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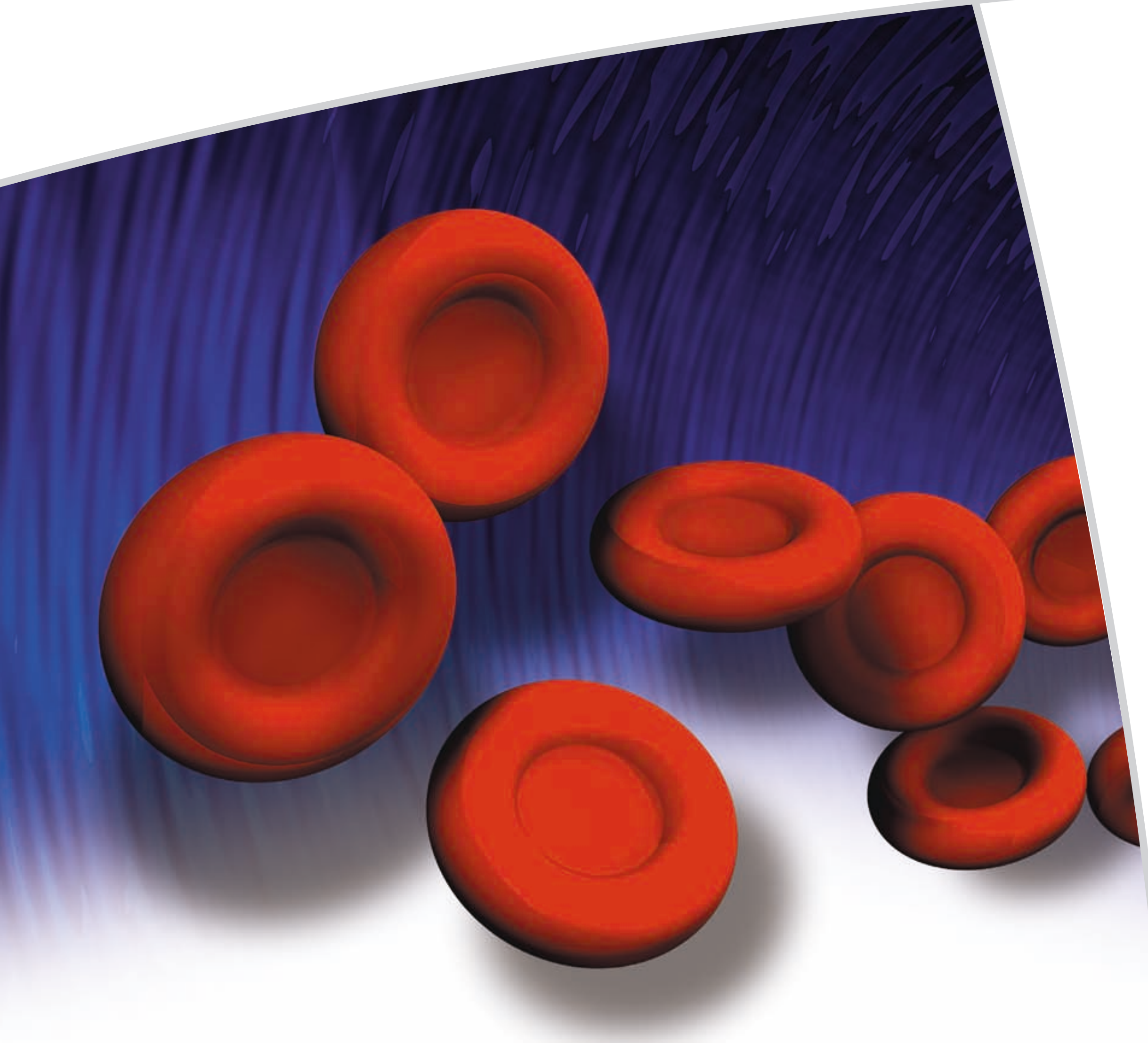

PREVENTING VENOUS THROMBOEMBOLISM WITH FLOWTRON® DVT PROPHYLAXIS SYSTEMS

ISSUE 4
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…with people in mind

The challenge……

More patients in England died from Venous Thromboembolism (VTE) than from breast cancer, HIV AIDS and road traffic accidents combined – this is 25 times greater than deaths from MRSA[1].

More than half of all hospitalised patients worldwide were at risk of VTE however, only half of these at risk patients received recommended [ACCP[2]] prophylaxis[3].

Around two thirds of symptomatic VTE can be avoided by provision of adequate prophylaxis[4].

There is a safe, efficacious and cost effective method of preventing VTE, which is not being as widely administered, as it should be[1].

Mechanical Prophylaxis: a safe and effective solution…..

NICE (2010)[5]
"Unlike pharmacological prophylaxis, none of the mechanical methods are associated with an increased risk of bleeding".

ECRI Institute (2009)[6]
"Based upon two [literature] reviews, our position remains the same: IPC is effective".

Morris (2008)[7]
"Intermittent compression has been shown to be clinically effective in a wide range of surgical and medical specialities".

Autar (2009)[8]
"There is an abundance of evidence that [anti-embolic stockings] AES are very efficacious in the prevention of VTE, either singly (monotherapy) or when used in conjunction with other methods of prophylaxis (adjuvant)".

Kakkos et al (2008)[9]
"The results of the [Cochrane Review] support, especially in high-risk patients, the use of combined modalities [IPC & pharmacological]".

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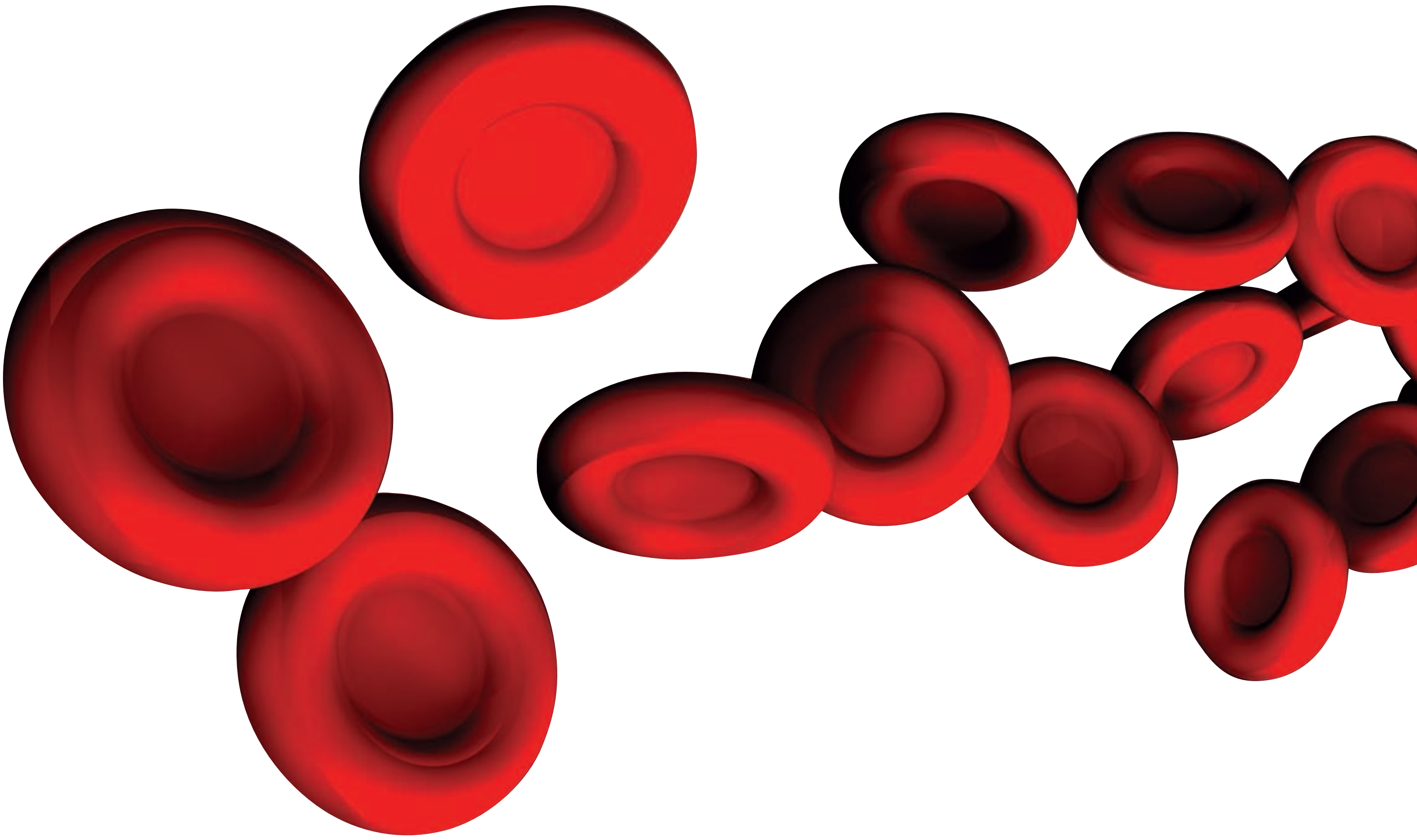


