Bayer AG
Investor Relations
51368 Leverkusen
Germany
www.investor.bayer.com

Backgrounder

Thromboembolic disorders: A major cause of morbidity and mortality

Ten percent of all deaths in hospital are caused by pulmonary embolism following deep vein thrombosis – almost all of these cases are preventable.[1]

Thromboembolic disorders are a major cause of morbidity and mortality worldwide. Despite a significant increase in the awareness of the clinical manifestations of these disorders, there is a desperate need for improved diagnostic techniques, advances in prevention and treatment strategies, and improved methods to reduce their impact.

Thromboembolic disorders include the following clinical manifestations:

- Venous thromboembolism (VTE), comprising deep vein thrombosis (DVT) and pulmonary embolism (PE)
- Cardiogenic stroke

DVT: up to 2 million cases per year in the US

A DVT is a blood clot, or thrombus, that forms in a deep vein (usually in the leg) [Figure 1] if the vein is damaged or if the flow of blood slows down or stops.

- Population studies suggest that the annual incidence of venous thromboembolic disease is as high as 2 per 1000 people,[2,3] giving an estimated VTE incidence in the US of 250,000 to 2 million cases per year[4]
- More than one-third of these cases represent recurrent disease[2]

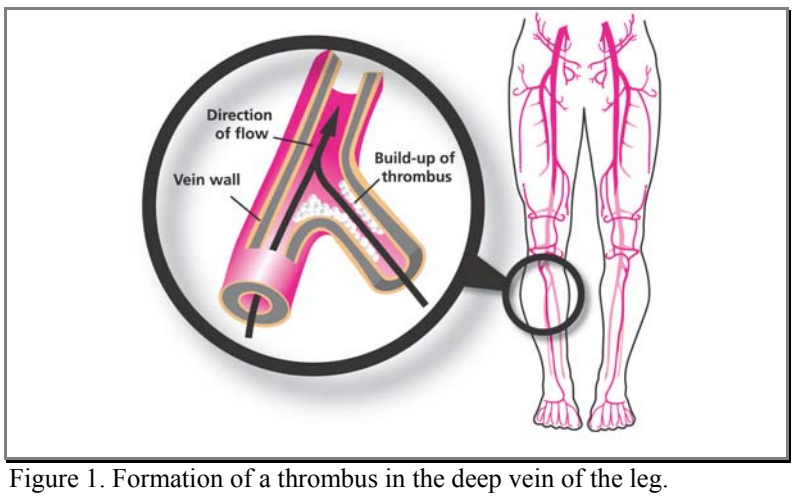

Figure 1. Formation of a thrombus in the deep vein of the leg.

PE: one of the most preventable causes of death in hospitalized patients
A PE is a life-threatening event that occurs when a section of a thrombus (an embolus) becomes detached from the vein in which it formed and travels to the lungs and blocks the pulmonary arteries

- PE is one of the most common, preventable causes of death among hospital inpatients;[3] it affects 0.5–1 per 1000 people in the general population each year
- 10% of patients with symptomatic PE die within 1 hour of the onset of symptoms. Among patients who are diagnosed with PE, the mortality rate is approximately 10% at 2 weeks and 25% at 1 year[5]
- Nearly 50% of patients with DVT have an asymptomatic PE at the time of their diagnosis.[6]

Stroke – someone dies of stroke every 3 minutes in the US
Stroke is the third leading cause of death and a leading cause of adult disability in the US

- Only heart disease and cancer cause more deaths annually
- Every year, about 700,000 Americans suffer a stroke; approximately 163,000 of these people die as a result of the stroke[7]

An ischemic stroke occurs when the blood supply to a part of the brain is interrupted or severely reduced, resulting in the brain tissue being deprived of oxygen and nutrients. Within a few minutes, brain cells begin to die and medical emergency ensues.

Stroke is associated with long-term morbidity – estimates indicate that in the US, approximately $57 billion will be spent on stroke-related medical costs and disability in 2005. Moreover, stroke is the biggest cause of long-term disability, with wide-ranging implications for patients and physicians.

- Stroke significantly reduces a patient's quality of life
- A stroke may impair mental status, perception, sensation, communication and motor ability
- Extra physician time and healthcare resources are needed to rehabilitate stroke patients and to monitor the many concomitant medications that will be prescribed

A cardiogenic stroke is a stroke that results from blood clots in the heart traveling to the brain.

