About Venous Thromboembolism (VTE)

Fast facts

- **Blood clots form to prevent bleeding in response to damage to a blood vessel; they act as a plug at the site of the blood vessel injury[1]**
- **However, if the blood clotting cascade is inappropriately activated, this can lead to the formation of potentially deadly blood clots[1]**
- **Venous blood clots are also known as venous thromboembolism (VTE)**
- **Venous blood clots kill more people in Europe each year than breast cancer, prostate cancer, HIV/AIDS and road traffic accidents combined[2]**
- **Current VTE treatments, although effective if managed properly, have significant drawbacks[3]**
- **Oral medicines that directly inhibit Factor Xa represent a potential new era of therapies to prevent and treat blood clots[3]**

What is venous thromboembolism (VTE)?

VTE or venous blood clots can present in two ways:

1. Deep vein thrombosis (DVT) - a blood clot in a deep vein, usually in the legs, that partially or totally blocks the flow of blood[4]

- DVT symptoms include pain, swelling and redness of the area and dilation of the surface veins. The skin may also feel warm to the touch
- The majority of patients suffering from a venous blood clot will experience a DVT alone, however in around one-third of patients it will progress to a potentially fatal pulmonary embolism (PE)[5]
- Even in the absence of a PE, DVT alone can have burdensome and costly consequences such as post-thrombotic syndrome[6] and an increased risk of reoccurrence[4]

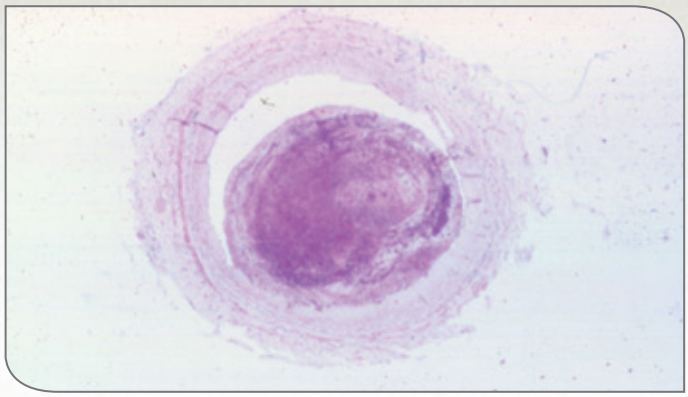

Fig. 1 Deep vein thrombosis micrograph image of vein with thrombus in lumen. Source: www.thrombosisadviser.com

2. Pulmonary embolism (PE) - a venous blood clot which breaks apart and travels to the lungs, ultimately blocking a blood vessel there[4]

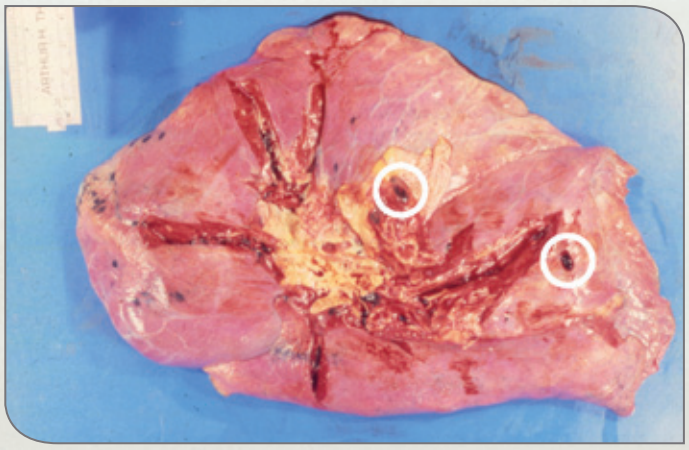

Fig. 2 Pulmonary Embolus. Whole lung in which pulmonary arteries are obstructed by fresh thrombus
Source: www.thrombosisadviser.com

Once in the lung, the blood clot may block the circulation, threatening sudden death or long-term damage to the lungs and other vital organs

- PE symptoms include acute shortness of breath, chest pain, and rapid heart rate; some people also cough blood
- 10–25% of PEs are rapidly fatal – usually within two hours from the onset of symptoms[5]
- PE can reoccur, and if it does, it is usually fatal[5, 6]

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- PE is the most common preventable cause of in-hospital death,[7] with 10% of all deaths in hospitals attributed to PE[8]

VTE is difficult to diagnose, as up to half of patients have no specific symptoms. Consequently, avoiding venous blood clots by preventative measures is the most economical and effective approach in current clinical practice.

