= Deep vein thrombosis =

Deep vein thrombosis , or deep venous thrombosis , (DVT) is the formation of a blood clot (thrombus) within a deep vein , predominantly in the legs . Non @-@ specific signs may include pain , swelling , redness , warmness , and engorged superficial veins . Pulmonary embolism , a potentially life @-@ threatening complication , is caused by the detachment (embolization) of a clot that travels to the lungs . Together , DVT and pulmonary embolism constitute a single disease process known as venous thromboembolism . Post @-@ thrombotic syndrome , another complication , significantly contributes to the health @-@ care cost of DVT . Prevention options for at @-@ risk individuals include early and frequent walking , calf exercises , anticoagulants , aspirin , graduated compression stockings , and intermittent pneumatic compression .

In 1856 , German pathologist Rudolf Virchow postulated the interplay of three processes resulting in venous thrombosis , now known as Virchow 's triad : a decreased blood flow rate (venous stasis) , increased tendency to clot (hypercoagulability) , and changes to the blood vessel wall . DVT formation typically begins inside the valves of the calf veins , where the blood is relatively oxygen deprived , which activates certain biochemical pathways . Several medical conditions increase the risk for DVT , including cancer , trauma , and antiphospholipid syndrome . Other risk factors include older age , surgery , immobilization (as with bed rest , orthopedic casts , and sitting on long flights) , combined oral contraceptives , pregnancy , the postnatal period , and genetic factors . Those genetic factors include deficiencies with antithrombin , protein C , and protein S , the mutation of Factor V Leiden , and the property of having a non @-@ O blood type . The rate of new DVTs increases dramatically from childhood to old age ; in adulthood , about 1 in 1000 adults develops it annually .

Individuals suspected of having DVT may be assessed using a clinical prediction rule such as the Wells score . A D @-@ dimer test may also be used to assist with excluding the diagnosis (because of its high sensitivity) or to signal a need for further testing . Diagnosis is most commonly done with ultrasound of the suspected veins . Anticoagulation is the standard treatment ; typical medications include a low @-@ molecular @-@ weight heparin and a vitamin K antagonist . Wearing graduated compression stockings appears to reduce the risk of post @-@ thrombotic syndrome .

= = Signs and symptoms = =

Common signs and symptoms of DVT include pain or tenderness , swelling , warmth , redness or discoloration , and distention of surface veins , although about half of those with the condition have no symptoms . Signs and symptoms alone are not sufficiently sensitive or specific to make a diagnosis , but when considered in conjunction with known risk factors can help determine the likelihood of DVT . In most suspected cases , DVT is ruled out after evaluation , and symptoms are more often due to other causes , such as cellulitis , Baker 's cyst , musculoskeletal injury , or lymphedema . Other differential diagnoses include hematoma , tumors , venous or arterial aneurysms , and connective tissue disorders .

Phlegmasia cerulea dolens is a very large and dangerous type of DVT . It is characterized by an acute and almost total venous occlusion of the entire extremity outflow , including the iliac and femoral veins . The leg is usually painful , blue tinged in color , and swollen , which may result in venous gangrene .

= = Causes = =

The three factors of Virchow 's triad ? venous stasis , hypercoagulability , and changes in the endothelial blood vessel lining (such as physical damage or endothelial activation) ? contribute to DVT and are used to explain its formation . Other related causes include activation of immune system components , the state of microparticles in the blood , the concentration of oxygen , and possible platelet activation . Various risk factors contribute to DVT , though many at high risk never

develop it .

Acquired risk factors include the strong risk factor of older age , which alters blood composition to favor clotting . Other important acquired risk factors include major surgery and trauma , both of which may increase the risk because of tissue factor from outside the vascular system entering the blood . In orthopedic surgery , venous stasis may be temporarily provoked by a cessation of blood flow as part of the procedure . Cancer can grow in and around veins , causing venous stasis , and can also stimulate increased levels of tissue factor . Pregnancy causes blood to favor clotting , and in the postpartum , placental tearing releases substances that favor clotting . Oral contraceptives and hormonal replacement therapy increase the risk through a variety of mechanisms , including altered blood coagulation protein levels and reduced fibrinolysis .