Introduction

Venous thromboembolism (VTE), which encompasses deep vein thrombosis (DVT) and pulmonary embolism (PE), is a major international health problem particularly affecting hospitalised patients: this group are more than 100 times more likely to develop VTE compared with the rest of the community[10].

Despite the fact that around two thirds of symptomatic VTE can be avoided by provision of adequate prophylaxis[4] PE is one of the commonest causes of death in hospital, accounting for around 10 percent of all hospital mortalities[11]. In the long term DVT can lead to post-thrombotic syndrome and leg ulceration, which affects patient quality of life as well as having significant healthcare costs.

Intermittent pneumatic compression and anti-embolic stockings are both proven and established non-invasive mechanical methods of DVT prophylaxis that are effective when used either alone or, for higher risk patients, used in combination with pharmacological prophylaxis. Mechanical methods have the additional advantage in that they are not associated with a risk of bleeding.

This booklet, written for the healthcare professional, presents an overview of the pathological processes behind VTE formation, identifies the population most at risk and explains the prophylactic mechanisms of anti-embolic stockings (AES) and intermittent pneumatic compression (IPC).

The global scale

Global:

An epidemiological study[3] involving 68,000 patients across 32 countries identified:

- More than half of all hospitalised patients are at risk of VTE.
- Less than half of those at risk have adequate [ACCP[2]] prophylaxis.
- Medical patients were particularly vulnerable with only 37% in the highest risk groups, malignancy and ischaemic stroke, adequately protected.
- 10% of patients with a high bleeding risk and not anti-coagulated could have been offered safe protection with mechanical prophylaxis.

Europe:

VTE: a substantial cause of mortality and morbidity.

- More than 1 million events or deaths attributed to VTE are estimated to occur annually across Europe, with more than three-quarters of these being hospital-acquired[3].
- Of the VTE related deaths only 7% are diagnosed before death, 34% are sudden and 59% follow undiagnosed PE[3].

UK:

25,000 people die annually from VTE:

- More than breast cancer, HIV AIDS and road traffic accidents combined and 25 times the number who die from MRSA[1].
- An estimated £640 million is spent on direct and indirect costs such as leg ulcers; a condition linked to previous DVT in up to 50% of cases[1].
- Up to 40% of patients undergoing major surgery in the UK may not receive adequate prophylaxis, with legal settlements for negligence awarding up to £500,000 per claimant[12].

Australia:

30,000 people are hospitalised annually and an estimated 2,000 patients die[13, 14].

USA:

VTE is the second most common medical complication in acute care.

- The second most common cause of extended length of stay.
- The third most common cause of excess mortality and charges[15].

The pathophysiology of VTE

Venous thrombus formation and propagation most usually depend on the presence of one or more of the following:

- venous stasis
- blood vessel wall trauma or abnormality
- increased risk of blood coagulation

These elements are known collectively as Virchow's triad (Figure. 1) and many predisposing factors can alter one or more of these factors.

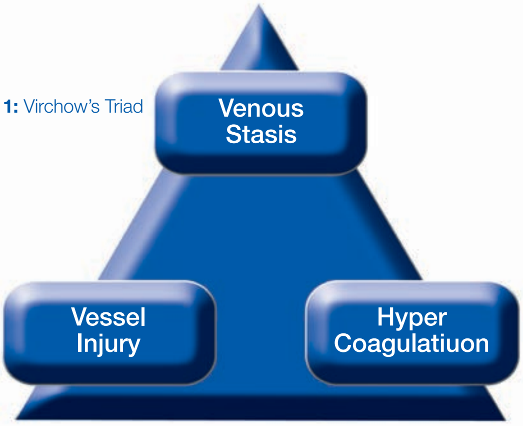


Figure 1: Virchow's Triad

Venous Stasis

Venous stasis occurs when there's a decrease in movement of blood, causing venous congestion in the lower extremities; this may occur after prolonged immobility or confinement to bed. Venous obstruction can also arise from external compression by enlarged lymph nodes, tumours or intravascular compression by previous thromboses[16].

Vein injury

The endothelium (lining) of a healthy vein is smooth and provides a physical barrier between the circulating blood and the thrombogenic tissues beneath. When the vein becomes injured the lining loses its normal negative charge, becoming rough and provoking platelet aggregation and adhesion. Endothelial injury may be caused by a previous DVT, venous distension, trauma and surgery.

Hypercoagulability

Changes in blood chemistry causing hypercoagulability (increased blood stickiness) can occur as a result of many factors including dehydration, malignancy, surgery or trauma, oestrogen therapy and systemic inflammatory diseases.

The risk of VTE by clinical speciality

Geerts et al (2008) representing the American College of Chest Physicians (ACCP) identified the frequency of DVT in hospitalised patients in the absence of prophylaxis[2]. Table 1 illustrates the high incidence of DVT and thus the requirement for effective prophylactic measures.

Patient group	Prevalence without prophylaxis
Medical patients	10-20%
General surgery	15-40%
Major gynaecological surgery	15-40%
Major urologic surgery	15-40%
Neurosurgery	15-40%
Stroke	20-50%
Hip/ knee arthroplasty/ surgery	40-60%
Major trauma	40-80%
Spinal cord injury	60-80%
Critical care patients	10-80%

Table 1: VTE incidence rates without prophylaxis

Preventing VTE with mechanical prophylaxis: Mode of Action

Unlike pharmacological methods, both IPC and AES work to mitigate not one but two of the risk factors associated with VTE development: venous stasis and hypercoagulability. These mechanical methods of VTE prophylaxis are attractive to clinicians as there is no risk of bleeding when used as a monotherapy and they can be used as an adjunct to pharmacological methods to increase effectiveness in high-risk patients.

Anti-embolic stockings (AES)

AES (Figure 2) are designed to exert sustained graduated compression to the legs decreasing from the ankle towards the knee and thigh. This mechanical support to the leg decreases the cross-sectional profile of the vein, which increases venous velocity[8] (Autar 2009). AES also prevents the pathological progression of passive venous distension to the point where sub-endothelial tears and activation of clotting factors might occur[17, 18]. In 1975 Sigel[19] identified an optimal stocking compression profile ranging from 18mmHg compression at the ankle to 8mmHg compression at the mid-thigh. Commonly known as the Sigel profile, this is the standard against which all AES performance is compared[8].

Despite the apparent simplicity as a modality, AES are heterogeneous with respect to length, compression profile and fit. To ensure therapeutic benefit and prevent complications (such as reverse pressure gradients and skin breakdown), a number of conditions must be satisfied including assessment and appropriate fitting using standardised protocols for measurement and application by trained staff[20, 21]. Poorly fitted stockings or those of an incorrect shape and size also have the potential to cause a tourniquet effect on the proximal part of the limb where the stocking is applied. This can result in ischaemia and an increased risk of thrombosis development[17]. AES should be worn immediately a risk is identified until a normal level of physical activity is resumed. Leg measurement should be reviewed regularly; if AES are too loose they will be ineffective and if they are too tight they may compromise vascular supply[22].

