



House of Commons
Health Committee

The Prevention of Venous Thromboembolism in Hospitalised Patients

Second Report of Session 2004–05

*Report, together with formal minutes, oral and
written evidence*

*Ordered by The House of Commons
to be printed 23 February 2005*

HC 99
Published on 8 March 2005
by authority of the House of Commons
London: The Stationery Office Limited
£15.50

The Health Committee

The Health Committee is appointed by the House of Commons to examine the expenditure, administration, and policy of the Department of Health and its associated bodies.

Current membership

Mr David Hinchliffe MP (*Labour, Wakefield*) (Chairman)

Mr David Amess MP (*Conservative, Southend West*)

John Austin MP (*Labour, Erith and Thamesmead*)

Mr Keith Bradley MP (*Labour, Manchester Withington*)

Simon Burns MP (*Conservative, Chelmsford West*)

Mrs Patsy Calton MP (*Liberal Democrat, Cheadle*)

Jim Dowd MP (*Labour, Lewisham West*)

Mr Jon Owen Jones MP (*Labour, Cardiff Central*)

Siobhain McDonagh MP (*Labour, Mitcham and Morden*)

Dr Doug Naysmith MP (*Labour, Bristol North West*)

Dr Richard Taylor MP (*Independent, Wyre Forest*)

Powers

The Committee is one of the departmental select committees, the powers of which are set out in House of Commons Standing Orders, principally in SO No 152. These are available on the Internet via www.parliament.uk.

Publications

The Reports and evidence of the Committee are published by The Stationery Office by Order of the House. All publications of the Committee (including press notices) are on the Internet at www.parliament.uk/parliamentary_committees/health_committee.cfm. A list of Reports of the Committee in the present Parliament is at the back of this volume.

Committee staff

The current staff of the Committee are Dr David Harrison (Clerk), Keith Neary (Second Clerk), Laura Hilder (Committee Specialist), Christine Kirkpatrick (Committee Specialist), Frank McShane (Committee Assistant), Darren Hackett, (Committee Assistant), and Rowena Macdonald (Secretary).

Contacts

All correspondence should be addressed to the Clerk of the Health Committee, House of Commons, 7 Millbank, London SW1P 3JA. The telephone number for general enquiries is 020 7219 6182. The Committee's email address is healthcom@parliament.uk.

Footnotes

In the footnotes of this Report, references to oral evidence are indicated by 'Q' followed by the question number. Written evidence is cited by reference in the form 'Ev' followed by the page number.

Contents

Report	<i>Page</i>
Summary	3
Glossary of terms	5
1 Introduction	7
2 The problem	9
What is venous thromboembolism?	9
Causes of venous thrombosis	10
Risk of venous thrombosis during surgery	11
Other risk areas for venous thrombosis in hospitalised patients	11
Cost of VTE to the nation	11
3 Availability of prophylaxis and current guidelines	13
Available prophylaxis	13
Efficacy of prophylaxis	14
Current guidelines	14
4 The current use of prophylaxis	17
Lack of awareness of the problem	17
Concerns about bleeding	18
Belief that VTE is no longer a problem	19
Inconsistent guidelines	19
Problems of funding	19
Department of Health	20
What should be done to improve the situation?	20
Education and awareness	20
Establishing guidelines	21
Counselling and risk assessment	23
Implementation of the guidelines	24
Thrombosis committees and thrombosis teams	26
Conclusions and recommendations	29
List of abbreviations used in the report	28
Formal Minutes	31
Witnesses	32
List of Written evidence	33
List of unprinted written evidence	34

Summary

Each year over 25,000 people in England die from venous thromboembolism (VTE) contracted in hospital. This is more than the combined total of deaths from breast cancer, AIDS and traffic accidents, and more than twenty-five times the number who die from MRSA. The figures are alarmingly high. Even more alarming is the fact that many of these deaths are preventable. There is a safe, efficacious and cost effective method of preventing venous thrombosis which is not being as widely administered as it should be.

There are various reasons for this situation. Witnesses told us that many physicians and surgeons were not aware of the extent of VTE. A substantial number of patients who develop VTE first show signs that they have the disease after they have been discharged from hospital. As a result the original physician or surgeon who treated the patient in hospital is often not informed that their patient suffered from the condition after leaving their care. Moreover, there are no national guidelines which would ensure that doctors consider the risk of VTE and the availability of prophylaxis.