The disease term venous thromboembolism (VTE) includes the development of either DVT or pulmonary embolism (PE) . Genetic factors that increase the risk of VTE include deficiencies of three proteins that normally prevent blood from clotting ? protein C , protein S , and antithrombin ? in addition to non @-@ O blood type and mutations in the factor V and prothrombin genes . Deficiencies in antithrombin , protein C , and protein S are rare but strong , or moderately strong , risk factors . These three thrombophilia increase the risk of VTE by about 10 times . Factor V Leiden , which makes factor V resistant to inactivation by activated protein C , and the genetic variant prothrombin G20210A , which causes increased prothrombin levels , are predominantly expressed in Caucasians . They moderately increase risk for VTE , by three to eight times for factor V Leiden and two to three times for prothrombin G20210A . Having a non @-@ O blood type approximately doubles VTE risk . Non @-@ O blood type is common in all races , making it an important risk factor . Individuals without O blood type have higher blood levels of von Willebrand factor and factor VIII than those with O blood type , increasing the likelihood of clotting .

Some risk factors influence the location of DVT within the body . In isolated distal DVT , the profile of risk factors appears distinct from proximal DVT . Transient factors , such as surgery and immobilization , appear to dominate whereas thrombophilias and age do not seem to increase risk . In upper @-@ extremity DVT , the most important risk factor is having a central venous catheter , and thoracic outlet syndrome also increases risk .

= = = Risk factors = = =

= = Pathophysiology = =

DVT often develops in the calf veins and " grows " in the direction of venous flow , towards the heart . When DVT does not grow , it can be cleared naturally and dissolved into the blood (fibrinolysis) . Veins in the calf or thigh are most commonly affected , including the femoral vein , the popliteal vein , and the iliofemoral vein (as with May ? Thurner syndrome) . Extensive lower @-@ extremity DVT can reach into the iliac vein of the pelvis or the inferior vena cava . Occasionally the veins of the arm are affected , as after central venous catheter placement and with the rare Paget ? Schrötter disease .

The mechanism behind arterial thrombosis , such as with heart attacks , is more established than the steps that cause venous thrombosis . With arterial thrombosis , blood vessel wall damage is required , as it initiates coagulation , but clotting in the veins mostly occurs without any such damage . The beginning of venous thrombosis is thought to be caused by tissue factor , which leads to conversion of prothrombin to thrombin , followed by fibrin deposition . Red blood cells and fibrin are the main components of venous thrombi , and the fibrin appears to attach to the blood vessel wall lining (endothelium) , a surface that normally acts to prevent clotting . Platelets and white blood cells are also components . Platelets are not as prominent in venous clots as they are in arterial ones , but they may play a role . Inflammation is associated with VTE , and white blood cells play a role in the formation and resolution of venous clots .

Often , DVT begins in the valves of veins . The blood flow pattern in the valves can cause low oxygen concentrations in the blood (hypoxemia) of a valve sinus . Hypoxemia , which is worsened

by venous stasis , activates pathways ? ones that include hypoxia @-@ inducible factor @-@ 1 and early @-@ growth @-@ response protein 1 . Hypoxemia also results in the production of reactive oxygen species , which can activate these pathways , as well as nuclear factor @-@ ?B , which regulates hypoxia @-@ inducible factor @-@ 1 transcription . Hypoxia @-@ inducible factor @-@ 1 and early @-@ growth @-@ response protein 1 contribute to monocyte association with endothelial proteins , such as P @-@ selectin , prompting monocytes to release tissue factor @-@ filled microvesicles , which presumably begin clotting after binding to the endothelial surface .