The choice between knee-high and thigh-length AES should be based upon clinical judgement, patient preference, concordance and surgical site, given the lack of evidence that any one type has superior efficacy[5].

Figure 2: *Flowtron* AES anti-embolic stockings

Intermittent Pneumatic Compression (IPC)

IPC therapy is delivered through inflatable, single-patient-use, garments containing one or more air chambers (Figure 3). These are applied to the foot, calf or calf and thigh and intermittently inflated with air by means of a powered pneumatic pump. The inflation - deflation cycle simulates the normal ambulatory calf and foot pump and propels the blood of the deep veins towards the heart.

This benefits the non-ambulatory patient by:

- Increasing blood flow velocity in the deep veins and reducing stasis
- Decreasing venous hypertension
- Flushing valve pockets where it is thought thrombi originate
- Decreasing interstitial oedema[23]

Figure 3: *Flowtron* DVT Prophylaxis System

Biochemical effect

The mechanical forces of shear and stress within the venous system are linked to physiological responses in the endothelial cells that are thought to contribute to the anti-thrombotic and pro-fibrinolytic effects of IPC[24] (Figure 4).

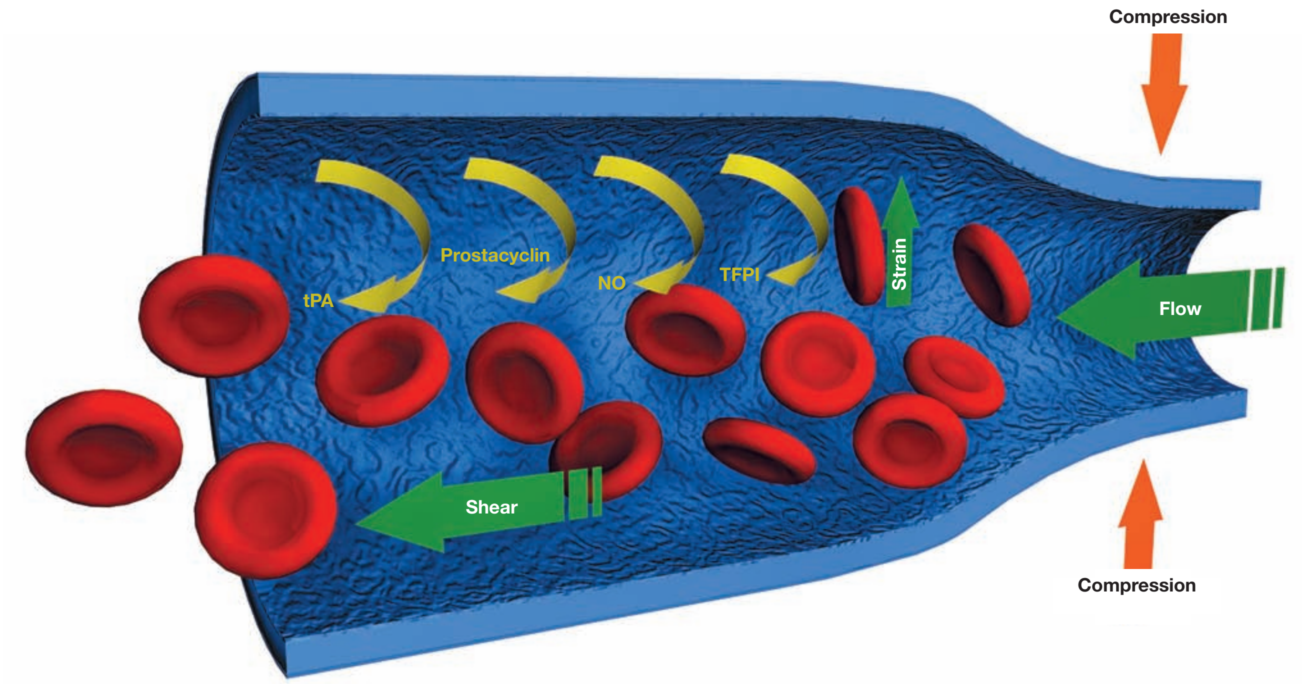


Figure 4: Mechanical and biochemical effects of IPC on a vein. Diagram adapted from Chen et al (2001)[24]

Figure 5: *Flowtron* DVT foot garment

Anti-thrombotic effect

IPC has been found to:

- Increase levels of tissue factor pathway inhibitor (TFPI)[25, 26] which is an important regulator of the initiating event in the blood coagulation system
- Decrease levels of thrombin-antithrombin complex (TAT)[27] increasing the anti-thrombotic properties of the blood

Another pathway, which IPC has been suggested to affect, is that of platelet disaggregation via the action of prostacyclin[24].

Maintaining haemostatic balance

Giddings et al (2004)[26] examined specific coagulation and fibrinolytic markers in 21 subjects comparing the status before (control) and after both 60 and 120 minutes of IPC using a *Flowtron* DVT Prophylaxis System. The results confirmed that physiological blood flow plays a significant role in maintaining a haemostatic balance and reflects the potential value of IPC in clinical thrombosis management.

Compression type

The *Flowtron* DVT Prophylaxis System delivers a single-pulse compression profile, and an optimised inflation-deflation sequence, which delivers proximal blood flow augmentation at a level known to be effective for DVT prophylaxis. The circumferential compression garment (Figure 3) is most commonly applied to the leg (calf-length or thigh-length) or, in some specialities such as orthopaedics, through application to the plantar plexus using a specialised foot garment (Figure 5).

While there has been some debate in the past about the relative merits of 'uniform' versus 'sequential' compression, studies have consistently shown little difference. Results indicate comparable blood velocity and a trend towards greater peak flow augmentation with the *Flowtron* DVT Prophylaxis System[30, 31, 32, 33, 34]. Both comparative patient studies and guideline consensus panels make little distinction between the two modalities; these will be discussed later in this booklet.

Intermittent Pneumatic Compression: consensus statements and guidelines

Given the high number of patients at risk of VTE, and the relatively simple measures which can be employed to improve patient safety, a number of National and International Best Practice Guidelines have been developed through systematic literature reviews and expert consensus panels. An example from the American College of Chest Physicians (ACCP) Consensus Conference[2] is presented in Table 2: other guidelines are introduced in Table 3 where the indications for IPC are summarised.

Level of risk	Recommended prophylaxis for optimal outcome
Low risk - Minor surgery in mobile patients - - Medical patients who are fully mobile	 No specific measures Early and aggressive mobilisation
Moderate risk - Most general, open gynaecology or urology surgery - Medical patients, bed rest or sick	**PC/AES** LDUH every 12 hours LMWH daily
Moderate VTE risk plus high bleeding risk	**IPC/AES**
High risk - Hip or knee arthroplasty, hip fracture surgery, major trauma, spinal cord injury	**LMWH** Fondaparinux Oral vitamin K antagonist
High VTE risk plus high bleeding risk	**IPC/AES**

Table 2: ACCP guidelines

Key:

IPC: Intermittent Pneumatic Compression
AES: Anti-Embolic Stockings
LDUH: Low Dose Unfractionated Heparin
LMWH: Low Molecular Weight Heparin

Consensus statement/guideline	Methodology	Recommendations relating to IPC & AES
NICE (UK) clinical guidelines (2010)[5]	Evidence based guideline for England and Wales based upon a systematic literature review.	• Effective in surgical patients • No risk of bleeding • Can be used in combination with pharmacological methods for many groups of patients.
Clinical practice guideline for the prevention of VTE in patients admitted to Australian hospitals (2009)[35]	Developed using internationally agreed methods for the development of evidence-based clinical practice guidelines.	• **AES and IPC** are recommended forms of prophylaxis used alone or in combination with pharmacological methods depending upon surgical procedure, medical condition and individual patient assessment.
8th ACCP conference on anti-thrombotic therapy (2008)[2]	North American consensus statement featuring risk stratification, recommendations and expert consensus where insufficient evidence exists	• Mechanical methods of prophylaxis **(AES & IPC)** are recommended for patients at high risk of bleeding. • Recommended as an adjunct to anticoagulant-based thromboprophylaxis in higher risk patients.
Australia and New Zealand Working Party on the Management and Prevention of Venous Thromboembolism. Best Practice Guidelines 4th Edition (2007)[36]	National guidelines developed by a working party to assist in the identification and treatment of patients at risk of developing DVT	• **IPC** is more effective than **AES** in high-risk patients when combined with anticoagulants or when anticoagulants are contraindicated.
International Consensus Statement (2006)[37]	An international group recommending prophylactic measures in surgical, medical and obstetric patients	• Both **IPC** and **AES** reduce the risk of asymptomatic DVT. • Combinations of prophylactic methods are more effective than when used alone.

