

THROMBOPROPHYLAXIS IN PAEDIATRIC SURGICAL AND TRAUMA PATIENTS - CHW PRACTICE GUIDELINE[®]

DOCUMENT SUMMARY/KEY POINTS

- Most paediatric patients are at very low risk for venous thromboembolism (VTE).
- Good hydration and early mobilisation after surgery or trauma are important in reducing the risk of VTE.
- Consider pharmacologic prophylaxis with low molecular weight heparin for patients at high risk for VTE, defined within this guideline; also see Enoxaparin (Clexane) – Low Molecular Weight Heparin – CHW.
- Mechanical methods of prophylaxis such as intermittent pneumatic compression are not routinely recommended but may be used at the discretion of the treating consultant.
- Thromboprophylaxis Guideline Summary - see [Flowchart](#) on page 3.

CHANGE SUMMARY

- Due for mandatory review

This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1 st May 2019	Review Period: 3 years
Team Leader:	Staff Specialist	Area/Dept: Haematology

READ ACKNOWLEDGEMENT

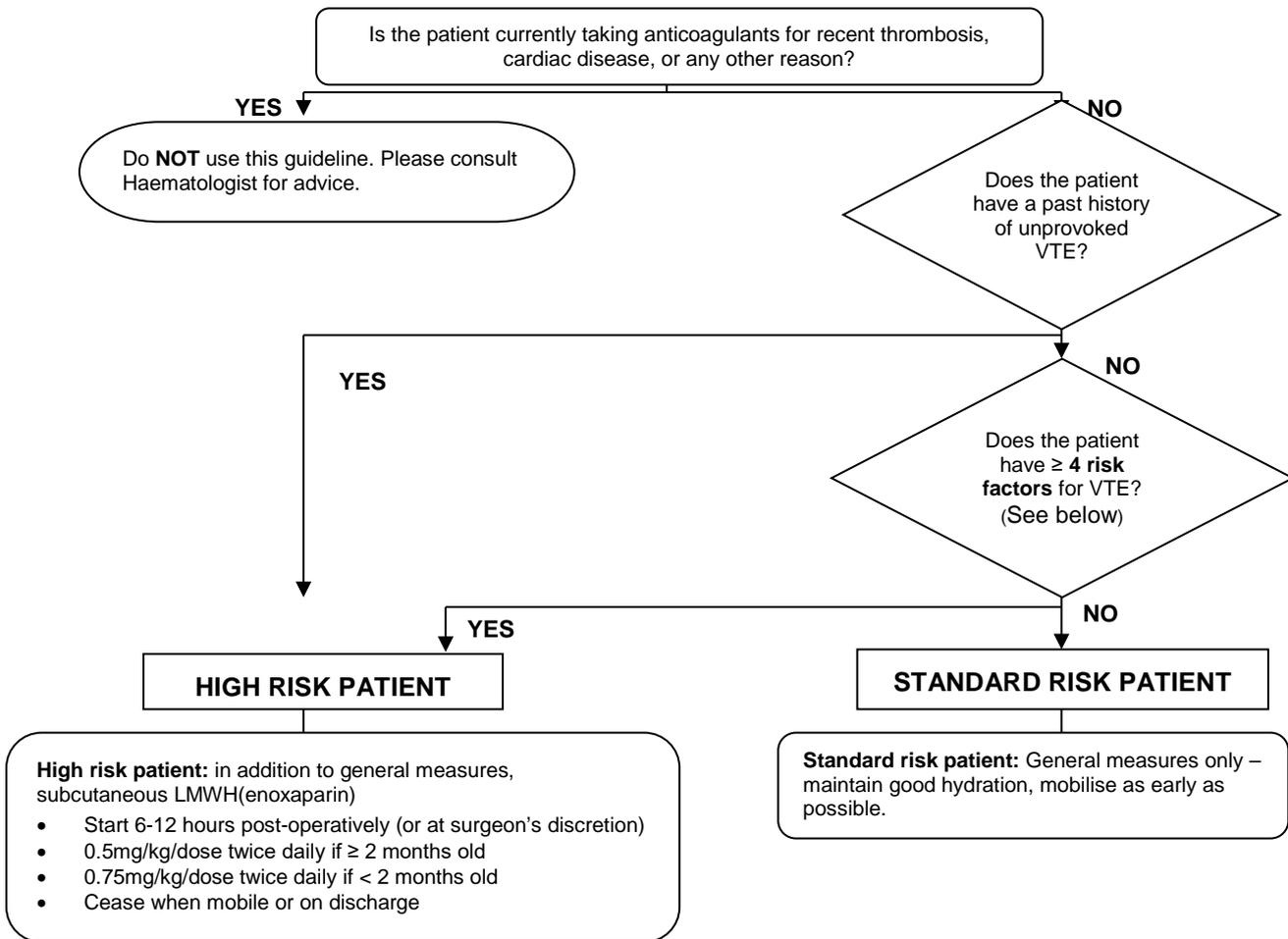
Read Acknowledge Only – Clinical staff involved in the care of surgical and trauma patients at risk of venous thromboembolism