= = Diagnosis = =

DVT diagnosis requires the use of imaging devices such as ultrasound . Clinical assessments , which predict DVT likelihood , can help determine if a D @-@ dimer test is useful . In those not highly likely to have DVT , a normal D @-@ dimer result can rule out a diagnosis .

= = = Classification = = =

Provoked DVTs occur in association with acquired risk factors , such as surgery , oral contraceptives , trauma , immobility , obesity , or cancer ; cases without acquired states are called unprovoked or idiopathic . Acute DVT is characterized by pain and swelling and is usually occlusive , which means that it obstructs blood flow , whereas non @-@ occlusive DVT is less symptomatic . The label of chronic has been applied to symptomatic DVT that persists longer than 10 or 14 days . DVT that has no symptoms , but is found only by screening , is labeled asymptomatic or incidental .

DVT in the legs is proximal (or iliofemoral) when above the knee and distal (or calf) when below the knee . DVT below the popliteal vein , a proximal vein behind the knee , is classified as distal and has limited clinical significance compared to proximal DVT . An initial episode of DVT is called incident and any subsequent DVT is termed recurrent . Bilateral DVT refers to clots in both legs while unilateral means that only a single leg is affected .

= = = Probability = = =

In those with suspected DVT , a clinical assessment of probability can be useful to determine which tests to perform . The most studied clinical prediction rule is the Wells score .

Wells score or criteria : (possible score ? 2 to 9)

Active cancer (treatment within last 6 months or palliative) : + 1 point

Calf swelling ? 3 cm compared to asymptomatic calf (measured 10 cm below tibial tuberosity) : + 1 point

Swollen unilateral superficial veins (non @-@ varicose , in symptomatic leg) : + 1 point

Unilateral pitting edema (in symptomatic leg) : + 1 point

Previous documented DVT : + 1 point

Swelling of entire leg : + 1 point

Localized tenderness along the deep venous system : + 1 point

Paralysis , paresis , or recent cast immobilization of lower extremities : + 1 point

Recently bedridden ? 3 days , or major surgery requiring regional or general anesthetic in the past 12 weeks : + 1 point

Alternative diagnosis at least as likely : ? 2 points

Those with Wells scores of two or more have a 28 % chance of having DVT , those with a lower score have 6 % odds . Alternatively , Wells scores can be categorized as high if greater than two , moderate if one or two , and low if less than one , with likelihoods of 53 % , 17 % , and 5 % respectively .

= = = D @-@ dimer = = =

D @-@ dimers are a fibrin degradation product , and an elevated level can result from plasmin

dissolving a clot ? or other conditions . Hospitalized patients often have elevated levels for multiple reasons . When individuals are at a high @-@ probability of having DVT , diagnostic imaging is preferred to a D @-@ dimer test . For those with a low or moderate probability of DVT , a D @-@ dimer level might be obtained , which excludes a diagnosis if results are normal . An elevated level requires further investigation with diagnostic imaging to confirm or exclude the diagnosis .

For a suspected first leg DVT in a low @-@ probability situation , the American College of Chest Physicians (ACCP) recommends testing either D @-@ dimer levels with moderate or high sensitivity or compression ultrasound of the proximal veins . These options are suggested over whole @-@ leg ultrasound , and D @-@ dimer testing is the suggested preference overall . The UK National Institute for Health and Care Excellence (NICE) recommends D @-@ dimer testing prior to proximal vein ultrasound .

For a suspected first leg DVT in a moderate @-@ probability scenario , a high @-@ sensitivity D @-@ dimer is suggested as a recommended option over ultrasound imaging , with both whole @-@ leg and compression ultrasound possible . The NICE guideline uses a two @-@ point Wells score and does not refer to a moderate probability group .

= = = Imaging = = =

Imaging tests of the veins are used in the diagnosis of DVT , most commonly either proximal compression ultrasound or whole @-@ leg ultrasound . Each technique has drawbacks : a single proximal scan may miss a distal DVT , while whole @-@ leg scanning can lead to distal DVT overtreatment . Doppler ultrasound , CT scan venography , MRI venography , or MRI of the thrombus are also possibilities .