The Department of Health has now commissioned the National Institute of Clinical Excellence to produce a set of guidelines for the administration of preventative measures which are expected to be published in May 2007. This is a remarkably tardy response to a serious situation and, moreover, the scope of the guidelines commissioned by the Department is limited to a subset of surgical patients, while the majority of sufferers are non-surgical patients. In contrast, in the United States the American College of Chest Physicians has recently published the 7th revision of their guidelines which were first produced in 1986. Based upon the effectiveness of the intervention and the cost-effectiveness of applying that intervention, routine thromboprophylaxis for appropriate potential groups in hospital was ranked the number one most important safety practice in that country by the US Health Agency for Research and Quality.

We recommend that the NICE VTE guidelines be extended in scope to cover the majority of hospital patients. We further recommend that on admission to hospital all patients, both medical and surgical, be counselled about the risks of VTE and undergo a risk assessment to determine if prophylaxis, to help prevent the onset of venous thrombosis, should be administered. To raise awareness among medical practitioners of the extent of the problem we recommend that all physicians and surgeons are informed if their patients contract VTE after they have been discharged from hospital.

During the inquiry we heard serious doubts as to the extent to which the guidelines will be implemented when they finally become available. This is a recurring problem which the Committee has come across in several inquiries. Accordingly, our report makes recommendations to ensure their effective implementation. The Department, NICE and the Royal Colleges should work together to raise awareness of the extent of VTE and to audit the use of the guidelines. Our most important recommendation is that thrombosis committees and thrombosis teams should be established in each hospital to promote best practice now, using accepted guidelines adapted for local practice, and to be a source of education and training for all staff dealing with patients at risk of VTE. When NICE guidelines are published the committees and teams will be in place to ensure adherence.

They should be modelled on the effective teams and committees dedicated to improving the use of blood transfusion. Finally we recommend that the Healthcare Commission audit the availability and use of venous thrombosis prophylaxis in hospitals.

Glossary of terms

Venous Thrombosis (VT): A condition in which a blood clot (thrombus) forms in a vein.

Deep Vein Thrombosis (DVT): venous thrombosis that occurs in the “deep veins” in the legs, thighs, or pelvis.

Pulmonary Embolism (PE): A blood clot that breaks off from the deep veins and travels round the circulation to block the pulmonary arteries (arteries in the lung). Most deaths arising from DVT are caused by PE.

Venous Thromboembolism (VTE): The blocking of a blood vessel by a blood clot dislodged from its site of origin. It includes both DVT and PE.

Prophylaxis: A measure taken for the prevention of a disease.

Thromboprophylaxis: A measure taken to prevent thrombosis.

Post-thrombotic (Post-phlebitic) Syndrome: Chronic pain, swelling, and occasional ulceration of the skin of the leg that occur as a consequence of previous venous thrombosis.

1 Introduction

1. In the UK Pulmonary Embolism (PE) following Deep Vein Thrombosis (DVT) in hospitalised patients causes between 25,000 and 32,000 deaths each year.¹ It is the immediate cause of death in 10% of all patients who die in hospital.² The figure exceeds the combined total of deaths from breast cancer, AIDS and traffic accidents.³ It is over twenty-five times greater than the 955⁴ annual deaths from MRSA and more than five times the total of all hospital acquired infections. The total cost (direct and indirect) to the UK of managing VTE is estimated at £640 million.⁵ Even more alarming than the scale of the problem is the fact that VTE in hospitalised patients is largely preventable through the use of thromboprophylaxis during the hospital stay of the patient and, in some cases, continuing after discharge. A study in over 4,000 patients who died of PE following major surgery, demonstrated that the use of perioperative⁶ low dose heparin⁷ reduced the frequency of fatal PE from 8 per 1000 to 1 per 1000 patients operated on — saving 7 lives per 1000 patients operated on.⁸ Thus thousands of lives could readily be saved by the use of a tried and tested treatment.

2. In view of the number of deaths from VTE and the apparent failure to apply the remedy on an appropriate scale, we decided in November 2004 to hold an inquiry with the following terms of reference:

The Committee will undertake a short inquiry into the prevention of venous thromboembolism in hospitalised patients.

We deliberately excluded from our terms of reference consideration of DVT in long haul air passengers, which has been the subject of considerable concern and attention recently.