Acronym	
CHW	The Children's Hospital at Westmead
CVAD	Central Venous Access Device
HITTS	Heparin-induced Thrombotic Thrombocytopenia Syndrome
IPC	Intermittent Pneumatic Compression
LMWH	Low Molecular Weight Heparin
PICC	Peripherally Inserted Central Catheter
TEDS	Thromboembolic Deterrent Stockings
UFH	Unfractionated Heparin
VTE	Venous Thromboembolism

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Thromboprophylaxis Guidelines Summary



Risk Factors for VTE

- Age less than 3 months **OR** post-pubertal
- Severe injury
- Major surgery – e.g. chest, abdominal, spinal, lower limb orthopaedic, craniotomy
- Coexisting disease – cancer (including leukaemia), severe infection, inflammatory disease, congenital heart disease, nephrotic disease, diabetes
- Obesity
- Prolonged immobilisation
- Central venous catheter
- Previous **line-related** proximal VTE
- Oestrogenic state – oral contraceptive pill, pregnancy, miscarriage/termination in last 3 months
- Inherited or acquired thrombophilia (see text for specific conditions)

Administration of Enoxaparin

DO NOT administer for **12 hours prior to** insertion or removal of epidural or spinal catheter

DO NOT administer for **2 hours after** insertion or removal of epidural or spinal catheter

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1 Purpose

To outline the epidemiology of venous thromboembolism (VTE).

To describe the available methods of thromboprophylaxis and their evidence base.

To recommend general measures suitable for all paediatric surgical or trauma patients to minimise risk of VTE.

To identify high risk paediatric surgical or trauma patients who may benefit from specific interventions to reduce their risk of VTE.

2 Principles

- VTE, including deep venous thrombosis and pulmonary embolism, is uncommon in children (in contrast to adults).
- VTE is a potentially preventable disease which, when it does occur, is associated with significant morbidity and mortality, even in children.
- Surgery and trauma are well described risk factors for VTE.
- **Simple, non-invasive general measures should be provided to all post-operative/trauma children in order to minimise the risk of VTE.**
- **Identify the small group of children who may be at increased risk of VTE, and provide effective interventions to ameliorate this risk.**

3 Recommendations

Note: The below recommendations have been drawn from the discussion in Sections 4 & 5.

3.1 Definition of Risk Groups

Most children are at **low risk** of VTE. These patients are referred to as "[standard risk](#)" for the purposes of this guideline.

"[High risk](#)" patients are considered to be those that have **4 or more risk factors** as outlined below **OR** a past history of non-line related/unprovoked VTE. All patients not fulfilling these criteria are standard risk.

3.1.1 Risk Factors for VTE

- Age: less than 3 months or post-pubertal.
- Severe injury – including severe chest, abdominal/pelvic or head injuries, spinal injuries, and lower limb fractures requiring open reduction and/or internal/external fixation.
- Major surgery – including chest, abdominal/pelvic, spinal, lower limb orthopaedic, craniotomy.

- Certain coexisting disease, including
 - Cancer, including haematological malignancy
 - Infection, particularly if severely unwell
 - Inflammatory disease, eg inflammatory bowel disease, rheumatological disease, Kawasaki disease
 - Congenital heart disease
 - Nephrotic syndrome
 - Diabetes
- Obesity.
- Prolonged immobilisation.
- Presence of a central venous catheter.
- Previous line-related proximal VTE – i.e., thrombosis at the site of a central venous catheter or PICC line.
- “Oestrogenic states” – use of the oral contraceptive pill, pregnancy, miscarriage or termination in the last 3 months.
- Thrombophilia
 - Inherited - protein C deficiency, protein S deficiency, antithrombin deficiency, factor V Leiden gene mutation, prothrombin gene mutation, raised plasma factor VIII, raised plasma homocysteine.
 - Acquired - antiphospholipid syndrome.

3.2 Thromboprophylaxis for Standard risk patients

Good hydration and mobilisation as early as possible should be employed in all patients, both standard risk and high risk.