Table 3: Recommendations for Mechanical Prophylaxis from consensus papers and guidelines

Scientific summaries

Meta-analyses and systematic reviews

Mechanical compression versus subcutaneous heparin therapy in postoperative and post-trauma patients: A systematic review and meta-analysis *(Eppsteiner et al 2010)*[38]

Years: 1966 – 2008

Objectives:

To systematically review the impact of mechanical compression versus subcutaneous heparin on VTE disease and bleeding in post-operative and trauma patients.

Outcomes:

- 16 eligible RCT's identified with nearly 4,000 participants.
- No difference in the risk of DVT or PE between mechanical compression and heparin.
- Heparin associated with a significantly increased risk of post-operative bleeding.

Intermittent pneumatic compression or graduated compression stockings for deep vein thrombosis prophylaxis *(Morris & Woodcock 2010)*[39]

Years: 1970 – 2008

Objectives:

To review the efficacy of IPC and graduated compression stockings in direct clinical comparisons.

Outcomes:

- 10 direct comparisons found.
- Considerable variation identified in type of AES, IPC device, DVT detection method and prophylaxis protocol.
- Both methods effective, however overall trend and cumulative rates favour IPC.

A review of the evidence for the efficacy of Anti-Embolism Stockings (AES) in venous thromboembolism prevention *(Autar 2009)*[8]

Objectives:

To review the efficacy and scientific basis of AES in the prevention of DVT when used either alone or in combination with other methods of prophylaxis.

Outcomes:

- When sized and correctly applied, AES are easy to use, acceptable to patients and safe (unless otherwise contraindicated).
- AES require a graduated pressure range from highest pressure at ankle to lowest at knee or thigh. The Sigel profile is the optimal range (18, 14, 10 & 8 mmHg). At this range, femoral venous blood flow is increased to 138% of base flow.
- AES used alone or as an adjuvant are very efficacious in DVT prophylaxis.
- Both calf and thigh-length AES offer similar therapeutic benefit.

Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high risk patients [Cochrane Review] *(Kakkos et al 2008)*[9]

Years: 1960 – 2007

Objectives:

This Cochrane Review assessed the efficacy of combined IPC and pharmacological prophylaxis versus single modalities in the prevention of VTE in high-risk patients.

Outcomes:

- 7,431 patients in 11 studies.
- The combined modalities of IPC and anticoagulant are more effective in reducing incidence of VTE than single modalities.
- This result endorses the recommendations of VTE prevention guidelines that high-risk patients should receive multi-modality prophylaxis.

Meta-analyses and systematic reviews - continued

Prevention of venous thromboembolism in neurosurgery: A meta-analysis *(Collen et al 2008)*[40]

Years: 1960 – 2007

Objectives:

To determine the relative efficacy of LMWH, UFH and mechanical devices in neurosurgical patients.

Outcomes:

- 7779 patients in 30 studies.
- In a mixed neurosurgical population, LMWH and IPC both effective in reducing rate of DVT.
- Isolated high-risk groups may benefit from combination therapy.

Knee versus thigh length graduated compression stockings for prevention of deep venous thrombosis: A systematic review *(Sajid et al 2006)*[41]

Years: 1976- 2005

Objectives:

To evaluate the efficacy of calf or thigh length AES in VTE prevention.

Outcomes:

- 14 randomised controlled trials identified.
- Both knee length and thigh length AES are efficient.
- Insufficient evidence exists to identify any differences between knee and thigh length AES.

Towards evidence-based guidelines for the prevention of venous thromboembolism: systematic reviews of mechanical methods, oral anticoagulation, dextran and regional anaesthesia as thromboprophylaxis *(Roderick et al 2005)*[42]

Years: Up to 2001

Objectives:

To determine if the use of different methods of VTE prophylaxis can reduce the risks of DVT and PE and reduce the risks of major bleeding in medical and surgical patients.

Outcomes:

- 39 papers reviewed: 17 (AES), 22 (IPC).
- Mechanical compression methods reduced the risk of DVT by two-thirds when used alone and by half when added to an anti-coagulant.
- Mechanical methods reduced the risk of proximal DVT by about half and the risk of PE by two-fifths.
- Unless contraindicated, and irrespective of their risk of VTE, patients undergoing a surgical procedure will benefit from mechanical prophylaxis.

Evidence based compression. Prevention of stasis and deep vein thrombosis (Morris and *Woodcock 2004)*[17]

Years: 1970 – 2002

Objectives:

To review published evidence on the venous flow effects of mechanical compression devices and determine their relevance in relation to DVT prevention.

Outcomes:

- In terms of efficacy, evidence does not support the view that:
    - Higher peak velocities equate to a more effective IPC system.
    - That graduated sequential compression is better than uniform compression
    - That thigh-compression is superior to calf compression.
- IPC is simple and complication free and compares favourably with pharmacological prophylaxis.
- Distal venous trapping might occur with any type of IPC device but is inconsistent and cannot be considered an important factor.

Elastic compression stockings for prevention of deep vein thrombosis [Cochrane Review]. *(Amaragiri and Lees 2003)*[43]

Years: 1971 - 2002

Objectives:

To evaluate the effectiveness and safety of AES as prophylaxis for DVT.

Outcomes:

- 16 randomised controlled trials (2211 subjects) from across a variety of medical and surgical in-patient units.
- Application of AES was identified as significantly decreasing the incidence of DVT.
- AES are even more effective when combined with another prophylactic modality.

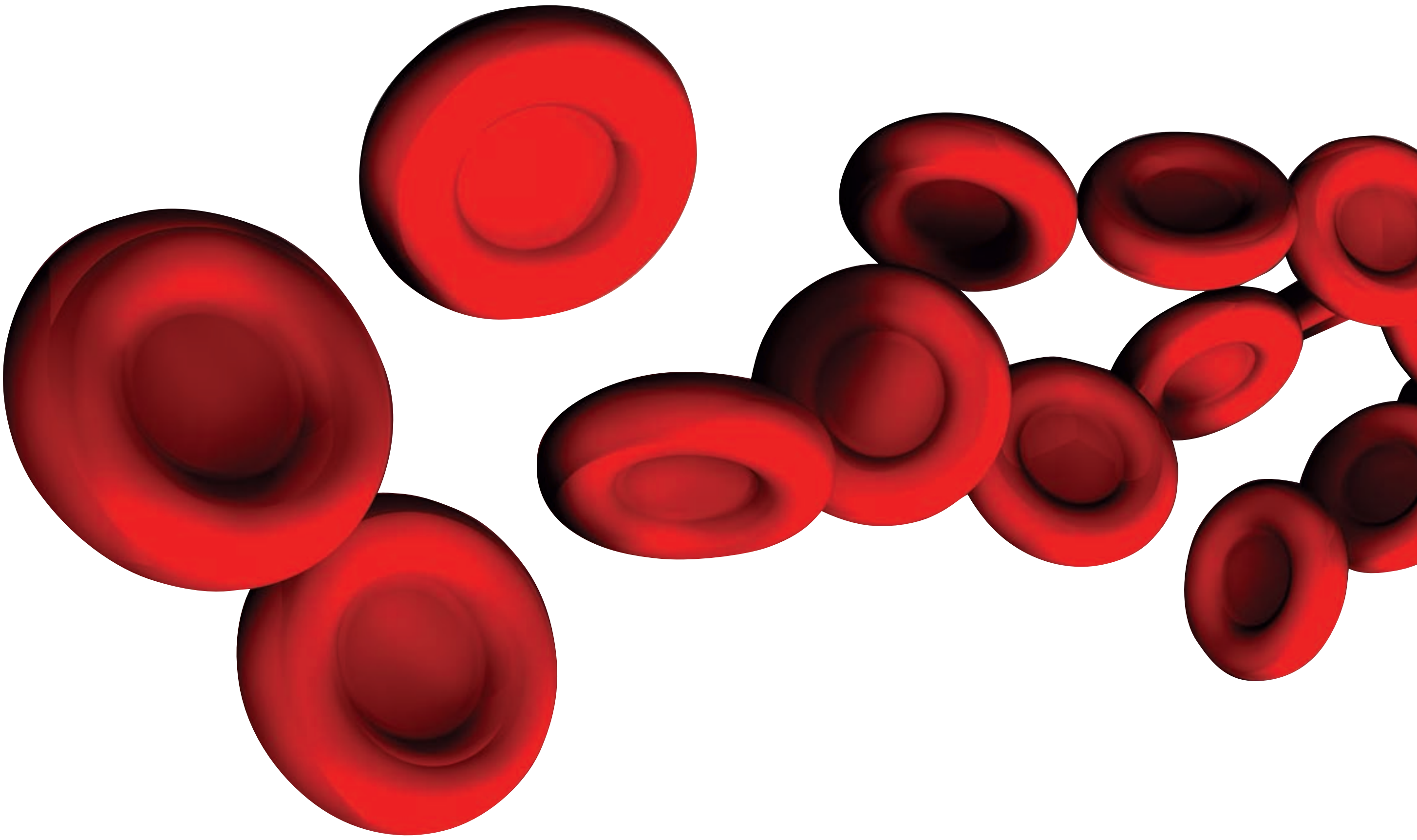
Prophylaxis of peri-operative venous thrombosis: role of venous compression *(Silleran-Chassany and Safran 2000)*[44]