The gold standard for judging imaging methods is contrast venography , which involves injecting a peripheral vein of the affected limb with a contrast agent and taking X @-@ rays , to reveal whether the venous supply has been obstructed . Because of its cost , invasiveness , availability , and other limitations this test is rarely performed .

A fibrinogen uptake test was formerly used to detect deep vein thrombosis . [move to history section ?]

= = Prevention = =

Depending upon the risk for DVT , different preventive measures are used . Walking and calf exercises reduce venous stasis because leg muscle contractions compress the veins and pump blood up towards the heart . In immobile individuals , physical compression methods improve blood flow . Anticoagulation , which increases the risk of bleeding , might be used in high @-@ risk scenarios . The risk of major bleeding with long @-@ term anticoagulation is about 3 % per year , and the point where annual VTE risk is thought to warrant long @-@ term anticoagulation is estimated to be between 3 and 9 % . Usually , only when individuals exceed a 9 % annual VTE risk is long @-@ term anticoagulation a common consideration . Antithrombin deficiency , a strong or moderately strong risk factor , carries an annual risk of VTE of only 0 @.@ 8 ? 1 @.@ 5 % ; as such , asymptomatic individuals with thrombophilia do not warrant long @-@ term anticoagulation .

Aside from anticoagulation , the anti @-@ platelet drug aspirin might be used in some people following orthopedic surgery and in those with a previous VTE . Statins might decrease the risk for people who are otherwise healthy , but the evidence is not clear . Following the completion of warfarin long term aspirin is useful to prevent re occurrence .

= = = Hospital = = =

In 2011 , the American College of Physicians (ACP) issued a clinical practice guideline making three strong recommendations based on moderate @-@ quality evidence : that hospitalized patients be assessed for their risk of thromboembolism and bleeding before prophylaxis is started ; that heparin or a related drug be used if potential benefits are thought to outweigh potential harms ; and

that graduated compression stockings not be used . The ACP also drew attention to a lack of support for any performance measures encouraging physicians to apply universal prophylaxis without regard to the risks .

A 2014 Cochrane review found that using heparin in medical patients did not change the risk of death or pulmonary embolism . While its use decreased people 's risks of DVTs it also increased people 's risks of major bleeding . The review thus recommended the need to balance risks and benefits .

The 2012 ACCP guidelines for non @-@ surgical patients recommend anticoagulation for the acutely ill in cases of elevated risk when there is neither bleeding nor a high risk of bleeding . Mechanical prophylaxis is suggested when risks for bleeding and thrombosis are elevated . For the critically ill , either pharmacological or mechanical prophylaxis is suggested depending upon the risk . Heparin is suggested in outpatients with cancer who have solid tumors and additional risk factors for VTE ? listed as " previous venous thrombosis , immobilization , hormonal therapy , angiogenesis inhibitors , thalidomide , and lenalidomide " ? and a low risk of bleeding .

= = = Post @-@ surgery = = =

Major orthopedic surgery ? total hip replacement , total knee replacement , or hip fracture surgery ? has a high risk of causing VTE . If prophylaxis is not used after these surgeries , symptomatic VTE has about a 4 % chance of developing within 35 days . Options for VTE prevention in people follow non @-@ orthopedic surgery include early walking , mechanical prophylaxis (intermittent pneumatic compression or graduated compression stockings) , and drugs (low @-@ molecular @-@ weight heparin [LMWH] and low @-@ dose @-@ unfractionated heparin [LDUH]) depending upon the risk of VTE , risk of major bleeding , and person 's preferences . Following major orthopedic surgery , the ACCP recommends treatment with drugs that reduce the risk of clots (such as fondaparinux and aspirin) with LMWH suggested as a preference . Intermittent pneumatic compression is also an option . Graduated compression stockings are effective after both general and orthopedic surgery .