Given the very low risk of VTE in paediatric patients, pharmacological thromboprophylaxis is **not** generally recommended for standard risk patients at The Children's Hospital at Westmead (CHW).

3.3 Thromboprophylaxis for High risk patients

Pharmacologic prophylaxis should be considered for high risk patients, in addition to maintenance of good hydration and early mobilisation. At CHW, the recommended pharmacologic thromboprophylaxis is:

- Age 2 months or more: subcutaneous enoxaparin 0.5 mg/kg/dose twice daily
- Age less than 2 months: subcutaneous enoxaparin 0.75 mg/kg/dose twice daily
- Consult the Haematologist on-call for dosage adjustment if there is co-existing renal impairment

Commencing 6-12 hours post-operatively once bleeding risk was considered low or at the surgeon's discretion and continuing until discharge. However, variation in the timing and duration may be appropriate in individual cases.

SAFETY OF NEURAXIAL ANAESTHESIA IN PATIENTS RECEIVING HEPARINS

Do **NOT** administer enoxaparin or any LMWH for at least 12 hours prior to insertion or removal of an epidural or spinal catheter.

Do **NOT** administer enoxaparin or any LMWH for at least 2 hours after insertion or removal of an epidural or spinal catheter.

3.4 Role of Mechanical Thromboprophylaxis

Mechanical thromboprophylaxis is not routinely recommended at CHW as it has not been demonstrated to be effective in children. There may, however, be indications for use in individual cases.

Given the lack of data demonstrating efficacy even in adults, TED stockings and graduated compression stockings are not generally recommended for patients at CHW. It may be appropriate to use them in certain individual cases at the discretion of the treating surgeon.

Intermittent pneumatic compression devices (IPC's) are not recommended for most patients at CHW. However, their use may be appropriate in certain individual cases, particularly in older children who may have contraindications to anticoagulation. They may also be employed in addition to pharmacologic thromboprophylaxis in certain cases. Again, this use is at the discretion of the treating surgeon.

4 Epidemiology of Venous Thromboembolism

The estimated incidence of VTE in hospital patients was 961 per 100 000 person-years for adults, compared with only 5.3 per 100 000 person-years for children. These rates are 50-100 times higher than those of VTE occurring in the general community (7 and 0.07-0.14 per 100 000 person-years for adults and children, respectively)¹.

Documented risk factors for VTE in children include the following²:

- Central venous access devices (CVAD)
- Age (neonates or post-pubertal)
- Surgery
- Trauma
- Acute infection or inflammatory states, including local infection
- Cancer and/or chemotherapy
- Thrombophilia (see below)
- Abortion/other oestrogenic states

However, as many as 90% of children with VTE have more than one risk factor³.

Although trauma is a known risk factor for VTE, the majority of children with trauma do not experience VTE. The incidence of VTE in paediatric trauma patients was described according to age in a level 1 US trauma centre⁴:

- Less than 13 years old – zero
- 13 to 17 years old – 0.2%
- Over 17 years old – 0.5%

Risk factors for VTE in the paediatric trauma population include⁵:

- Severity of injury
- Major vascular surgery
- CVAD
- Craniotomy
- Age greater than 10 years

In the above review, an injury severity score (ISS) of 25 or greater was associated with a 21 fold increased risk of VTE on multivariate analysis. The relative risks of VTE were 16 for major vascular surgery, and 5 for CVAD, craniotomy or age over 10 years. In addition, it was noted that the types of injury particularly associated with VTE were severe spinal injury, severe head injury, severe thoracic injury, and lower limb fracture requiring open reduction/internal fixation.

“Thrombophilia” refers to the state of having certain inherited or acquired prothrombotic factors or conditions. These include, but are not limited to, the following:

- Protein C deficiency
- Protein S deficiency
- Antithrombin deficiency
- Antiphospholipid syndrome (this is NOT the same as simply having positive tests for either anticardiolipin antibodies or the lupus anticoagulant; certain clinical criteria must coexist)
- Factor V Leiden gene mutation
- Prothrombin gene mutation
- Raised plasma factor VIII levels
- Raised plasma homocysteine levels

Whilst it is becoming apparent that these factors increase the risk of VTE in both children and adults, particularly when multiple factors coexist, it is far from clear as to how significant this risk is in any one given individual. Few universally recognised recommendations exist as to when and under what circumstances these individuals should receive pharmacologic thromboprophylaxis. Therefore, thrombophilia should be considered in the overall context of a given patient's clinical features and other risk factors, but should **never be regarded** as an automatic indication for pharmacologic thromboprophylaxis or anticoagulation.

