VOL 04/2018

# PHARMACY BULLETIN

## HOSPITAL SEGAMAT

# Tetanus

- **Tetanus is caused by Clostridium tetani which produces a potent toxin that has 2 components, ie tetanospasmin (a neurotoxin) and tetanolysin (a haemolysin).**
- **Microorganisms usually gain entry through open wounds and lacerations or via penetrating injuries.**
- **Tetanospasmin is mainly responsible for the features of tetanus which manifests as rigidity and painful spasms of skeletal muscles. The muscle stiffness usually involves the jaw (lockjaw) and neck and then becomes generalised.**
- **The transmission of tetanus is not from person to person. It occurs when the tetani spores are introduced into acute wounds from trauma, surgeries, injections, chronic skin lesions and infections.**

## IN THIS ISSUE:

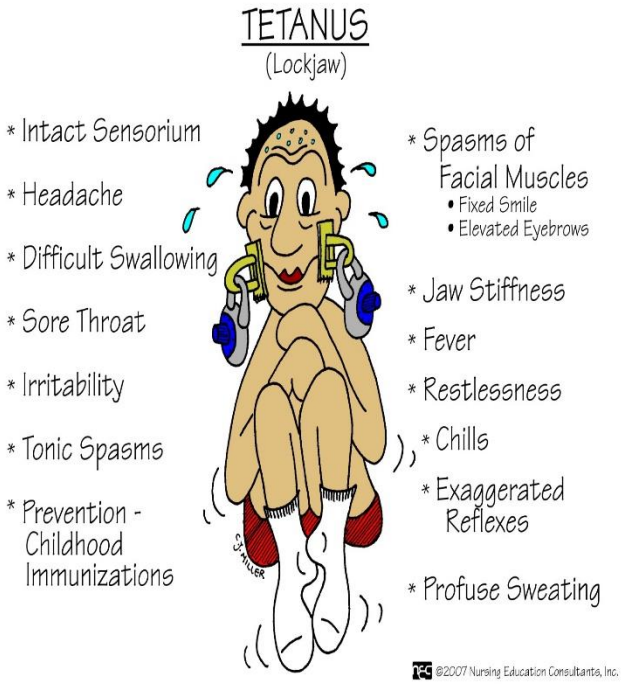


## EDITORIAL BOARD

## Diagnosis

**Tetanus diagnosis is strictly clinical**; there are no confirmatory laboratory tests. The WHO definition of adult tetanus requires at least one of the following signs: trismus (inability to open the mouth) or risus sardonicus (sustained spasm of the facial muscles); or painful muscular contractions. However, tetanus may also occur in patients who are unable to recall a specific wound or injury.

## Sign and Symptoms




## Incubation period

### Children and adult

- **Usually between 3 to 21 days (median 7 days).**
- **Shorter incubation periods (<7 days) along with delays in seeking treatment are associated with fatal outcomes**

### Neonates

- **In 90% cases, symptoms appear within 3 to 14 days of birth**

Reference : Clinical Guideline Practice, Childhood Immunization, December 2004

# Treatment

**General measures:** if possible a separate ward/location should be designated for tetanus patients. Patients should be placed in a quiet shaded area and protected from tactile and auditory stimulation as much as possible. All wounds should be cleaned and debrided as indicated.

**Immunotherapy:** if available, administer human TIG 500 units by intramuscular injection or intravenously (depending on the available preparation) as soon as possible; in addition, administer age-appropriate TT-containing vaccine, 0.5 cc by intramuscular injection at a separate site.

**Antibiotic treatment:** metronidazole is preferred (500 mg every six hours intravenously or by mouth); Penicillin G (100,000–200,000 IU/kg/day intravenously, given in 2–4 divided doses). Tetracyclines, macrolides, clindamycin, cephalosporins and chloramphenicol are also effective.

**Muscle spasm control:**

*benzodiazepines* are preferred. For adults, intravenous diazepam can be given in increments of 5 mg, or lorazepam in 2 mg increments, titrating to achieve spasm control without excessive sedation and careful monitoring to avoid respiratory depression or arrest is needed.

*Magnesium sulphate* can be used alone or in combination with benzodiazepines to control spasm and autonomic dysfunction: 5 gm (or 75mg/kg) intravenous loading dose, then 2–3 grams per hour until spasm control is achieved.