= = = Pregnancy = = =

The risk of VTE is increased in pregnancy by about five times because of a more hypercoagulable state , a likely adaptation against fatal postpartum hemorrhage . Additionally , pregnant women with genetic risk factors are subject to an approximate three to thirty times increased risk for VTE . Preventative treatments for pregnancy @-@ related VTE in hypercoagulable women were suggested by the ACCP . Homozygous carriers of factor V Leiden or prothrombin G20210A with a family history of VTE were suggested for antepartum LMWH and either LMWH or a vitamin K antagonist (VKA) for the six weeks following childbirth . Those with another thrombophilia and a family history but no previous VTE were suggested for watchful waiting during pregnancy and LMWH or ? for those without protein C or S deficiency ? a VKA . Homozygous carriers of factor V Leiden or prothrombin G20210A with no personal or family history of VTE were suggested for watchful waiting during pregnancy and LMWH or a VKA for six weeks after childbirth . Those with another thrombophilia but no family or personal history of VTE were suggested for watchful waiting only . Warfarin , a common VKA , can cause harm to the fetus and is not used for VTE prevention during pregnancy .

= = = Travelers = = =

The 2012 ACCP guidelines offered weak recommendations . For at @-@ risk long @-@ haul travelers ? those with " previous VTE , recent surgery or trauma , active malignancy , pregnancy , estrogen use , advanced age , limited mobility , severe obesity , or known thrombophilic disorder " ? suggestions included calf exercises , frequent walking , and aisle seating in airplanes to ease walking . The use of graduated compression stockings that fit below the knee and give 15 ? 30 mm Hg of pressure to the ankle was suggested , while aspirin or anticoagulants were not . Compression

stockings have sharply reduced the levels of asymptomatic DVT in airline passengers , but the effect on symptomatic VTE is unknown , as none of the individuals studied developed symptomatic VTE .

= = Treatment = =

= = = Anticoagulation = = =

Anticoagulation , which prevents further coagulation but does not act directly on existing clots , is the standard treatment for DVT . Balancing risk vs. benefit is important in determining the duration of anticoagulation , and three months is generally the standard length of treatment . In those with an annual risk of VTE in excess of 9 % , as after an unprovoked episode , extended anticoagulation is a possibility . Those who finish VKA treatment after idiopathic VTE with an elevated D @-@ dimer level show an increased risk of recurrent VTE (about 9 % vs. about 4 % for normal results) , and this result might be used in clinical decision @-@ making . Thrombophilia test results rarely play a role in the length of treatment .

For acute cases in the leg , the ACCP recommended a parenteral anticoagulant (such as LMWH , fondaparinux , or unfractionated heparin) for at least five days and a VKA , the oral anticoagulant , the same day . LMWH and fondaparinux are suggested over unfractionated heparin , but both are retained in those with compromised kidney function , unlike unfractionated heparin . The VKA is generally taken for a minimum of three months to maintain an international normalized ratio of 2 @.@ 0 ? 3 @.@ 0 , with 2 @.@ 5 as the target . The benefit of taking a VKA declines as the duration of treatment extends , and the risk of bleeding increases with age .

The ACCP recommended treatment for three months in those with proximal DVT provoked by surgery . A three @-@ month course is also recommended for those with proximal DVT provoked by a transient risk factor , and three months is suggested over lengthened treatment when bleeding risk is low to moderate . Unprovoked DVT patients should have at least three months of anticoagulation and be considered for extended treatment . Those whose first VTE is an unprovoked proximal DVT are suggested for anticoagulation longer than three months unless there is a high risk of bleeding . In that case , three months is sufficient . Those with a second unprovoked VTE are recommended for extended treatment when bleeding risk is low , suggested for extended treatment when bleeding risk is moderate , and suggested for three months of anticoagulation in high @-@ risk scenarios .