Objectives:

A literature review to examine the effectiveness of IPC in general and orthopaedic surgery.

Outcomes:

- IPC reduces the calibre of superficial and deep veins resulting in accelerated blood flow, reduced venous reflux and reduced oedema through interstitial fluid drainage.
- IPC is inexpensive, easy to use and has few contraindications.
- IPC does not increase bleeding risk so is particularly suitable for patients in whom anticoagulation is contraindicated e.g. neurosurgery.
- Randomised trials have shown compression and anticoagulation used together to be better than the respective methods alone (25% DVT in combination, compared to 38% in LMWH alone).



Meta-analyses and systematic reviews - continued

A meta-analysis of thromboembolic prophylaxis following elective hip arthroplasty *(Freedman et al 2000)*[45]

Years: 1966 – 1998

Objectives:

To define the efficacy and safety of agents used for DVT prophylaxis in total hip arthroplasty patients – LMWH, warfarin, aspirin, low dose heparin (LDH) and IPC. No combination therapies were included.

Outcomes:

- 10,929 subjects in 52 studies: DVT outcomes were:
    - LMWH - 17.7%
    - IPC - 20.7%
    - Warfarin - 23.2%

These were the only agents that significantly decreased the risk of symptomatic PE.

- Anticoagulants were associated with the highest risk of minor and major wound bleeding
- IPC had the lowest risk of distal DVT (7.7%); risk of proximal DVT was 13.3%.
- IPC had the second lowest risk of symptomatic PE (0.26%) and lowest risk of minor wound bleeding (1.1%) and major wound bleeding (0%).
- IPC provided a superior balance of efficacy and safety, matched by warfarin.

Meta-analysis of effectiveness of intermittent pneumatic compression devices with a comparison of thigh-high to knee-high sleeves *(Vanek 1998)*[46]

Years: 1966 – 1996

Objectives:

To examine the effectiveness of IPC devices in the prevention of DVT and PE.

Outcomes:

- 57 papers reviewed
- IPC was more effective than placebo, AES and low dose heparin in preventing DVT. *(It was not clear if IPC was protective against PE as only 2 studies included ventilation/perfusion scans.)*
- IPC devices reduced the relative risk of DVT by:
    - 62% when compared with placebo
    - 47% compared with AES
    - 48% compared with heparin
    - 28% when compared with warfarin (not significant)
- IPC significantly decreased proximal and calf DVT in neurosurgery and major orthopaedic surgery.
- Knee-length sleeves reduced the relative risk by 64% compared to thigh-length garments at 56% concluding that no one method is superior to another.
- Meta-analysis clearly reveals that IPC devices are effective in reducing incidence of DVT in patients at moderate to high risk of DVT, and are probably more efficacious than AES or low dose heparin. A much larger number of patients would need to be studied to demonstrate the effect of IPC on PE incidence.

Haematological, biochemical and microbiological studies

Intermittent pneumatic compression in stable claudicants: effect on hemostasis and endothelial function *(Sutkowska et al 2009)*[27]

- The effect of IPC using the *Flowtron* Plus garment and AC 200 pump were evaluated.
- Blood coagulation parameters were assessed alongside walking distance in a group of 25 claudicants and results compared to a cohort of 11 healthy volunteers.
- Limb compression was found to increase levels of nitric oxide from the endothelium in both groups.
- Use of the *Flowtron* system also decreased platelet activity and decreased thrombin-antithrombin complex levels.
- IPC enhances the antithrombotic profile of the blood and stimulates release of nitric oxide from the endothelium that acts as a vasodilator and improves leg circulation.

Re-using intermittent pneumatic compression garments designed for single-patient use is a potential source of cross infection *(Tweed & Wigglesworth 2009)*[47]

- Bacterial bio-burden present on IPC garments from 3 different manufacturers examined & compared to the results of a sample of un-used (clean) garments.
- Used IPC garments (foot and leg) were collected from 3 unrelated hospital sites after a single-patient use.
- 94% of used garments carried some level of bioburden and 30% exceeded 100 colony-forming units (CFU).
- Used IPC garments carry a significant level of bioburden compared to clean (unused) garments

The influence of inflation rate on the hematologic and hemodynamic effects of intermittent pneumatic calf compression for deep vein thrombosis prophylaxis *(Morris et al 2006)*[48]

- A rapidly inflating IPC device (Aircast Venaflow™) was compared to a gentler IPC device (*Flowtron* DVT prophylaxis system) in a group of 20 male volunteers to determine if there were any differences in the haematological and haemodynamic profiles of the two IPC devices.
- Fibrinolytic and coagulation markers were obtained immediately before and after IPC therapy: blood velocity was assessed by Doppler to quantify the haemodynamic impact of the IPC devices.
- Both IPC systems reduced procoagulant activity but only *Flowtron* therapy significantly increased global fibrinolysis.
- Devices with rapid inflation profiles may not provide optimal DVT prophylaxis.

Systemic haemostasis after intermittent pneumatic compression. Clues for investigation of DVT prophylaxis and travellers thrombosis *(Giddings et al 2004)*[26]

- A volunteer, repeated measures, study investigated the haematological response to IPC using a *Flowtron* calf garment. Subjects (n=21) had peripheral blood samples obtained pre-treatment and after 60 and 120 minutes of IPC. Tests were repeated with the subjects resting and no IPC. Blood sampling technique, which can affect coagulation markers, was controlled to avoid confounding the results.
- The *Flowtron* Excel DVT Prophylaxis system elicited a beneficial haematological effect, suppressing pro-coagulant activation whilst enhancing fibrinolytic mechanisms.

Haematological, biochemical and microbiological studies - continued

Intermittent pneumatic compression for bariatric patients – the Huntleigh DVT60 compression garment *(Morris and Woodcock 2003)*[49]

- A haemodynamic evaluation took place in 3 subjects (1 UK; 2 USA) using DVT60 Bariatric Fit™ garments from ArjoHuntleigh. Subjects weighed between 150 kg and 210 kg.
- Blood flow augmentation, between 83% and 120%, was observed in the femoral and popliteal veins; similar to that for non-bariatric subjects.
- The compressibility of fat is not very different to that of most other body constituents and it is unlikely to prevent emptying of the veins.
- Evidence from these evaluations suggests that the DVT60 garment would provide as effective prophylaxis as the DVT10 or DVT20 garments.