Finally, it is important to remember that perhaps the most important single risk factor for VTE is a personal past history of VTE (particularly, if unprovoked). Recurrent VTE is as high as 30% in adults⁶ and between 6-23% in children⁷.

5 Methods Used For Thromboprophylaxis

5.1 Hydration and early mobilisation

A change in blood composition is one of the elements of Virchow's triad which may predispose to thrombosis. Dehydration may increase blood viscosity. Therefore, it is rational to maintain good hydration status in all patients.

Immobility is a described risk factor for VTE, and mobilisation of post-surgical or trauma patients as early as possible is generally recommended as a way of modifying this risk factor.

5.2 Thromboembolic deterrent stockings (TEDS) or graduated compression stockings

These are often recommended as an adjunctive measure for thromboprophylaxis in adults. However, there is no good evidence that they are effective in adults⁸. No good data exist for children. In addition, whilst these stockings are generally safe, complications such as pressure ulcers and peripheral neuropathy have been reported in adults with poorly fitting stockings^{9,10}.

5.3 Intermittent pneumatic compression devices

These have been shown to reduce the risk of post-operative VTE in high risk adult patients, although it was less effective than prophylaxis with heparin¹¹. The advantage of these devices is that they have almost no side effects, making them attractive in patients with contraindications to heparins and/or at high risk of bleeding. IPC's may also be used in conjunction with heparin prophylaxis but data of its use in children are sparse.

IPC's may be commenced pre-operatively, intra-operatively, or post-operatively. There is at present no firm evidence that timing of commencement influences risk of VTE. It is more important to continue the IPC's until the patient is fully ambulatory¹². If IPC's are started post-operatively, they should be instituted soon after surgery, as there is a hypothetical risk of them dislodging preformed thrombus in a patient who has had a prolonged period without thromboprophylaxis.

5.4 Pharmacologic – heparins and warfarin

Heparins – both unfractionated heparin (UFH) and low molecular weight heparins (LMWH) such as enoxaparin ("Clexane") – are well documented to decrease the risk of post-operative VTE in adults¹³⁻¹⁶. UFH and LMWH both indirectly inhibit thrombin formation via potentiation of the action of antithrombin, increasing its activity several thousand fold. UFH is typically administered subcutaneously 2-3 times a day, whilst LMWH is generally given once daily in adults. With prophylactic usage of UFH or LMWH, monitoring can be performed but does not need to be done routinely.

Side effects are minimal, but do include pain at the injection site, local reactions, risk of bleeding, and, extremely rarely in children, heparin-induced thrombotic thrombocytopenia syndrome (HITTS)¹⁷. Lastly, these agents have a financial cost, particularly LMWH.

Fondaparinux is a synthetic analogue of the antithrombin-binding pentasaccharide region of heparin. It is used for thromboprophylaxis of adults undergoing major orthopaedic surgery, and may have greater efficacy than enoxaparin in this regard¹⁸. Mature data in children are not available.

Warfarin is an orally administered anticoagulant whose mechanism of action is the inhibition of vitamin K dependent clotting factors. It is effective in the prevention of VTE in adults but it is generally not used in post-surgical or trauma thromboprophylaxis.

5.4.1 Timing and Duration of Pharmacologic Thromboprophylaxis

There is no good data to guide the timing of first dose or duration of thromboprophylaxis in children. The following is a summary of what is known in adults.

The timing of the first dose of peri-operative thromboprophylaxis has undergone a number of changes over the last fifty years. Unfractionated heparin given 2 hours pre-operatively was shown to be safe and effective in the 1970's; however, this schedule resulted in increased post-operative bleeding when used with LMWH. This resulted in a shift in practice by adult orthopaedic surgeons to administer prophylactic LMWH 12 hours either pre or post-operatively.²²

More recent studies in adults undergoing orthopaedic surgery have shown that LMWH administered 12 hours or more either before or after surgery was less effective than if it was administered 4 – 6 hours post-operatively. Furthermore, an increased bleeding risk was only observed if LMWH was administered within 2 hours of surgery, and that pre-operative administration provided no benefit compared to administration 4 – 6 hours post-operatively^{23,24}.

The duration of thromboprophylaxis in adult surgical patients has traditionally been until discharge. However, clinical studies in high risk adult surgical patients, particularly those undergoing hip surgery, have shown that extended post-discharge thromboprophylaxis of up to 4 – 6 weeks significantly reduces the incidence of VTE (including both venographically detected and symptomatic deep venous thrombosis)^{25, 26}.

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