3. On 9 December 2004 we took oral evidence from Mrs Linda de Cossart and Mr David Warwick, both representing the Royal College of Surgeons; Professor Ajay Kakkar, Barts and the London Medical School; Dr David Keeling, representing the Royal College of Physicians; Dr Beverley Hunt, representing Lifeblood: the Thrombosis Charity; Dr Roger Boyle, Department of Health (hereafter ‘the Department’); Professor Sir Michael Rawlins and Professor David Barnett, both of the National Institute of Clinical Excellence; and Professor David Cousins, National Patient Safety Agency. In addition we received written memoranda from a variety of professional bodies, companies, charities and clinicians. We are most grateful to all who provided written or oral evidence.

¹ Ev 14

² Ev 9, Ev 14, Ev 55 and Ev 70

³ Ev 66

⁴ Health Statistics Quarterly Spring 2005, National Statistics, 24 February 2005

⁵ Ev 69

⁶ Perioperative - Around the time of surgery; usually lasts from the time of going into the hospital or doctor's office for surgery until the time the patient goes home.

⁷ Low dose heparin – 5,000 international units given by subcutaneous injection three times daily

⁸ Ev 10

4. Our specialist adviser in this inquiry was Professor K John Pasi, Professor of Haemostasis and Thrombosis and Honorary Consultant Haematologist at Barts and the London, Queen Mary's School of Medicine, University of London. We wish to express our gratitude to Professor Pasi for his help on technical matters, for giving us the benefit of his knowledge of the treatment of venous thromboembolism, and for the enthusiasm and expertise with which he assisted us at the evidence session.

2 The problem

What is venous thromboembolism?

5. Venous thrombosis is a condition in which a blood clot (thrombus) forms in a vein. Blood flow through the affected vein can be limited by the clot, causing swelling and pain. Venous thrombosis most commonly occurs in the “deep veins” in the legs, thighs, or pelvis. This is known as a deep vein thrombosis. An embolism is created if a part or all of the blood clot in the deep vein breaks off from the site where it is created and travels through the venous system. If the clot lodges in the lung a very serious condition, pulmonary embolism (PE), arises. Untreated PE has a mortality rate of 30%, treated the mortality rate is reduced to 2%.⁹ Venous thrombosis can form in any part of the venous system. However, deep vein thrombosis (DVT) and PE are the most common manifestations of venous thrombosis. DVT and PE are known as venous thromboembolism (VTE).

6. VTE is common and a cause of many deaths in hospitalised patients. Table One presents some remarkable and shocking information about the incidence of DVT. For example, 45 to 51% of patients undergoing orthopaedic surgery develop DVT if they are not provided with thromboprophylaxis. Until the recent introduction of guidelines produced by the Royal College of Obstetricians and Gynaecologists (RCOG), thromboembolism was the single biggest killer of pregnant women.¹⁰

Table 1: Incidence of DVT by specialities

Speciality	DVT % (weighted mean)
General Surgery	25
Orthopaedic surgery	45-51
Urology	9-32
Gynaecological surgery	14-22
Neurosurgery. including strokes	22-56
Multiple trauma	50
General medicine	17 ¹¹

Data - International Consensus Statement 1997/2002¹²

⁹ www.surgical-tutor.org/system/vascular/venous_thromb.htm

¹⁰ “Why Mothers Die 2000-2002”, *CEMACH*, November 2004

¹¹ Average of all medical cases

¹² Ev 55

7. VTE is recognised internationally to be a serious health issue. Research in Australia has found that the incidence of VTE is 135 times greater in hospitalised patients than the community. The Australian National Institute for Clinical Studies has identified the under use of preventative measures as a clinical priority.¹³ In France all patients who undergo a joint replacement receive preventative treatment¹⁴ and the French Government has set a target to reduce the incidence of VTE by 15%.¹⁵

Causes of venous thrombosis

8. There are many reasons for people to be at an increased risk of developing a blood clot. Inherited thrombophilia refers to a genetic problem affecting 1 in 20 of the population¹⁶ that causes the blood to clot more easily than it should. There are a number of other acquired conditions which can cause a person to be at increased risk of developing a venous thrombosis. The risk factors — typically, there is more than one factor affecting any given patient — can now be identified in over 80% of patients with venous thrombosis. The acquired risk factors for VTE are well-defined and include:

- previous surgery (especially orthopaedic surgery and neurosurgery) trauma
- pregnancy
- obesity
- use of certain medications, including birth control pills, hormone replacement therapy, or tamoxifen
- immobilisation
- cancer
- heart failure
- elevated blood levels of homocysteine (partially genetic)
- certain disorders of the blood, such as polycythemia vera or essential thrombocythemia
- kidney problems, such as nephrotic syndrome
- antiphospholipid antibodies (antibodies in the blood that can affect the clotting process)
- a previous episode of thromboembolism, such as a clot in the leg (deep vein thrombosis) or lung (pulmonary embolism).