Haematological and haemodynamic comparison of the Kendall A-V Impulse™ and the Huntleigh FP5000 Intermittent Pneumatic Foot Compression Systems *(Morris et al 2003)*[50]

- Despite differences in cuff design and inflation patterns, both systems increase fibrinolysis and prevention of venous stasis with no statistically significant differences.

Venous haemodynamics after total knee arthroplasty: evaluation of active dorsal to plantar flexion and several mechanical compression devices *(Westrich et al 1998)*[33]

- The haemodynamic effect of 7 different IPC systems (including the *Flowtron* Excel system) was examined in 10 patients who had a total knee arthroplasty at the Hospital for Special Surgery in New York City.
- The results indicated calf compression is sufficient for the augmentation of venous velocity….

"Based upon the results of our study, we doubt whether the addition of thigh compression is necessary"

The effect of the Kendall (Tyco) SCD™ and Huntleigh DVT30 garments on femoral and popliteal vein blood flow measurements *(Woodcock and Morris 2002)*[34]

- Popliteal and femoral vessels were scanned using duplex Doppler ultrasound in healthy volunteers with both *Flowtron* Excel DVT30 thigh-length and Tyco SCD thigh-length garments.
- Little difference was detected between the 2 systems with respect to the response in the femoral vein or the volume flow rate of blood ejected from the lower limb.
- The *Flowtron* system reduced venous flow to very low levels, indicating refilling of veins. This was not observed with the Tyco SCD System.
- The findings indicate that the Flowtron thigh-garment is more efficient than the Tyco SCD System at emptying veins.

Venous hemodynamic effects of pneumatic compression devices *(Proctor et al 2001)*[30]

- 15 healthy volunteers tested 9 different IPC pumps and 15 different compression garments from a total of 5 different suppliers. Venous haemodynamic parameters were assessed at the common femoral vein using duplex ultrasound.
- Although baseline velocities all changed, there was no significant difference in the haemodynamic outcomes with respect to compression cycle, type and length of garment.
- Neither the length of garment, nor the type of compression (rapid graduated sequential, graduated sequential and intermittent compression) affected the haemodynamic parameters of peak and mean velocity and peak volume flow.

Intermittent pneumatic compression devices of the foot: a comparison of various systems on femoral vein blood flow velocity augmentation in the supine and dependent, non-weight bearing positions *(Flam et al 2000)*[51]

- Four commercially available foot compression garments were evaluated in 4 healthy adult subjects: Kendall A-V Impulse™, KCI Plexipulse™ system, Currie ALP™ and *Flowtron* FP5000 systems. Blood velocity augmentation was measured at the femoral vein.
- Systems delivered an average of 32% blood velocity augmentation in the supine position except the Currie ALP System, which performed poorly compared to the other devices.
- In particular, the average velocity augmentation for the *Flowtron* FP5000 garment was 219.5% while the Currie ALP device was just 36.5% in a dependent non-weight bearing position.

The fibrinolytic effects of intermittent pneumatic compression. Mechanism of enhanced compression *(Comerota et al 1997)*[29]

- A study designed to quantify and clarify the mechanisms of fibrinolytic enhancement after 180-minutes of IPC and to also determine whether post-thrombotic subjects had the same capacity for fibrinolytic enhancement as normal subjects.
- There was a significant increase in fibrinolytic activity in both normal and post-thrombotic subjects.
- tPA levels only increased in normal subjects while decreases in PAI-1 were seen in both groups.
- Fibrinolytic activity was reduced significantly at baseline in post-thrombotic subjects compared with normal subjects.
- Following IPC, fibrinolytic activity of the post-thrombotic subjects only increased to the equivalent of the baseline level seen in the normal subjects.
- It is the balance of PAI-1 to tPA, which determines fibrinolytic activity. IPC induces a reduction in PAI-1, which in turn increases the availability of tPA

Blood flow augmentation of intermittent pneumatic compression systems used for the prevention of deep vein thrombosis prior to surgery *(Flam et al 1996)*[32]

- A prospective, randomly assigned, crossover study, using duplex ultrasonography to measure and compare blood velocity associated with the *Flowtron* DVT calf compression System and the Tyco SCD thigh compression System in 26 healthy volunteers.
- Average flow augmentation
  - 107% - *Flowtron* DVT system (superior)
  - 77% - Tyco SCD system.
- Peak compression velocity
  - 39.5 cm/sec *Flowtron* DVT system (significant)
  - 34.2 cm/sec Tyco SCD

DVT prophylaxis: comparison of two thigh-high intermittent pneumatic compression systems *(Flam et al 1993)*[33]

- This study was conducted to directly compare the femoral venous blood flow generated by 2 IPC devices, *Flowtron* DVT Prophylaxis System and the Tyco SCD System in 20 healthy subjects
- Peak compression velocity was equal and the *Flowtron* single-pulse IPC system produced a significantly higher (23%) venous blood flow augmentation than the vinyl sequential pulse system

Clinical outcome studies: *Flowtron* IPC Prophylaxis Systems

Over the past 30 years, a number of international clinical studies by independent specialists have compared ArjoHuntleigh's *Flowtron* DVT Prophylaxis systems (Figure 6) to other methods of DVT prophylaxis; these are reported in the next section. The results demonstrate that *Flowtron* IPC Therapy provides a cost-effective method of DVT prophylaxis while avoiding the humanitarian and financial cost associated with side effects such as bleeding.

Figure 6: *Flowtron* IPC Prophylaxis Systems

A meta-analysis of thromboembolic prophylaxis following elective hip arthroplasty *(Pagella et al 2007)*[52]

Design: Randomised controlled trial.

Objective: To evaluate whether patient comfort and satisfaction correlated to concordance in wearing IPC devices.

Setting: Trauma unit/orthopaedic medical-surgical unit.

Method: Two different types of effective IPC devices, Tyco SCD compression system (with thick plastic sleeves) and the *Flowtron* Excel system (with soft breathable garments), were randomly assigned to 65 patients to determine whether comfort and satisfaction correlated to compliance in wearing of the garments. The evaluation was driven by anecdotal reports that patients removed the plastic garments and so were exposed to DVT risk.

Results: The *Flowtron* DVT system was associated with better concordance (wear time), with greater satisfaction expressed by patients and clinicians.

Conclusion: The facility used the results objectively to switch to *Flowtron* DVT systems and noted a downward trend of VTE despite a rise in the number of hospital admissions.

Thromboembolism in patients undergoing total knee arthroplasty [TKA] with epidural analgesia *(Brooks et al 2007)*[53]

Design: A retrospective, consecutive chart review.

Objective: To compare the early post-operative VTE rates for orthopaedic patients undergoing unilateral or bilateral TKA.

Method:
Group 1: Spinal anaesthesia, LMWH and *Flowtron* DVT prophylaxis (calf garment).
Group 2: Epidural anaesthesia (indwelling catheter) and *Flowtron* DVT prophylaxis (calf garment).

All patients had early postoperative lower extremity ultrasound.

Results:
Group 1: Of 224 unilateral and bilateral TKA patients, 5 patients (2.2%) had a DVT.
Group 2: Of 157 patients, all bilateral TKA, 6 (3.8%) developed DVT.

There were no reported PE's in either group.

Conclusion: The data suggest that epidural analgesia with IPC alone is an effective method of post-operative pain control without a significant increase in DVT as compared to spinal anaesthesia followed by LMWH administration.

Venous thrombosis prophylaxis for urological laparoscopy: Fractionated heparin versus sequential compression devices *(Montgomery and Wolf 2005)*[54]

Design: Retrospective chart review.

Objective: To examine post-operative haemorrhagic and thrombotic complications after laparoscopic urological procedures in patients treated with LMWH or *Flowtron* DVT Prophylaxis System

Method:
Group 1: 172 subjects received 40 mg LMWH daily, starting peri-operatively.
Group 2: 172 subjects received thigh-length IPC applied immediately pre-operatively.

Symptomatic VTE was confirmed by ultrasound / radiology; patients were followed up for 3 months postoperatively.

