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| **Module** | Management of VKAs (HCP) |
| **Topic** | Indications for oral anticoagulation  |
| **Audience** | Healthcare professional |
| **Type** | Topic content |
| **Version** | 4 |

**1. Introduction**

The aim of this topic is to give you an understanding of the indications for anticoagulation (excluding atrial fibrillation). If you would like to learn about the use of vitamin K antagonists for the prevention of stroke and systemic emboli in those with atrial fibrillation, please go to *(-> link to Topic 1: The use of oral antcoagulants for stroke prevention)*

By the end of this topic you should be able to:

1. Describe the clinical features of an acute deep vein thrombosis
2. Describe the clinical features of an acute pulmonary embolism
3. List the main complications of a venous thromboembolism
4. List the disorders of hypercoagulability
5. Summarise the use of anticoagulation to reduce the risk of thrombosis in those with a replacement heart valve

 **2. Check your understanding**

Before you start reading this topic check how much you already know by taking a short quiz. You will have an opportunity to take the quiz again at the end of the module, where we will reveal the correct answers.

**a) The most common site of origin of a deep vein thrombosis is the deep vein is of the calf (distal DVT)**

**True** / False

**b) Which of the following are signs or symptoms of a DVT (select all that apply**

i) **Hot, painful leg**

**ii) Leg oedema**

**iii) Skin discolouration**

iv) Numbness

**c) When treating a DVT, heparin can be stopped once the INR in in therapeutic range**

True / **False**

**d) All those who have a DVT should have a thrombophilia screen**

True / **False**

**e) Which of the following are signs or symptoms of a PE (select all that apply**

i) **Shortness of breath**

ii) Rash

iii) **Tachycardia**

**iv) Apprehension**

**f) Antiphospholipid syndrome (Hughes Syndrome) is an inherited thrombophilia**

True / **False**

**g) All patients with bioprosthetic heart valve replacements require lifelong anticoagulation**

True / **False**

**h) There is a higher risk of systemic embolisation with a valve in the mitral position compared with an aortic valve replacement**

**True** / False

**VENOUS THROMBOEMBOLISM**

**3. Venous thromboembolism (VTE)**

A **deep vein thrombosis (DVT**) is a clot that develops in one of the deep veins of the body. The most serious consequence of a DVT is a **pulmonary embolism (PE**), which results from a piece of the blood clot breaking off into the bloodstream and blocking one of the blood vessels in the lungs.

Deep vein thrombosis and pulmonary embolism are known collectively as venous thromboembolism (VTE).

**4. Deep vein thrombosis (DVT)**

The most common site of a DVT is the deep vein of the calf (**distal DVT**). An isolated distal DVT only rarely causes serious late or early morbidity, and the risk of PE is low. However, studies suggest that 15 – 25 % of untreated symptomatic distal DVTs will extend into the proximal vein **(proximal DVT).** There is a 50% chance that a proximal DVT will be associated with a pulmonary embolus.

Now take a look at this 2-minute animation that describes how a DVT is formed. (https://www.youtube.com/v/Ru6BAfcN2sA)

**4.1 What are the risk factors for developing a DVT**

The common risk factors for developing a DVT are listed below:

* Age. Being over age 60 increases the risk of DVT, although it can occur at any age
* A previous history of deep vein thrombosis or pulmonary embolism.
* A family history of deep vein thrombosis or pulmonary embolism.
* An inherited blood-clotting disorder
* Medical conditions such as cancer and heart failure and inflammatory bowel disease
* Inactivity. For example, Sitting for long periods of time, such as when driving or flying, prolonged bed rest (e.g. after an operation)
* Pregnancy
* Birth control pills or hormone replacement therapy
* Being overweight or obese
* Smoking

**4.2 What are the clinical signs of a DVT?**

*(image - Deep\_vein\_thrombosis\_of\_the\_right\_leg.jpg. DVT of the right leg. By James Heilman, MD (Own work)*

*[CC-BY-SA-3.0 (http://creativecommons.org/licenses/by-sa/3.0))*

Diagnosing a DVT can difficult, and many DVTs progress to PE without any clinical signs. In those with classic clinical signs, only about 50% are subsequently proven to have a DVT. These clinical signs generally result from from obstruction to venous drainage.