= = = Home treatment , stockings , walking , and repeat imaging = = =

The ACCP recommended initial home treatment instead of hospital treatment for those with acute leg DVT . This applies as long as individuals feel ready for it , and those with severe leg symptoms or comorbidities would not qualify . An appropriate home environment is expected : one that can provide a quick return to the hospital if necessary , support from family or friends , and phone access .

In addition to anticoagulation , the ACCP suggested graduated compression stockings ? which apply higher pressure (30 ? 40 mm Hg) at the ankles and a lower pressure around the knees ? for those with symptomatic DVT . Use should begin as soon as possible after anticoagulation . Evidence however does not support that these stockings reduce the risk of post @-@ thrombotic syndrome nor do they indicate a reduction in recurrent VTE . Use is suggested for two years , though inconvenience and discomfort can reduce compliance . Walking is also suggested for those without severe pain or edema .

Unless a person has medical problems preventing movement , after a person starts anti @-@ coagulation therapy bed rest should not be used to treat acute deep vein thrombosis . There are clinical benefits associated with walking and no evidence that walking is harmful , but people with DVT are harmed by bed rest except when it is medically necessary .

Instead of anticoagulation , a follow @-@ up imaging test (typically ultrasound) about one @-@

week post @-@ diagnosis is an option for those with an acute isolated distal DVT without a high risk for extension ; if the clot does not grow , the ACCP does not recommend anticoagulation . This technique can benefit those at a high risk for bleeding . Patients may choose anticoagulation over serial imaging , however , to avoid the inconvenience of another scan if concerns about the risk of bleeding are insignificant . When applied to symptomatic patients with a negative initial ultrasound result , serial testing is inefficient and not cost effective .

= = = IVC filters , thrombolysis , and thrombectomy = = =

Inferior vena cava filters (IVC filters) are used on the presumption that they reduce PE , although their effectiveness and safety profile are not well established . In general , they are only recommended in some high risk scenarios . The ACCP recommended them for those with a contraindication to anticoagulant treatment but not in addition to anticoagulation , unless an individual with an IVC filter but without a risk for bleeding develops acute proximal DVT . In this case , both anticoagulation and an IVC filter are suggested . NICE recommends caval filters in settings where someone with an acute proximal DVT or PE cannot receive anticoagulation , and that the filter is removed when anticoagulation can be safely started . While IVC filters themselves are associated with a long @-@ term risk of DVT , they are not reason enough to maintain extended anticoagulation .

Thrombolysis is the administration of an enzyme (intravenous or directly into the affected vein through a catheter) , which acts to enzymatically break up clots . This may reduce the risk of post @-@ thrombotic syndrome by a third , and possibly reduce the risk of leg ulcers , but is associated with an increased risk of bleeding . The ACCP currently suggests anticoagulation rather than thrombolysis , but patients may choose thrombolysis if prevention of post @-@ thrombotic syndrome outweighs concerns over the complexity , bleeding risk , and cost of the procedure . NICE recommends that thrombolysis is considered in those who have had symptoms for less than two weeks , are normally well , have a good life expectancy and a low risk of bleeding .

A mechanical thrombectomy device can remove venous clots , although the ACCP considers it an option only when the following conditions apply : " iliofemoral DVT , symptoms for < 7 days (criterion used in the single randomized trial) , good functional status , life expectancy of ? 1 year , and both resources and expertise are available . " Anticoagulation alone is suggested over thrombectomy .

= = Prognosis = =

The most frequent complication of proximal DVT is post @-@ thrombotic syndrome , which is caused by a reduction in the return of venous blood to the heart . Some symptoms of post @-@ thrombotic syndrome are pain , edema , paresthesia , and in severe cases , leg ulcers . An estimated 20 ? 50 % of those with DVT will develop it , and 5 ? 10 % will develop the severe form . PE is the most serious complication of proximal DVT , and the risk of PE is higher when clots are present in the thigh and pelvis . Distal DVT itself is hardly if ever associated with post @-@ thrombotic syndrome or PE . Untreated lower extremity DVT has a 3 % PE @-@ related mortality rate , while deaths associated with upper extremity DVT are extremely rare . The presence of a remaining thrombus after a DVT frequently occurs in a minority of people , and it increases the risk of recurrence , though to a lesser extent than an elevated D @-@ dimer . In the 10 years following a VTE , approximately a third of individuals will have a recurrent episode .