Results: A total of 344 patients (172 in each group) were treated over a 30-month period: VTE outcomes were the same for both groups at 1.2%.

The LMWH group was significantly more likely to experience a major bleed (p = 0.045) and required more transfusions.

Conclusion: LMWH is associated with significantly increased haemorrhagic complications without a reduction in VTE. Mechanical compression devices are the prophylaxis of choice in this patient speciality.

Intermittent pneumatic compression in the prevention of venous thromboembolism in high-risk trauma and surgical ICU patients *(Kurtoglu et al 2005)*[55]

Design: Prospective study.

Objective: To evaluate the efficacy of *Flowtron* DVT Prophylaxis System in the prevention of VTE in high-risk surgical ICU patients (major abdominal surgery or multiple trauma) for whom anticoagulation is contraindicated.

Method: Patients were provided with a *Flowtron* Excel System. Venous duplex ultrasonography was performed on days 3 and 7 and again at discharge. Chest radiology was undertaken to screen for PE.

Results: Over a 9-month period 38 patients, with multiple trauma (n=21); major surgery (n=11) or gastrointestinal bleeding (n=6), were evaluated. No patient developed a DVT while one patient (2.6%) had an asymptomatic PE.

Conclusion: IPC is a safe and effective modality in preventing both DVT and PE in high-risk ICU patients: IPC should be used when there is a clear contraindication to chemoprophylaxis.

Venous thromboembolism prophylaxis after head and spinal trauma: Intermittent pneumatic compression devices versus low molecular weight heparin *(Kurtoglu et al 2004)*[56]

Design: Prospective randomised controlled clinical trial.

Objective: To compare the safety and efficacy of IPC and LMWH for DVT prophylaxis in Intensive Care Unit (ICU) patients with serious head and spinal trauma.

Method:
Group 1: IPC (e.g. *Flowtron* DVT prophylaxis).
Group 2: LMWH (enoxaparin).

All patients had daily leg circumference measured plus Doppler ultrasound on admission and weekly thereafter until 1-week post-discharge. Patients showing signs of continued cerebral bleeding were excluded from the study.

Results:
Group 1: 4 patients developed DVT and 2 patients a fatal PE.
Group 2: 3 patients developed a DVT and 4 patients a fatal PE. The VTE results were not statistically significant.

The IPC group required statistically significant (p = <0.03) fewer blood transfusions (0.9 ± 1.7) compared to the LWMH group (2.8 ± 1.3).

Conclusion: The data suggests that IPC was as effective as LMWH in decreasing the risk of DVT and PE. However, IPC carries no risk to the patient (haemorrhage), is non invasive and has a lower cost than LMWH and therefore may be the preferred option in head and spinal trauma.

Clinical outcome studies: Flowtron IPC Prophylaxis Systems - continued

Evaluating an intermittent compression system for thromboembolism prophylaxis *(Van Blerk 2004)*[57]

Design: Prospective study.

Objectives: To evaluate use and acceptance of the *Flowtron* Universal System in patients undergoing elective joint replacement surgery.

Method: High-risk VTE patients were provided with either a calf or foot garment, with or without anticoagulation and/or compression stockings as directed by the surgeon.

Results: 30 patients were recruited: 19 received calf garments, 10 had foot garments, and a single patient used a foot garment on the operative leg and a calf garment on the other. Half of the patients received mechanical prophylaxis alone. There were no VTE episodes reported.

Patients: Most (85%) found the *Flowtron* Universal System to be comfortable or very comfortable, with calf garments preferred over foot garments. This latter finding is not device specific and reflects the higher pressures required to empty the plantar plexus in foot compression.

Nurses: All 20 nurses rated the device highly positively due to its favourable ergonomics, lightweight, low vibration and noise and safety features.

Conclusion: Patient satisfaction led to good compliance and positive clinical outcomes in this high-risk group. Compared with chemical prophylaxis, the *Flowtron* Universal System offers a cost-effective solution while avoiding the potential complications of altered coagulation.

Randomized clinical trial of intermittent pneumatic compression and low molecular weight heparin in trauma *(Ginzburg et al 2003)*[58]

Design: Randomised controlled trial.

Objective: To compare the effects of LMWH versus IPC in severe trauma patients.

Method: 442 patients were prospectively randomised and treatment was continued until patients were walking independently or discharged.

Group 1: LMWH (enoxaparin 30 mg twice daily).
Group 2: *Flowtron* Excel System with DVT10 calf garments.

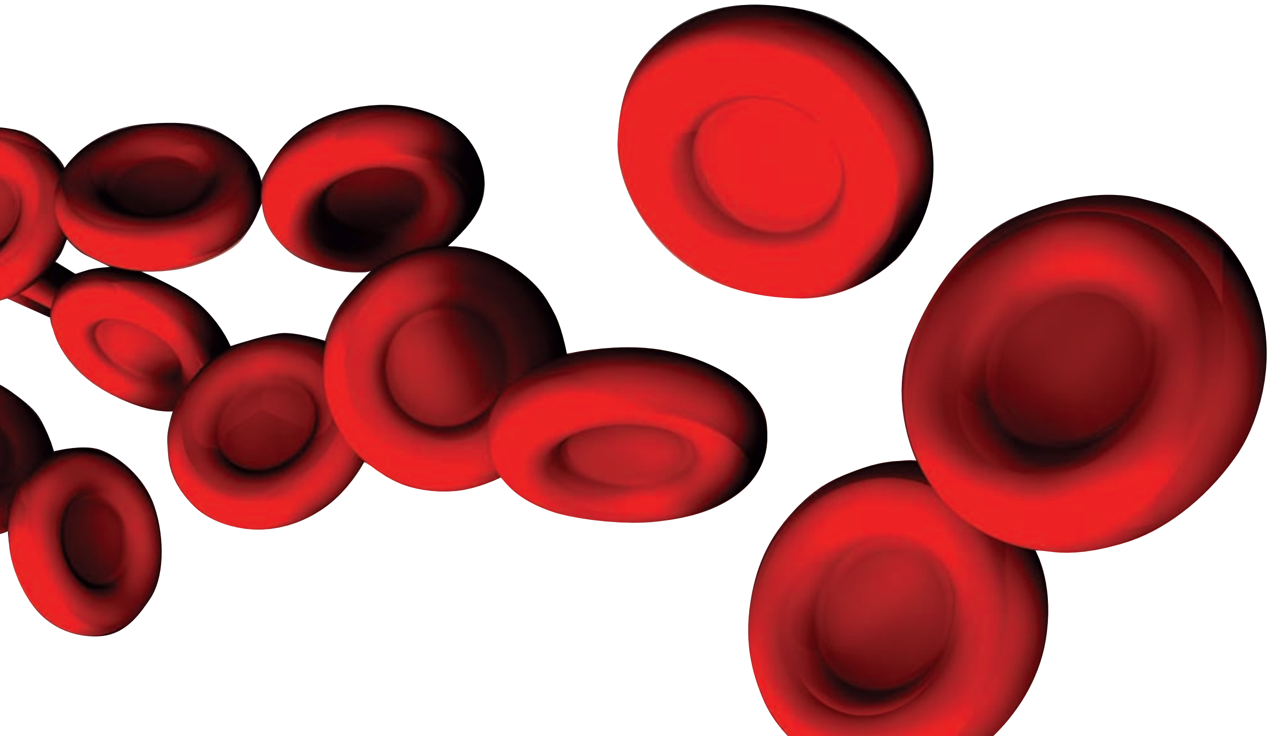
Duplex study of lower extremities was conducted on admission and weekly until discharge or at 30 days.

Results:
Group 1: DVT 2.7%; 1 patient had a PE.
Group 2: DVT 0.5%; 1 patient had a PE.

VTE rates were not statistically significant.

The cost of providing LMWH was US$73,000 compared to US$6,272 for the IPC representing a cost saving of $67,300 in the IPC group.

Conclusion: The low rate of thromboembolic events supports the use of IPC as a low cost alternative method of DVT prophylaxis in trauma patients.