*Other agents* used for spasm control include baclofen, dantrolene (1–2 mg/kg intravenous or by mouth every 4 hours), barbiturates, preferably short-acting (100–150 mg every 1–4 hours in adults; 6–10 mg/kg in children; by any route), and chlorpromazine (50–150 mg by intramuscular injection every 4–8 hours in adults; 4–12 mg every by intramuscular injection every 4–8 hours in children).

**Autonomic dysfunction control:** magnesium sulphate as above; or morphine. Note: β-blockers such as propranolol were used in the past but can cause hypotension and sudden death; only esmolol is currently recommended.

**Airway / respiratory control:** drugs used to control spasm and provide sedation can result in respiratory depression. If mechanical ventilation is available, this is less of a problem; if not, patients must be carefully monitored and medication doses adjusted to provide maximal spasm and autonomic dysfunction control while avoiding respiratory failure. If spasm, including laryngeal spasm, is impeding or threatening adequate ventilation, mechanical ventilation is recommended when possible. Early tracheostomy is preferred as endotracheal tubes can provoke spasm and exacerbate airway compromise.

**Adequate fluids and nutrition** should be provided, as tetanus spasms result in high metabolic demands and a catabolic state. Nutritional support will enhance chances of survival.

Prior to the availability of a vaccine and mechanical ventilation (during the 1920s–30s), careful monitoring and nursing care improved survival. If patients can be supported through one to two weeks of spasm and other complications, the chances of complete recovery greatly increase, particularly in non-elderly and previously healthy patients.


## Tetanus vaccines available in Malaysia

| Tetanus toxoid | Combination vaccine | Tetanus Immune Globulin (TIG) |
|---|---|---|
| • **Tetavax® (Adsorbed tetanus vaccine)**<br>• **TT Vaccine® (Adsorbed tetanus vaccine)**<br>• **Tetanus Toxoid Vaccine® (Adsorbed tetanus vaccine)** | • **Adacel® (Tdap; tetanus-diphtheria-acellular pertussis)**<br>• **Adacel® Polio (Tdap-IPV; tetanus-diphtheria-acellular pertussis-inactivated polio)** | • **Sero-Tet® (Human tetanus immune globulin)**<br>• **Igantet® (Human antitetanus Ig)** |

## Tetanus vaccines available in Hospital Segamat


### Tetanus toxoid vaccine

**Brand name and strength:** TT Vaccine 0.5 ml
**Reconstitution and dilution:** Not required
**Administration:** IM injection; Inject in the area of the vastus lateralis (mid-thigh laterally) or deltoid. Do **NOT** inject into gluteal area
**Storage and stability: 1. Intact vial**
Store at 2-8°C. Do **NOT** freeze
**2. Multidose vial**
Stable for 4 weeks if kept as per stated above and used aseptically
**Cautions :** 1) The vaccine **MUST** be shaken well before use
2) Do **NOT** use if product does not form a suspension

## Mode of Administration

**Primary vaccination in adults:** 3 doses of vaccine are required with an interval of 4-6 weeks between the 1st and 2nd doses, and 6-12 months between the 2nd and 3rd doses. Tdap can be used for the 1st dose with Td vaccine for the subsequent doses.

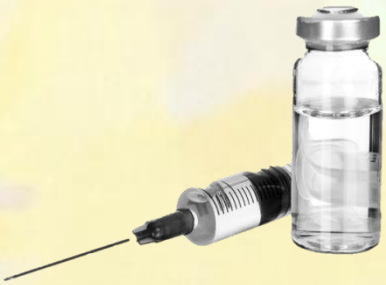
**Booster vaccination:** Booster dose of Tdap vaccine is usually given at 10 and 20 years after the primary course. All adults who reach the age of 50 years without having received a booster dose Td in the previous 10 years should receive a further tetanus booster dose.

## Co-administration With Other Vaccines

Several vaccines can be given together as long as there are no contraindications for individual agents. There are no contraindications to simultaneous administration of live attenuated vaccines with inactivated or toxoid vaccines. Do not mix tetanus toxoid with other vaccines in the same syringe, unless approved for mixing by manufacturer.

## Contraindications and Adverse Effects

- The only absolute contraindication to tetanus containing vaccines is anaphylaxis reaction after the previous dose, or to any component of the vaccine.
- Common adverse effects include pain, tenderness, localised erythema and discomfort at the injection site. Uncommon general adverse effects following Td vaccination include headache, lethargy, malaise, myalgia and fever. Anaphylaxis, urticaria and peripheral neuropathy occur very rarely.
- The adverse reactions to a single dose of Tdap are similar in adults and adolescents, whether administered shortly (18 months) or at a longer interval after a previous dose of a vaccine containing tetanus/diphtheria toxoids. Thus, frequent administration of tetanus toxoid does not increase the risk of developing injection site reaction as had been perceived previously.
- To date, the most frequently reported adverse events for tetanus toxoid vaccines received by National Adverse Drug Reactions Monitoring Centre, NPCB include local site reactions such as injection site pain and swelling, fever and rash.



Reference: Malaysian Society of Infectious Diseases and Chemotherapy, Guidelines For Adult Immunisation, 2nd Edition, 2014

## Prevention

1) Post-exposure prophylaxis
– In all cases:
• Cleansing and disinfection of the wound, and removal of any foreign body.
• Antibiotics are not prescribed routinely for prophylaxis. The decision to administer an antibiotic (metronidazole or penicillin) is made on a case-by-case basis, according to the patient's clinical status.
– Depending on pre-exposure vaccination status:
Tetanus vaccine (TV) and immunoglobulin: see indications below.

| Risk | **Complete immunisation** (3 or more doses) Time since administration of latest dose: | | | **Incomplete immunisation** (less than 3 doses) or **no immunisation** or **unknown status** |
|---|---|---|---|---|
| | < 5 years | 5-10 years | > 10 years | |
| **Minor clean wound** | None | None | TV one booster dose | Initiate or complete TV |
| **All other wounds** | None | TV one booster dose | TV one booster dose | Initiate or complete TV and administer tetanus immunoglobulin |

## Tetanus Vaccine (IM)

**Children and adults:** 0.5 ml per dose
If no immunisation or unknown immunisation status: administer at least 2 doses at an interval of 4 weeks.
If incomplete immunisation: administer one dose.
Then, to ensure long-lasting protection, administer additional doses to complete a total of 5 doses, as indicated in the table below.

## Human Anti-tetanus Immunoglobulin (IM)

**Children and adults:** 250 IU single dose; 500 IU for wounds more than 24 hours old.
Inject the vaccine and the immunoglobulin in 2 different sites, using a separate syringe for each.

Reference : Véronique Grouzard., et al. (2018) Clinical guidelines - Diagnosis and treatment manual., 2018 edn., : Médecins Sans Frontières., Chapter 7: Bacteria Disease

# Directive : Restriction Of Metoclopramide Use In View Of Adverse Neurological Side Effects

**1.1 Indication**

Adult population

Indicated for the use in adults for:

• prevention of post-operative nausea and vomiting,

• symptomatic treatment of nausea and vomiting, including nausea and vomiting induced by migraine attack

•Prevention of radiotherapy-induced nausea and vomiting.

Pediatric population

Indicated for the in children aged 1 to 18 years for:

• prevention of delayed chemotherapy-induced nausea and vomiting as a second-line option,

• prevention of post-operative nausea and vomiting as a second-line option.

**1.2 Dose and Administration**

**Parenteral**

•The solution can be administered by the intravenous or intramuscular route.

•The intravenous doses must be administered as a slow bolus (for at least 3 minutes)

**All indications (Adults)**

•A single 10mg dose is recommended for the prevention of post-operative nausea and vomiting.

•The recommended dose for the symptomatic treatment of nausea and vomiting, including nausea and vomiting induced by migraine attack and for the prevention of radiotherapy induced nausea and vomiting is 10mg pr dose, 1 to 3 times daily.

•The maximum recommended daily dose is 30mg or 0.5mg/kg.

•Treatment of duration when administering by injection should be as short as possible and a switch to administration via oral or rectal route should be instituted as quickly as possible.

**All indications (Children from 1 to 18 years of age)**

•The recommended dosage is 0.1 to 0.5mg/kg, 1 to 3 times daily, by intravenous route.

•The maximum daily dose is 0.5mg/kg.

•For prevention of delayed chemotherapy-induced nausea and vomiting, the maximum treatment duration is 5 days.

•For the prevention of post-operative nausea and vomiting, the maximum treatment duration is 48 hours.

Dosing table

| Age | Body Weight | Dose | Frequency |
|---|---|---|---|
| 1-3 years | 10-14kg | 1mg | Up to 3 times daily |
| 3-5 years | 15-19kg | 2mg | Up to 3 times daily |
| 5-9 years | 20-29kg | 2.5mg | Up to 3 times daily |
| 9-18 years | 30-60kg | 5mg | Up to 3 times daily |
| 15-18 years | Over 60kg | 10mg | Up to 3 times daily |

**Frequency of administration:**

A minimum interval of 6 hours between two administration is to be respected, even if vomiting or rejection of the dose occurs.