How common is VTE?

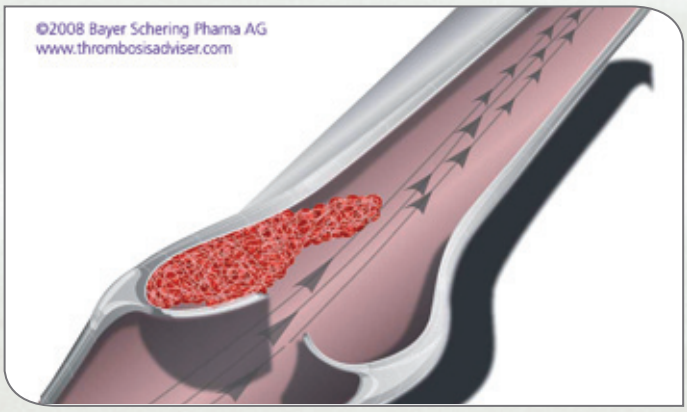

Fig. 3 Venous thrombus formation
Source: www.thrombosisadviser.com

- VTE is estimated to be the third most common cardiovascular disease after heart disease and stroke[9]
- Each year about 1 in 1,000 people will experience a VTE for the first time[4]
- Every year, VTE kill nearly 1 million people: around 300,000 people in the US and 544,000 in Europe[2,10]

Who is at risk from VTE?

People most likely to experience a VTE include those who have undergone surgery, those admitted to hospital for an acute medical condition, the elderly, pregnant women, and those using certain medications or therapies.[11] Prolonged immobility and cancer also increase the risk of developing blood clots

- VTE occurs in 40–60% of patients undergoing orthopedic surgery who do not receive preventative care due to factors such as vascular damage and reduced mobility[12]
- Up to 30% of general medical patients may develop DVT or PE[13]
- The threat of a blood clot does not go away just because a patient leaves the hospital. Out of a total of 1,897 patients who experienced a venous blood clot:[14]
  - 74% developed a VTE in the outpatient setting
  - A substantial proportion of these outpatients had undergone surgery (23%) or hospitalization (37%) in the preceding three months[14]

Costs associated with VTE

The complications associated with VTE and its treatment are frequent and costly. The main drivers of these VTE costs are initial and recurrent events requiring hospitalization.

- In the US, total cumulative inpatient costs related to venous blood clots over 3, 6 and 12 months amount to $4,696,[15,16] $10,072[17] and $33,000,[17,18,19] respectively
- Studies in Europe showed comparatively lower but still significant additional inpatient costs following VTE of €1,804 after 3 months[20] and €3,220 after 12 months[21]

In light of the high overall costs of treatment, using more effective VTE prevention strategies after major orthopedic surgery could reduce the economic burden of VTE.

How is VTE prevented and treated?

Anticoagulants

Anticoagulants help prevent the formation and halt the progression of a blood clot. This allows the body's natural clot-dissolving activity to take effect. The key to treatment with anticoagulants is to manage the acute crisis and prevent recurrent VTE as this risk is heightened after an initial episode.[6]

- VTE recurrence rates in the first year post-initial event are 3–10%[2]

The current standard treatment for VTE is injectable heparin followed by an oral vitamin K antagonists (VKA).[22] These agents, although effective if managed properly, have significant drawbacks including:

- Complexities of drug administration[23]
- Routine monitoring[23]
- Food and drug interactions[23]

Direct Factor Xa therapies: a new potential era of oral anticoagulants

Factor Xa has emerged as an attractive target for new anticoagulants due to its pivotal role in the blood-clotting cascade, where it stimulates the production of thrombin, the enzyme that promotes clot formation.[3,4] One molecule of Factor Xa leads to the formation of about 1,000 thrombin molecules.[3]

By targeting Factor Xa at a pivotal stage in the blood clotting process, direct Factor Xa inhibitors prevent the so-called 'thrombin burst' that dramatically increases clot formation, while allowing for other coagulation processes to continue, such as wound healing following surgery.[3]

- Oral medicines that directly inhibit Factor Xa represent a potential new era of therapies to prevent and treat blood clots[3]
- Xarelto® (rivaroxaban), a Factor Xa inhibitor, has been shown to be:
  - Well tolerated and effective in robust Phase III clinical trials in the prevention of VTE in patients undergoing major orthopedic surgery[17]

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