A clinical comparison of pneumatic compression devices: The basis for selection *(Proctor et al 2001)*[59]

Design: Comparative evaluation.

Objective: To evaluate 5 IPC devices in surgical patients with respect to effectiveness, compliance, patient and nursing satisfaction, and potential clinical selection.

Method: 1350 patients were evaluated, using 5 manufacturers' devices, including the *Flowtron* Excel System and FP5000 System. Each manufacturer's device was tested for a 4-week period. Tests included venous duplex ultrasound, DVT risk assessment, device evaluation, compliance using pump meters, and ranking matrix for compression pattern. Patients were asked to complete 7 questions about acceptability including comfort, mobility, sleep interference and noise. Nurses also completed a questionnaire with questions including frequency of alarms, patient complaints and ease of use.

Results: The *Flowtron* Excel System with calf garments was ranked the best with respect to DVT rate with only a 1.1% incidence. It also ranked highest in the patient and nurse satisfaction surveys and gained the highest compliance rates.

Conclusion: This is the largest known study to have evaluated all marketed IPC devices. ArjoHuntleigh was awarded the contract for IPC at the University of Michigan hospitals based upon clinical outcomes and patient/nurse satisfaction.

External pneumatic compression therapy for DVT prophylaxis *(Capper 1998)*[60]

Design: Retrospective & prospective audit.

Objective: To evaluate the effectiveness of the *Flowtron* DVT System in the prophylaxis of DVT in elective hip and knee surgery, compared to the previous use of anticoagulants in elective hip and knee replacements.

Method:
Retrospective group: 825 patients received LDH, LMWH or hydroxychloroquine.
Prospective group (IPC): 375 patients had *Flowtron* calf garments worn pre-operatively until discharge.

All patients were mobilised after 48 hours.

Results:
Retrospective group: VTE rate was 2.6%.
Prospective group (IPC): VTE rate was 1.06%.

The *Flowtron* garments were well tolerated by patients with no risk of haematoma or bruising, whilst proving to be cost effective.

Conclusion: When selecting a method of DVT prophylaxis, clinical effectiveness, patient comfort, reduction of the risk of infection, and compliance with treatment all need to be considered. The benefits of IPC warrant serious consideration.

Pneumatic sequential compression reduces the risk of deep vein thrombosis in stroke patients *(Kamran et al 1998)*[61]

Design: Three-phase study.

Objective: To determine if IPC combined with subcutaneous heparin and AES reduces the risk of thromboembolic disease in acutely hospitalised patients with non-haemorrhagic stroke.

Method:
Group 1: retrospective review of 233 stroke patients who received sub-cutaneous heparin and AES.

Group 2: prospective study of 432 subjects who received the same prophylaxis as group 1 but with the addition of IPC (calf garments) for non-ambulatory patients.

Group 3: prospective study of 16 patients who were given the same therapy as group 1.

Results: Using additional IPC for non-ambulatory stroke patients reduced the incidence of VTE by more than 40 times.

Conclusion: Non-ambulatory stroke patients have an increased risk for DVT and PE and using *Flowtron* therapy can significantly reduce this risk without appreciably increasing patient care cost. IPC should be considered for adjunctive DVT prophylaxis in all non-ambulatory stroke patients.

Clinical outcome studies: Flowtron IPC Prophylaxis Systems - continued

Sequential mechanical and pharmacological thromboprophylaxis in the surgery of hip fractures
(Eskander et al 1997)[62]

Design: Randomised controlled trial.

Objective: To compare combined therapy (IPC and LMWH) with LMWH alone in traumatic femoral neck fracture patients.

Method:
Group 1: IPC (calf) until 48 hours post-operatively, then enoxaparin to day 7.

Group 2: Enoxaparin from admission to day 7.

Blood transfusions, wound drainage and haemoglobin levels were reported pre-operatively, then on days 2 and 7. Colour duplex Doppler scans of the femoral and popliteal venous system were carried out post-operatively at weeks 1 and 6.

Results:
Group 1: VTE occurred in 14% of patients.

Group 2: VTE occurred in 17% of patients.

There was no significant fall in haemoglobin, or difference in operative field, but group 1 had less wound drainage (mean 314 ml), compared to group 2 (mean 402 ml).

Conclusion: The study demonstrated the benefit of using a combination of *Flowtron* Excel System in the peri-operative period, followed by pharmacological treatment during mobilisation. IPC avoids the peri-operative complications associated with pharmacological agents.

A comparison of intermittent calf compression and enoxaparin for thromboprophylaxis in total hip replacement
(Stone et al 1996)[63]

Design: Randomised controlled trial.

Objective: To compare enoxaparin with IPC in elective primary hip replacement.

Method: 50 patients were randomised to either group.
Group 1: IPC with *Flowtron* DVT Prophylaxis (calf garment).

Group 2: Enoxaparin 40 mg daily.

Operative field bleeding was monitored, as were haemoglobin levels pre-operatively and on days 2 and 5. Blood loss into drains, blood transfusions, infection and haematoma were also recorded. All patients underwent a colour duplex ultrasound scan at weeks 1 and 6 post-operatively to assess for popliteal and femoral thrombus.

Results: One DVT was detected in each group.

Group 1: The operative field was judged by the surgeons to be drier in IPC group, with no significant wound drainage or haemoglobin difference: 3 patients required blood transfusions.

Group 2: 7 patients receiving Enoxaparin required blood transfusions.

Conclusion: “The use of intermittent calf compression garments is a safe method of prophylaxis for general use in a unit performing total hip replacement.”

A prospective study on intermittent pneumatic compression in the prevention of deep vein thrombosis in patients undergoing total hip or total knee replacement
(Pidala et al 1992)[64]

Design: Prospective study.

Objective: To evaluate the effectiveness of IPC (*Flowtron* Systems) as a cost effective method for preventing DVT in elective hip and knee replacement patients.

Method: 112 patients undergoing elective hip replacements and 234 patients undergoing total knee replacements all received IPC pre-operatively through to discharge. Venous Doppler ultrasound and impedance plethysmography were performed pre-operatively and on days 4 and 7 post-operatively.

Results: DVT was found in 8/112 total hip replacement patients, and 6/234 total knee replacement patients, giving an incidence of 4%. No PE were diagnosed.

Conclusion: The study supports the use of the *Flowtron* System in patients undergoing total hip and total knee replacements.

Independent Technology Review

Intermittent pneumatic compression devices –ECRI evaluation *(2007[65] & 2009[6])*

- ECRI (www.ecri.org) is a North American, independent, organisation that undertakes medical device evaluations as well as offering guidance on patient safety, quality and risk management issues. The ECRI mission is to research the best approaches for safety, quality and cost effectiveness in healthcare.
- In June 2007, a 28-page detailed evaluation report of IPC devices was published. The following devices were tested and rated:
  - Aircast VenaFlow™ system
  - *Flowtron* Excel system and the *Flowtron* Universal system
  - KCI Plexipulse™ all-in-1 system and Pulse SC™ system
  - Tyco S.C.D EXPRESS™ system and S.C.D Response™ system
- Each product was evaluated using specific and detailed parameters: patient safety, ease of use, patient comfort, performance, quality of construction and battery (if applicable). Detailed reports are given of the testing procedures and ratings achieved as well as an overall recommendation.
- The *Flowtron* Universal system was the "Top Choice", best overall product tested and is the (single) preferred IPC product on the market. Patient safety and ease of use were evaluated as excellent. Patient comfort, product performance and construction of the product were rated as good. The *Flowtron* Excel system was rated as "worth considering" offering good performance.
- The report highlights that there is currently no reason to believe that one type of IPC therapy (uniform or sequential; calf or thigh) is more effective than any other in preventing deep vein thrombosis. Therefore, the type of therapy a device provides is not necessarily a significant factor when deciding among models. Instead, choice should be based on the other factors such as product performance, ease of use, patient comfort, adequate safety features and quality of construction.
- A second literature review undertaken in 2009 focused on studies comparing IPC devices with different sleeve types and compression cycles. ECRI comment that their position remains the same, IPC is effective in general but no evidence identified that any one type of IPC therapy or device is superior.

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