1.2 Dose and Administration

**Oral- tablet/syrup**

**Adults:**

•The recommended single dose is 10mg, repeated up to three times daily.
•The maximum recommended daily dose is 30mg or 0.5mg/kg body weight.
•The maximum recommended treatment is 5 days.

**Prevention of delayed chemotherapy induced nausea and vomiting (CINV) (Pediatric patients aged 1-18 years)**

•The recommended dose is 0.1 to 0.15mg/kg body weight, repeated up to three times daily by oral route.
•The maximum dose in 24 hours is 0.5mg/kg body weight.

Dosing table

| Age | Body Weight | Dose | Frequency |
|---|---|---|---|
| 1-3 years | 10-14kg | 1mg | Up to 3 times daily |
| 3-5 years | 15-19kg | 2mg | Up to 3 times daily |
| 5-9 years | 20-29kg | 2.5mg | Up to 3 times daily |
| 9-18 years | 30-60kg | 5mg | Up to 3 times daily |
| 15-18 years | Over 60kg | 10mg | Up to 3 times daily |

•The maximum treatment duration is 5 days for prevention of delayed chemotherapy induced nausea and vomiting (CIVN).
•Tablets are not suitable for use in children weighing less than 30kg.
•Other pharmaceutical forms may be more appropriate for administration to this population.

**Frequency of administration:**

A minimum interval of 6 hours between two administration is to be respected, even if vomiting or rejection of the dose occurs.

**Special Warnings and Precautions For Use**

**Neurological disorders**
Extrapyramidal disorders may occur, particularly in children and young adults, and/or when high doses are used. These reactions generally occur at the beginning of treatment, and can occur after a single dose. If extrapyramidal symptoms occur, metoclopramide should be discontinued immediately. These effects are generally completely reversible after treatment discontinuation; however, symptomatic treatment may be required (benzodiazepines in children, and/or anticholinergic antiparkinsonian medicinal products in adults).

An interval of at least six hours should be respected between each dose even if vomiting or rejection of the dose occurs, in order to avoid overdose.

Long-term treatment with metoclopramide may cause potentially irreversible tardive dyskinesia, particularly in elderly subjects. Treatment should not exceed 3 months because of the risk of tardive dyskinesia. Treatment must be discontinued if clinical signs of tardive dyskinesia occur.

Neuroleptic malignant syndrome has been described with metoclopramide in combination with neuroleptics and with metoclopramide monotherapy. Metoclopramide must be immediately discontinued if symptoms of neuroleptic malignant syndrome develop, and appropriate treatment should be initiated.

Particular caution should be exercised in patients with underlying neurological disorders, and in patients receiving other centrally-acting drugs.

Symptoms of Parkinson's disease may also be exacerbated by metoclopramide.

**Methemoglobinemia**
Methemoglobinemia, which could be related to NADH-cytochrome b5 reductase deficiency, has been reported. If this occurs, treatment must be immediately and permanently discontinued, and appropriate measures initiated (such as treatment with methylene blue).

**Cardiac disorders**
Serious cardiovascular undesirable effects, including cases of severe bradycardia, circulatory collapse, cardiac arrest and QT prolongation have been reported during administration of metoclopramide by injection, particularly via the intravenous route.

Particular caution should be exercised when administering metoclopramide, particularly via the intravenous route, in elderly subjects, patients with cardiac conduction disorders (including QT prolongation), patients with electrolyte imbalance, bradycardia, and patients taking other drugs known to prolong QT interval.

The intravenous injection must be given as a slow bolus (of at least 3 minutes' duration) in order to reduce the risk of undesirable effects (e.g. hypotension, akathisia).

**Kidney or liver failure**
In patients with kidney failure or severe liver failure, a dose reduction is recommended.

# PRODUCT BRAND CHANGES:

*AUGUST-SEPTEMBER 2018*

## Telmisartan 80 mg Tablet


**Previous brand : Micardis**

Manufacturing company: Boehringer Ingelheim


**Current brand: Teleact**

Manufacturing company: Ranbaxy

## Mometasone Furoate 50 mcg Aqeous Nasal Spray


**Previous brand: Nasonex**

Manufacturing company: MSD Pharmaceuticals


**Current brand: Nasehaler**

Manufacturing company: Cipla

## Pravastatin Sodium 20 mg Tablet


**Previous brand: Pravatas 20**

Manufacturing company: Intas


**Current brand: Apo-Pravastatin**

Manufacturing company: Apotex

# PRODUCT BRAND CHANGES

*August-September 2018*

## Salbutamol 100 mcg/dose Inhalation


**Previous brand: Ventolin**

Manufacturing company: GlaxoSmithKline


**Current brand: Biomol 100**

Manufacturing company: Beximco Pharmaceuticals LTD

## Noradrenaline Acid Tartrate 4mg/4 ml Injection


**Previous brand: Cardiamed**

Manufacturing company: Chemical Company of Malaysia (CCM)