* Limb pain and tenderness
* Swelling of the calf or thigh (usually unilateral)
* Distension of superficial veins
* Increase in skin temperature
* Leg oedema
* Skin discolouration (erythema or occasionally purple or cyanosed).

**Common clinical signs of DVT**

**4.3 How is a DVT treated?**

The aims of **initial treatment** are prevention of thrombosis extension and acute recurrence. As warfarin has a delayed onset of action, **heparin** is used for at least 5 days until warfarin can take its effect. In rare instances the initiation of warfarin, particularly with large loading doses, can paradoxically cause clot extension through rapid depletion of Protein C and Protein S. To prevent this from happening, heparin should be continued for at least two days after the INR is therapeutic.

In many places, the treatment of DVT is conducted through an **integrated care pathway (ICP)**, with many patients treated on an ambulatory care basis. The low molecular weight heparin and warfarin are started on day one. The first INR is taken on day three and the dose adjusted according to protocol

Warfarin prevents extension and embolisation of the clot. It does not have a significant effect on existing clots.

In contrast to warfarin, **a NOAC can be used for acute treatment of DVT**. If heparin is used for acute treatment and then followed up by rivaroxaban, this should be started 0 to 2 hours before the time of the next scheduled administration of the low molecular weight heparin, or at the time of discontinuation of a continuous infusion of unfractionated heparin.

**WHAT HAPPENS NEAR ME?**

Now please find out how DVTs are treated near you? (If you work in primary care, try to find out what happens at your nearest hospital) Is there a clinical guideline? Is there an integrated care pathway? Which heparin is used?

**4.4 What are the complications of a DVT?**

Post-thrombotic syndrome (PTS) is the development of lower-limb symptoms secondary to DVT and occurs in about a third of patients .

* Heaviness and swelling of the leg
* Inflammation around ankle
* Oedema
* Itching
* Varicose veins
* Ulceration

 **Signs of post-thrombotic syndrome**

**How can post-thrombotic syndrome be prevented?**

To prevent PTS, graduated **compression stockings** should be worn for as long as the patient tolerates them, but ideally for at least 2 years after the event. They may remove the stocking when they go to bed. Below-knee stockings are usually sufficient except when the venous damage is very extensive, when thigh length ones may be necessary. They are available in three strengths: Class 1, 2 and 3. Class 2 are usually sufficient to control the swelling.

Regular **exercise** is also often helpful, as is **weight loss** if overweight, **leg elevation** and **stopping smoking.**

**4.5 Travellers’ DVT**

There is some evidence that long-haul flights, especially when passengers have little or no exercise, may increase the risk of developing DVT. There are similar risks associated with long journeys by car, coach or train. It is difficult to determine the proportion of people who develop DVT related to air travel.

Simple in-flight exercises and getting up and walking around regularly are advised. And avoid dehydration - take regular non-alcoholic drinks. There is some evidence that flight socks of elastic stockings (Class 1) may be useful.

**5. Pulmonary embolism (PE)**

Pulmonary embolism (PE) can occur without warning or as a complication of a confirmed DVT. A large embolus lodged in a major pulmonary artery may result in a major pulmonary embolus which can present as a sudden collapse or in unconsciousness, and the patient may die of acute circulatory failure unless rapidly treated.

Now take a look at this 2-minute animation that describes a DVT can lead to a PE (https://www.youtube.com/watch?v=V9wt1yFt0FQ)

**5.1 What are the clinical signs and symptoms of a PE?**

Clinical diagnosis of PE is often difficult because of the non-specificity of symptoms. The most frequently observed features of a PE are summarised below.

* Dyspnoea
* Tachypnoea (> 20/minute)
* Pleuritic chest pain
* Tachycardia (> 100 beats/minute)
* Pain
* Apprehension
* Cough
* Haemoptysis
* Pleural ‘rub’ (a sound like Velcro being torn apart when the patient breathes in)

 **Common signs and symptoms of a non-major PE**

**5.2 How is a PE treated?**

The principles of treatment for PE are similar to those for DVT. Additional **haemodynamic and respiratory support** may be necessary, particularly for a major pulmonary embolus.

