volume measurements (tape measurements, novel digital equipment for measuring limb volume) in quantifying and monitoring local swelling, and in assessing the effect of antivenom on local swelling after snakebite. It will also explore potential associations between the degree/severity of swelling and wound necrosis. 200 participants will be assessed at randomisation, 8h, 14h, 24h, 48h, daily whilst in hospital, at discharge or Day 7 (whichever is earlier), and at Day 42.
4. Respiratory muscle assessment (neurotoxicity only): This substudy will investigate the utility of a diagnostic tool which measures tongue strength (as a proxy for neurotoxicity-driven cranial nerve impairment) and a portable respiratory diagnostic device to objectively measure respiratory muscle strength and assess worsening respiratory compromise, at randomisation, 3h, 8h, 14h, 24h, 48h in 50 participants.

Intervention Type
Biological/Vaccine

Phase
Phase III

Drug/device/biological/vaccine name(s)
EchiTAb Plus ICP, EchiTab G, Fav Afrique, Antivipmyn Africa, Premium Pan-Africa, Inoserp Pan-Africa

Primary outcome(s)
In participants with signs of systemic envenoming at presentation, specifically coagulopathy or shock, the primary endpoint, reflecting “success”, will be defined by the participant being alive and having:
1. Resolution of shock at 3h from randomisation in participants with evidence of shock at baseline (defined by age-specific systolic blood pressure) (note: all participants presenting with shock must receive weight-dependent fluid boluses, so primary endpoint reflects resolution with

antivenom and fluid bolus)
2. International normalised ratio (INR) <3 at 8h from randomisation in those without shock and with evidence of coagulopathy at presentation (defined by baseline INR >1.4 (diagnostic criteria based on external evidence) but no evidence of shock)

In participants with only neurotoxicity at presentation (exploratory outcome):
The primary endpoint, reflecting "success", will be defined by the participant having no requirement for mechanical or manual ventilation within 48h from randomisation

Key secondary outcome(s))
Efficacy will be measured in all participants using:
1. All-cause mortality through 42 days from randomisation
2. WHO 12-item disability assessment scale 2.0 (WHO-DAS) at 42 days from randomisation (5 years and older) or Washington Child Functioning Module (aged 2-4 years)
3. Patient-specific functional scale (PSFS) at 14 and 42 days from randomisation

Efficacy (any evidence of coagulopathy):
• INR <3 at 14h from randomisation
• Mean change in INR from baseline to 8h and 14h from randomisation
• Fibrinogen >0.5 g/L at 8h and 14h from randomisation
• Mean change in fibrinogen from baseline to 8h and 14h from randomisation
• Cessation of bleeding at 8h from randomisation (in those with evidence of active bleeding at randomisation)
• Development of new major or clinically relevant non-major bleeding 8-48h from randomisation (major bleeding as defined by International Society on Thrombosis and Haemostasis (ISTH) criteria)
• Development of new major bleeding from 8 hours through 7 days from randomisation

Efficacy (neurotoxicity only):
• Requirement for intubation within 48h from randomisation
• Duration of any mechanical or manual ventilation given through 42 days from randomisation

Safety (all)
• Severe (Grade 3/4 following the Brown grading) allergic reactions (hypotension, hypoxia, or neurological compromise) within 6h of first administration following randomisation
• Severe (Grade 3/4) allergic reactions (hypotension, hypoxia, or neurological compromise) within 6h of any administration following randomisation (Brown grading)
• Allergic reactions (any grade) within 6h of first administration following randomisation (Brown grading)
• Allergic reactions (any grade) within 6h of any administration following randomisation (Brown grading)
• Serum sickness through 14 and 42 days from randomisation (defined by the Australian Snakebite Project (ASP))

Completion date
01/06/2029

Eligibility

Key inclusion criteria

1. ≥2 years of age
2. Presenting to the hospital reporting having been bitten by a snake and with evidence of systemic envenoming, defined as any of the following:
2.1. Coagulopathy, defined as no evidence of clotting on a 20-minute whole blood clotting test (20WBCT) (performed as part of standard clinical practice)
2.2. Shock defined by systolic blood pressure (see below) persisting 30 mins after a weight-dependent fluid bolus. A single post-bolus blood pressure reading will be used to determine eligibility.
2.2.1. 2-5 years of age <60 mmHg
2.2.2. 6-12 years of age <70 mmHg
2.2.3. >13 years <90 mmHg
2.3. Neurotoxicity, defined as one or more of the following symptoms: bilateral ptosis, ophthalmoplegia, airway compromise or ventilatory failure presenting within 24 hours of a bite
3. Not received antivenom for this snakebite, at the presenting hospital or any other healthcare facility (including a local health centre)
4. Participant or proxy or parent/guardian willing and able to provide consent (written or, depending on severity of presentation, verbal consent confirmed by written consent as soon as possible). Verbal consent allows for the administration of antivenom at no or minimal delay.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
2 years

Upper age limit
100 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. If presenting with coagulopathy: currently known to be receiving anti-coagulant therapy including warfarin, heparin or heparin derivatives or direct oral anticoagulants (DOAC)
2. Active (current) participation in another trial of antivenom or small molecule treatments for envenoming
3. Previous participation in this trial with a reaction to trial antivenom

Date of first enrolment
01/03/2026

Date of final enrolment
01/06/2029

Locations

Countries of recruitment
Ghana

Togo

Study participating centre
Site and additional country selection ongoing
Togo
-

Sponsor information

Organisation
Liverpool School of Tropical Medicine

ROR
https://ror.org/03svjbs84

Funder(s)

Funder type
Research council

Funder Name
Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

Data release requests should be directed to mrcctu.anysnakes@ucl.ac.uk. The data-sharing policy will be summarised in the study protocol. The study team intend to make the protocol available via the registry in due course, providing clarification on the details of individual participant data (IPD) sharing.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes