

# A randomised, open, comparison of penicillin and metronidazole for the treatment of tetanus

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<b>Registration date</b> 14/10/2005	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 25/10/2022	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**Clinical Trials Information System (CTIS)**  
Nil known

**Protocol serial number**  
077166

## Study information

**Scientific Title**

A randomised, open, comparison of penicillin and metronidazole for the treatment of tetanus

**Acronym**

TS Study

**Study objectives**

Penicillin given parenterally has been the standard antibiotic treatment for tetanus for more than 50 years. However there are several theoretical disadvantages to its use. Because many patients with tetanus cannot take medicines orally, penicillin must be administered by injection, either IntraMuscular (IM) or IntraVenous (IV). Any noxious stimulus, such as an injection, has the potential to induce potentially lethal spasms.

Penicillin is known to block post-synaptic Gamma-AminoButyric Acid (GABA) and thus is pro-convulsant. It could lower the threshold for convulsions, which may be seen in severe tetanus. Since GABA transmission occurs in skeletal muscles as well as the central nervous system, penicillin could in theory worsen spasms as well. Metronidazole may be given rectally by suppository, thus obviating the need for painful injections. Bioavailability by this route is reasonably high. Metronidazole is known to be effective against Clostridia species. In a small study from Indonesia metronidazole was at least as effective as penicillin in patients with tetanus of moderate severity, although many patient details were not given in the published report. This study aimed to compare IV penicillin and metronidazole suppositories for the treatment of tetanus.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Not provided at time of registration

**Study design**

Randomised controlled trial

**Primary study design**

Interventional

**Study type(s)**

Treatment

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

Tetanus

**Interventions**

Patients entered into the study were randomised to receive:

1. Benzylpenicillin 2 million units (child 25,000 units/kg) IV six-hourly for seven days
  2. Metronidazole 1 g (child):
    - a. 125 mg age four weeks to less than 12 months
    - b. 250 mg age one to four years
    - c. 500 mg age five to 12 years
- Rectally (PR) eight-hourly for three days then 12-hourly for four days.

Once the patient could reliably tolerate oral medicines the appropriate dose of penicillin G or metronidazole was given by mouth instead of IV or PR, respectively. Patients who were known to be allergic to penicillin received erythromycin instead.

### **Intervention Type**

Drug

### **Phase**

Not Specified

### **Drug/device/biological/vaccine name(s)**

Penicillin and metronidazole

### **Primary outcome(s)**

The primary endpoint was mortality.

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

The secondary endpoints were recovery times and complication rates.

### **Completion date**

01/01/1997

## **Eligibility**

### **Key inclusion criteria**

1. Clinical diagnosis of tetanus
2. Aged more than one month
3. Informed consent from patient or attendant relative (if comatose or aged less than 16 years)

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

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Not Specified

### **Sex**

All

### **Key exclusion criteria**

Lack of informed consent or age less than one month

### **Date of first enrolment**

01/04/1993

### **Date of final enrolment**

01/01/1997

## Locations

### Countries of recruitment

Bangladesh

Thailand

### Study participating centre

c/o Dr Nick Day

Bangkok

Thailand

10400

## 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: 077166)

## Results and Publications

### Individual participant data (IPD) sharing plan

Not provided at time of registration

### IPD sharing plan summary

Not provided at time of registration

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
	conference abstract				

[Abstract results](#)

01/03/2002

23/10/2019

No

No