We were told that smoking and increased age may also increase the risk of venous thromboembolism, but it is uncertain what role these factors play.

¹³ "Preventing venous thromboembolism in hospitalised patients", *National Institute of Clinical Studies*, 2003

¹⁴ Q14 (Mr Warwick)

¹⁵ Ev 15

¹⁶ "Investigation and Management of Heritable Thrombophilia", *British Journal of Haemophilia*, Vol 114 (2001), pp 512-528 and "World distribution of factor V Leiden", *Lancet*, Vol 346 (1995), pp 1133-34

Risk of venous thrombosis during surgery

9. Before the introduction of specific preventative measures almost one third of all surgical patients developed a DVT.¹⁷ Without prophylaxis the rate of fatality from a PE after hip and knee replacement is approximately 0.4%. While this may appear to be a low figure, with 1.25 million hip and knee replacements in Europe each year this represents 5,000 fatalities annually.¹⁸

Other risk areas for venous thrombosis in hospitalised patients

10. There has been more emphasis on the occurrence and prevention of VTE in surgical, especially orthopaedic, patients, but the majority of hospitalised patients who experience VTE are medical patients. The risk of developing DVT in certain patients immobilised with a medical illness is high. We were informed that patients at particular risk for the development of VTE in an acute medical illness include those with severe heart failure, chronic respiratory disease, sepsis and cancer.¹⁹ Historically, approximately 40-50% of patients admitted with stroke or myocardial infarction²⁰ developed detectable venous thrombosis without prophylaxis. Professor David Barnett, Chair of the Appraisals Committee of NICE, told us that “70 to 80 per cent of...venous thrombosis may be in non-surgical cases.”²¹ A recent trial has shown that even ‘moderate risk’ medical patients admitted to hospital have a 15% chance of developing detectable venous thrombosis after 14 days.

11. Cancer patients are at particular risk. Those who develop a thrombosis are at three times greater risk than a non-cancer patient of getting a recurrent thrombosis and are more susceptible to significant bleeding complications while receiving treatment for thrombosis. Professor Kakkar, Professor of Surgical Science and Consultant Surgeon, stated that this: “has a devastating impact on their quality of life.”²²

Cost of VTE to the nation

12. Estimates of the number of deaths in the UK due to VTE vary. The evidence we received put the figures at between 24,000²³ and 32,000²⁴ per year. Precise numbers are difficult to gauge because many deaths are not followed up by a post-mortem.²⁵ As a result the number of deaths resulting from VTE is probably underestimated. Deaths caused by VTE are recorded as having another cause, such as acute respiratory problem or a heart attack. A consequence is that it would be difficult to monitor the progress made through any initiatives to decrease the number of deaths from VTE.

¹⁷ Ev 14

¹⁸ Ev 1

¹⁹ Ev 11

²⁰ Myocardial infarction - destruction of heart tissue resulting from obstruction of the blood supply to the heart muscle

²¹ Q86 (Professor Barnett)

²² Q 46

²³ Ev 66

²⁴ Ev 14

²⁵ Qq 4, 5, 6 (Mrs de Cossart), 59, 60

13. We were told that the problem has been caused in part by the fall in the number of post-mortems undertaken since the Alder Hey scandal. Hospital post-mortem rates have declined and coroners are no longer demanding such thorough investigation of deaths. **We are concerned that the number of post-mortems being performed has decreased since Alder Hey. As a result the true cause of death is not being determined in many cases. We recommend that the Department encourage the increased use of post-mortems where appropriate. This would enable accurate identification of the cause of death in more patients and more reliable assessment of the current incidence of death through VTE, thereby providing a base from which to monitor progress.**

14. VTE is very costly. Most patients with VTE require one or more diagnostic tests, treatment with the anticoagulant heparin (low molecular weight heparin [LMWH] or unfractionated heparin) and a variable or prolonged hospital stay (if already an inpatient) and then subsequent oral anticoagulation with attendant regular hospital visits and blood tests.²⁶

15. The Office for Healthcare Economics estimated in 1993 that the annual cost in the UK of treating patients who developed post-surgical DVT and PE was in the region of £204.7 to £222.8 million.²⁷ The total cost (direct and indirect costs) to the UK for the management of VTE is currently estimated at approximately £640 million.²⁸

16. In addition to the cost associated with the initial treatment of VTE there are significant costs to the NHS for the long-term treatment of patients who develop the disease. The International Consensus Statement stated that approximately 25% of patients who have in the past suffered from deep vein thrombosis would later in life develop the debilitating condition of venous leg ulceration.²⁹ They estimated that the annual costs of the treating venous leg ulcers in the UK were in the region of £400 million.³⁰

²⁶ "Low Weight Molecular Heparin in Preventing and Treating DVT", *American Family Physician*, 15 March 1999

²⁷ Ev 61 and see Alexander Cohen comments about costs (Ev 69)

²⁸ Ev 69

²⁹ "Prevention of Venous Thromboembolism. International Consensus Statement. (Guidelines According to Scientific Evidence)", *Int Angiol*, 1997, 16(1), pp 3-38

³⁰ Ev 61

3 Availability of prophylaxis and current guidelines

Available prophylaxis

17. Lifeblood informed us: “There is a huge body of research showing that use of specific treatments to prevent clots (thromboprophylaxis) reduces the frequency of death and post phlebotic syndrome³¹ substantially if given at times of high risk such as after surgery or during an in-patient stay.”³² Thromboprophylaxis is available in both mechanical and pharmacological form.

18. For patients with moderate to low risk of blood clots mechanical prophylaxis may be used instead of, or in combination with, pharmacological prophylaxis. For example, some surgical and medical patients may be treated with special plastic devices that fit around the legs and fill with air, exerting gentle pressure, which boost circulation and helps prevent clots. Mechanical methods of thromboprophylaxis include pneumatic calf compression and compression stockings. A systematic review of trials using such methods indicated that mechanical thromboprophylaxis did reduce the frequency of DVT, but these methods have not been as extensively investigated as pharmacological thromboprophylaxis and have not been shown to reduce the frequency of fatal pulmonary embolism.³³

19. Mechanical prophylaxis may also be considered in general surgical patients at high risk for bleeding.³⁴ However Mr David Warwick, Consultant Hand and Orthopaedic Surgeon at Southampton University Hospital NHS Trust, in his written evidence stated:

The advantages of mechanical prophylaxis such as the Foot Pump (no bleeding side effects, no interactions, reasonable efficacy) must be weighed against the disadvantages (compliance, refitting when mobilising, impracticality of extended use). A sensible approach would be to use the Foot Pump as soon as possible after injury or surgery and then to switch to chemical prophylaxis once the risk of bleeding has subsided and for as long as the risk of thromboembolism pertains.³⁵

20. The most common form of prophylaxis used in England is pharmacological. Surgical patients (especially those undergoing orthopaedic surgery) and medical patients classified as medium or high risk may be given anticoagulants to decrease the risk of blood clots. Anticoagulants may also be given to pregnant women at high risk of venous thrombosis during and after their pregnancy. Pharmacological agents for thromboprophylaxis include unfractionated heparin, LMWH, thrombin inhibitors, oral anticoagulants, and specific factor Xa inhibitors. Studies have shown that low-dose unfractionated heparin and LMWHs are an effective and safe prophylaxis for deep vein thrombosis. They have proven safe and cheap, and do not require laboratory monitoring and their cost is low.

³¹ The Post Phlebotic Syndrome occurs following a blood clot in the vein to the leg (Deep Vein Thrombosis).

³² Ev 14

³³ Ev 11

³⁴ Ev 11

³⁵ Ev 3

Efficacy of prophylaxis

21. Most importantly, the use of prophylaxis for VTE is efficacious. As we have seen, the risk of developing DVT after hip replacement surgery has been estimated to be as high as 50% of patients when thromboprophylaxis is not used. The use of appropriate thromboprophylaxis can reduce this risk to between 10 and 15% of patients. The risk of developing DVT in certain patients immobilised with a medical illness is also high. There is now evidence that combining mechanical and pharmacological thromboprophylaxis in some situations can reduce death and morbidity rates, and increase efficacy without increasing the risk of bleeding.³⁶ In general medical patients, including heart failure and respiratory failure patients, both unfractionated heparin and LMWH have been shown to be effective in reducing the risk of venous thromboembolism. Low dose heparin has been shown to be effective in acute myocardial infarction.³⁷ The administration of a thromboprophylaxis before general or orthopaedic surgery, or during medical treatment is also very cost-effective.³⁸

22. Many surgeons now advocate that prophylaxis after joint replacement should continue after the patient is discharged from hospital (extended prophylaxis), especially now that patients often leave hospital before regaining full mobility. The duration of extended prophylaxis depends on the risk category of the patient and the treatment that is undertaken. Extended prophylaxis normally lasts for five weeks but in high risk patients, or in those who have previously experienced DVT, prophylaxis can be administered for a significantly longer period.

23. While our witnesses agreed that thromboprophylaxis for patients while in hospital was cost-effective, there was some dispute as to whether this was true of prophylaxis for patients after they had been discharged. Apart from the cost of the drugs, concerns were expressed about its administration, because it has to be injected. Some discharged patients cannot, or will not, self-inject subcutaneous LMWH. Additional costs, and demands on scarce resources, may be incurred through the use of district nurses to visit and administer the drug to those patients who will not self-administer.³⁹

24. Despite this uncertainty, there is little doubt about the efficacy of thromboprophylaxis. The United States Agency for Health Care Research and Quality recently undertook a process that ranked 79 safety practices in hospitals. Based upon the effectiveness of the intervention and the cost-effectiveness of applying that intervention, routine thromboprophylaxis for appropriate patient groups in hospital was ranked the number one most important safety practice.⁴⁰

Current guidelines

25. For some specialities in the UK and in other countries, effective VTE guidelines already exist. A number of professional bodies have analysed results from clinical trials and

³⁶ Ev 70

³⁷ "Venous Thromboembolism: pathophysiology, clinical features, and prevention", *BMJ* 2002; 325, pp 887-890

³⁸ Q 15

³⁹ Q 37

⁴⁰ Q 12

produced guidelines that make recommendations for the prevention of VTE. The guidelines consider which groups of hospital patients should receive thromboprophylaxis, how it should be administered and the type of drug or other methods that should be used. An assessment of the level of risk for specific patient groups forms a basis for each recommendation and a grading based on the strength of the clinical evidence that supports it is supplied.

26. The Royal College of Obstetricians and Gynaecologists have drawn up and successfully implemented a series of guidelines for different types of thromboprophylaxis and for the treatment of venous thromboembolism during pregnancy. These include:

- Venous Thrombosis and Hormonal Contraception
- Hormone Replacement Therapy and Venous Thrombosis
- Thromboprophylaxis during Pregnancy, Labour and after Vaginal Delivery

An essential element in the wide-acceptance of these guidelines within the obstetric community was that they were introduced and supported by obstetricians themselves.⁴¹

27. Other guidelines have been introduced outside England and Wales. The most comprehensive on the prevention of VTE currently available are the seventh American College of Chest Physicians (ACCP) guidelines.⁴² These provide multiple recommendations based on evidence drawn from about 800 references. They are considered by many as “state of the art” within the field. Guidelines were also developed in Scotland after the Scottish Intercollegiate Guidelines Network (SIGN) identified the need for a national guidance on prophylaxis following a study of fatal PE in surgical patients up to 1995. The study showed that 56% of patients who died of PE did not receive thromboprophylaxis, despite having major risk factors and no contraindications to standard thromboprophylaxis.⁴³ Some hospitals and Strategic Health Authorities have also developed local protocols based upon existing guidelines, in particular those of SIGN and ACCP.

28. A key part of any guidelines is the incorporation of risk factors. Those for VTE are well defined — immobility, acute illness, major surgery (especially long operations) and orthopaedic surgery, malignancy, pregnancy, increasing age and obesity. The overall risk is increased further where the patient has several risk factors.⁴⁴ Risk assessment has been identified in the guidelines as an important process for administration of thromboprophylaxis. When determining if patients require thromboprophylaxis physicians and surgeons classify patients into risk factor groups to determine their potential susceptibility to VTE and then establish if thromboprophylaxis is recommended for the patient. Patients can be classified into one of three (or four — depending on which guidelines are being followed) risk factor groups, low, medium or high (highest). The

⁴¹ Q 87 (Sir Michael Rawlins)

⁴² “The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy: Evidence-Based Guidelines”, *Chest*, 2004, Vol:126, Supplement 3, pp 3385-4005. i.e. these are the 7th revision; the first guidelines were issued in 1986

⁴³ Prophylaxis of Venous Thromboembolism, <http://www.sign.ac.uk/guidelines/fulltext/62/index.html>

⁴⁴ Ev 14

resultant categorisation is used to determine the relevant prophylaxis to be administered to the patient. An example of the type of categorisation is given below.