= = Epidemiology = =

About 1 in 1000 adults per year has DVT , but as of 2011 , available data is dominated by North American and European populations . VTE is rare in children , with an incidence of about 1 in 100 @,@ 000 a year . From childhood to old age , incidence increases by a factor of about 1000 , with almost 1 % of the elderly experiencing VTE yearly . During pregnancy and after childbirth , acute

VTE occurs about once per 1000 deliveries . After surgery with preventative treatment , VTE develops in about 10 of 1000 people after total or partial knee replacement , and in about 5 of 1000 after total or partial hip replacement . About 300 @,@ 000 ? 600 @,@ 000 Americans develop VTE each year , with about 60 @,@ 000 ? 100 @,@ 000 deaths attributable to PE . In England , an estimated 25 @,@ 000 a year die from hospital @-@ related VTE . For unclear reasons , people of Asian descent have a lower VTE risk than whites .

In North American and European populations , around 4 ? 8 % of people have a thrombophilia , most commonly factor V leiden and prothrombin G20210A . For populations in China , Japan , and Thailand , deficiences in protein S , protein C , and antithrombin predominate . Non @-@ O blood type is present in around 50 % of the general population and varies with ethnicity , and it is present in about 70 % of those with VTE . Altogether , global data is incomplete .

= = Economics = =

Initial DVT costs for an average hospitalized patient in the U.S. are around $ 7 @,@ 700 ? $ 10 @,@ 800 . VTE follow @-@ up costs at three months , six months , and a year are about $ 5 @,@ 000 , $ 10 @,@ 000 , and $ 33 @,@ 000 respectively ; in Europe , the three and six @-@ month figures are about ? 1 @,@ 800 and ? 3 @,@ 200 . Post @-@ thrombotic syndrome is a significant contributor to DVT follow @-@ up costs . Annual DVT costs in the U.S. are an estimated $ 5 billion or in excess of $ 8 billion , and the average annual cost per treated individual is thought to be about $ 20 @,@ 000 . As an example , if 300 @,@ 000 symptomatic DVT patients were treated at costs averaging $ 20 @,@ 000 annually , that would cost $ 6 billion a year .

= = History = =

The earliest case of DVT was described by Sushruta in his book Sushruta Samhita around 600 ? 900 BC . Another documented case is thought to have occurred in the 13th century , in the leg of a 20 @-@ year @-@ old male . At some point , the increased incidence of DVT in women after childbirth was noticed , and in the late 1700s , a public health recommendation was issued to encourage women to breastfeed as a means to prevent this phenomenon ; the DVT was called " milk leg " , as it was thought to result from milk building up in the leg .

In 1856 , German physician and pathologist Rudolf Virchow published what is referred to as Virchow 's triad , the three major causes of thrombosis . The triad provides the theoretical framework for the current explanation of venous thrombosis , although it was focused on the effect of a foreign body in the venous system and the conditions required for clot propagation .

Multiple pharmacological therapies for DVT were introduced in the 20th century : oral anticoagulants in the 1940s , subcutaneous LDUH in 1962 and subcutaneous LMWH in 1982 . Diagnoses were commonly performed by impedance plethysmography in the 1970s and 1980s , but the use of Doppler ultrasound techniques , with their increased sensitivity and specificity , largely superseded this method .

= = Research directions = =

As of 2011 , three large randomized controlled trials ? the Norwegian CaVent trial , the North American ATTRACT trial , and the Dutch CAVA trial ? are studying the effectiveness and safety of catheter @-@ directed thrombolysis . In 2012 , two studies found a clinical benefit in taking aspirin to prevent recurrent VTE .

= = = Cited literature = = =