**Current brand: Levophed**

Manufacturing company: Hospira Malaysia Sdn. Bhd.

# AKTIVITI JABATAN FARMASI HOSPITAL SEGAMAT:

## PHARMILY DAY 2018

14 SEPTEMBER-15 SEPTEMBER 2018


# WORLD PHARMACIST DAY (HOSPITAL SEGAMAT)

25 September 2018


# PERTANDINGAN PSYCHODRAMA

30 September 2018

Sempena Kempen Kesedaran Kesihatan Mental dan Pencegahan Bunuh Diri Peringkat Daerah Segamat 2018, Jabatan Farmasi telah menyertai Pertandingan 'Pscychodrama' dan telah memenangi tempat ketiga.

## AKTIVITI KENALI UBAT ANDA (SEKOLAH KEBANGSAAN KAMPUNG JAWA)

1 Oktober 2018

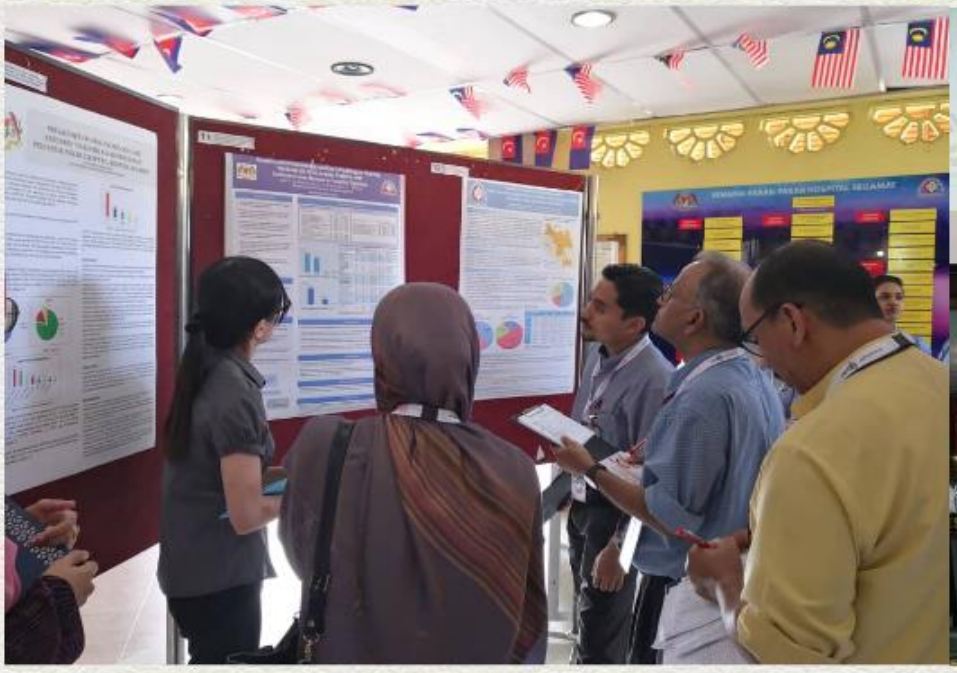

## AKTIVITI KENALI UBAT ANDA (SEKOLAH KEBANGSAAN BANDAR PUTRA)

30 Oktober 2018

# HOSPITAL SEGAMAT RESEARCH WEEK

1 Oktober 2018

Jabatan Farmasi yang diwakili oleh Cik Soh Fang Yu dan Cik Gan Fong Nee, telah menyertai 'Hospital Segamat Research Week 2018'. Tahniah kepada Cik Soh Fang Yu [Tajuk kajian:Assessment of Knowledge and Use of Sublingual Glyceryl Trinitrate (S/L GTN) among Patients with Coronary Heart Disease in Hospital Segamat] yang memenangi tempat pertama dalam kategori poster.



# JOHOR RESEARCH DAY

30 Oktober 2018