**6. Disorders of hypercoagulability (thrombophilias)**

Hypercoagulability is a contributory factor in many instances of thrombotic disease. This can be **acquired** or **inherited.**

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| Inherited*Accounts for 10% of VTE in those < 45 yrs old* | Acquired*Secondary to wide range of disorders (e.g. cardiac disease, inflammatory bowel disease, malignancy, pregnancy*) |
| Antithrombin deficiency | Antiphospholipid syndrome (Hughes Syndrome) |
| Protein C deficiency |  |
| Protein S deficiency |  |
| Activated Protein C resistance (Factor V Leiden) |  |

**Disorders of hypercoagubility**

**6.1 Common hypercoagulability disorders**

**Antithrombin deficiency**

* Patients have a predisposition to developing VTEs at a young age.
* Patients with antithrombin deficiency are relatively resistant to heparin as antithrombin is necessary for its mode of action.

**Protein C and S deficiency**

* An inherited blood disorder that predisposes to VTEs, often in patients less than 40 years of age.

**Factor V Leiden**

* Factor V is a cofactor for the formation of thrombin in the clotting cycle, and the failure to inactivate factor V with activated protein C leads to a greater tendency to form blood clots.
* Factor V Leiden is found in 3-5% of healthy individuals in Western countries.
* In patients who have presented with a VTE of unknown origin, 20% are found to suffer with factor V Leiden.

**Antiphospholipid syndrome (Hughes Syndrome)**

* Antiphospholipid syndrome is associated with autoantibodies which have specificity for negatively charged phospholipids. A small percentage of patients with antiphospholipid syndrome have systemic lupus erythematous. The hallmark of this syndrome is recurrent venous thromboembolism and miscarriages.

**6.2 When should thromobophilia screening be done?**

Thrombophilia screening will detect most causes of a prothrombotic state, but should not be used indiscriminately. It is expensive and time-consuming. Positive results often cause unjustified concern to the individual, and a negative result may provide false reassurance. There should be a plan of how the results will affect management.

Its main indications are:

* VTE at age < 40 yrs
* Recurrent VTE
* VTE in an unusual anatomical site
* Positive family history of VTE
* Recurrent miscarriage
* Skin necrosis

Thrombophilia screening cannot be carried out during the acute episode, and the person has to be off warfarin for at least 4 weeks before if can be done.

**WHAT HAPPENS NEAR ME?**

Now please find out what the criteria for thrombophilia screening are near you? How would you refer a patient for thrombophilia screening?

**HEART DISEASE**

### 7. Replacement heart valves

There are four valves in the heart, and their job is to ensure that blood flows through the heart in the correct direction. If a valve does not open fully – valve **stenosis** - it will obstruct the flow of blood. If a valve does not close properly – valve i**ncompetenc**e or **regurgitation** - it will allow blood to leak backwards.

Valve replacement is when a diseased valve is replaced with a new valve. Replacement heart valves can either be in the **mitral position (MVR**), or in the **aortic position (AVR).** Replacement valves can be either **mechanica**l or **bioprosthetic** (tissue valves)

*(image - Diagram\_of\_the\_human\_heart\_(valves\_improved).svg)*

Structural abnormalities of the heart and foreign surfaces, such as prosthetic valves, predispose to thrombus formation, which becomes clinically manifests through systemic embolisation.

**Which factors affect the risk of systemic embolism with heart valve replacements?**

The risk of systemic embolism from mechanical heart valves depends on the **position** of the valve, the **type of valve**, and other factors that contribute to the patients’ risk of developing thrombosis, such as **cardiac rhythm** and **dilatation**. These factors will dictate the target INR.

There is a greater risk of thromboembolism with mitral valve replacements than with ones in the aortic position.

Mechanical valves have a higher thrombogenic potential than bioprosthetic (tissue) valves, and all patients with mechanical heart valves need long-term anticoagulation.

The risk of systemic embolisation is less with bioprosthetic valves. In the absence of other risk factors, long-term warfarin is not required. As the reported risk of thromboembolism is highest in the months just after valve replacement, patients with a  bioprosthetic MVR should be anticoagulated for 3 months after the replacement. Although, warfarin may not be needed for valves in the aortic position in patients in sinus rhythm, many centres anticoagulate patients for 3-6 months after *any* tissue valve implant.

**DEMONSTRATE YOUR KNOWLDEGE**

Now try answering the questions at the start of this topic again. Did you get a higher score?