- Cardiogenic stroke accounts for approximately 15–20% of all ischemic strokes, and is significantly more common in the elderly, in whom it is estimated to represent approximately 40% of all strokes[8–10]
- Certain conditions – atrial fibrillation (AF) in particular – place patients at high risk of cardiogenic stroke

Who is at risk?
Orthopaedic surgery is a major risk factor for VTE. Total hip and knee replacements are common – over 350,000 were carried out in the US alone during 2000,[11] and UK estimates indicate that over 80,000 are carried out annually.[12] Over the next 30 years,

the number of these procedures is predicted to increase dramatically as both the age and weight of populations increase.[13] The risk of VTE after major orthopaedic surgery is also compounded by increased age.

Atrial fibrillation is a major risk factor for cardiogenic stroke, and is responsible for 15–20% of all strokes.[14] Atrial fibrillation is predominantly a disease of old age [Figure 2]; the results of long-term population studies indicate that the lifetime risk of developing this condition increases from <1% in people aged under 60 years to 10% in those aged over 80 years.[15]

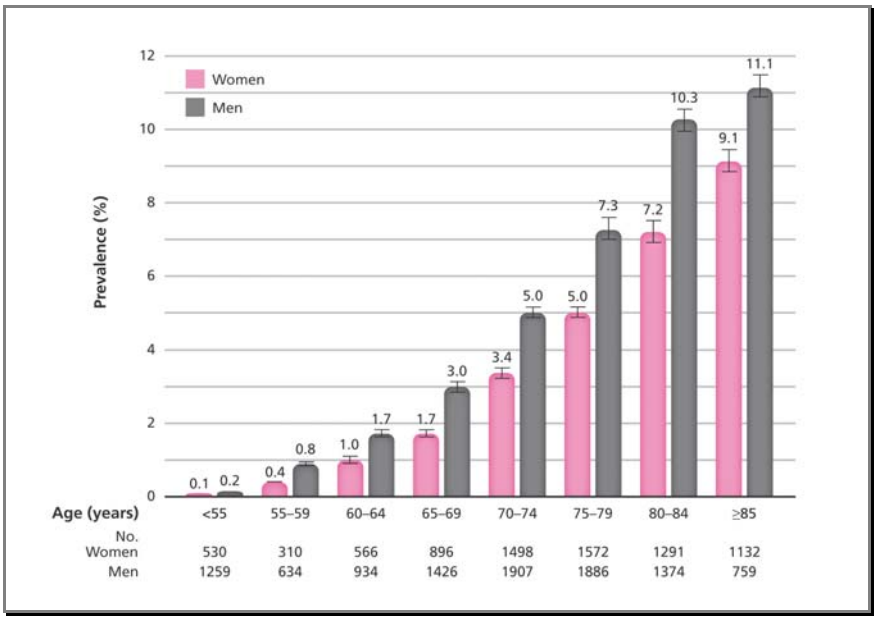

Figure 2. Prevalence of diagnosed atrial fibrillation, stratified by age and sex.[15]
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Medical history and concomitant illnesses: patients with mechanical replacement heart valves and acute coronary syndromes (especially after a heart attack) are at increased risk of stroke; prior stroke/transient ischemic attack and prior VTE also heighten the risk of further VTE and carry a high risk of death. Several medical conditions, including circulation or heart problems, and cancer and its treatments also place patients at increased risk of VTE or stroke.

Other risk factors for VTE

Strong risk factors	**Moderate risk factors**	**Weak risk factors**
Fracture (hip or leg)	Arthroscopic (keyhole) knee surgery	Bed rest >3 days
Hip or knee replacement	Central venous lines	Prolonged car or air travel
Major general surgery	Chemotherapy	Increasing age
Spinal cord injury	Congestive heart or respiratory failure	Laparoscopic surgery (e.g. cholecystectomy)
	Hormone replacement therapy	Obesity
	Oral contraceptive therapy	Varicose veins

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Bayer AG, Investor Relations contacts:

Dr. Alexander Rosar (+49-214-30-81013)
Dr. Juergen Beunink (+49-214-30-65742)
Peter Dahlhoff (+49-214-30-33022)
Ute Krippendorf (+49-214-30-33021)
Ilia Kürten (+49-214-30-35426)
Judith Nestmann (+49-214-30-66836)