- Low risk
 - Minor surgery (<30 min⁴⁵) + no risk factors other than age
 - Major surgery (> 30 min), age <40 yrs + no other risk factors
 - Minor trauma or medical illness

- Moderate risk
 - Major general, urological, gynaecological, cardiothoracic, vascular or neurological surgery + age >40 yrs or other risk factor
 - Major medical illness or malignancy
 - Major trauma or burn
 - Minor surgery, trauma or illness in patients with previous DVT, PE or thrombophilia

- High risk
 - Fracture or major orthopaedic surgery of pelvis, hip or lower limb
 - Major pelvic or abdominal surgery for cancer
 - Major surgery, trauma or illness in patient with previous DVT, PE or thrombophilia
 - Major lower limb amputation⁴⁶

In the absence of a nationally recognised set of guidelines risk assessment remains variable and prophylactic regimes continue to be inconsistent.

⁴⁵ i.e. surgery lasting less than 30 minutes.

⁴⁶ www.surgical-tutor.org.uk/system/vascular/venous_thromb.htm

4 The current use of prophylaxis

29. During the inquiry we were struck forcibly by the very variable use of prophylaxis. There are variations between regions and between hospitals. Within some hospitals the application of thromboprophylaxis may vary between individual surgeons and physicians. Professor David Barnett, of NICE, pointed out that the application of thromboprophylaxis in “the whole hospital environment is very patchy and it is particularly true within the medical framework(i.e. in non-surgical cases).”⁴⁷

30. Despite the high risk of VTE in patients undergoing major surgery, some 40% or more of patients still do not receive an effective form of thromboprophylaxis. Indeed last year the Department estimated that 4 out of every 10 orthopaedic patients do not receive any thromboprophylaxis at all — where the risks of DVT are in the order of 1 in 2.⁴⁸ Only 40% of medical at risk patients eligible for preventive treatment (approx 25% of all those in hospital for an acute medical condition) receive an effective thromboprophylactic agent.⁴⁹ Most do not receive any form of risk assessment either.

31. This variability is caused by a number of factors: the lack of awareness of the problem; concerns about bleeding when thromboprophylaxis is administered; funding issues; the inaction of the Department; the lack of a nationally recognised set of thromboprophylactic guidelines, which we have already noted; and the failure to implement what guidelines there are. These factors are considered in detail below.

Lack of awareness of the problem

32. Although there is much evidence for the high incidence rate of VTE and the availability of thromboprophylaxis, a number of submissions stressed that many surgeons and physicians were not aware that their patients suffered from this condition. A hospitalised patient who has contracted a DVT will often have no outward signs that show that they have developed the condition. The manifestation of the condition often occurs when the patient has been discharged from hospital. The first indication may be chest pain from a pulmonary embolus or even sudden death if the embolus is massive. Professor Kakkar told us that: “The problem is that the silent disease can still be deadly and it is bridging that gap between the silence of the disease and the low frequency of the clinical symptoms that I think has been the great problem in persuading large numbers of clinicians about the seriousness of the disease.”⁵⁰ Mr David Warwick, a Consultant Orthopaedic Surgeon representing the Royal College of Surgeons (RCS), told us:

..if you are an orthopaedic surgeon about four in a thousand hip replacement patients will die from a pulmonary embolism if you do not use prophylaxis. That, I suppose is quite a small number in as much as if you are a busy hip surgeon and you do a hundred hip replacements a year you will not see a pulmonary embolism for

⁴⁷ Q 72

⁴⁸ Ev 15

⁴⁹ Ev 67

⁵⁰ Q 4

three or four years and when you do it may have happened at home. So for you individually it is not a problem, but the thing is that we do 90,000 hip and knee replacements per annum in the United Kingdom, so 90,000 times 0.4% is 360 deaths per year.⁵¹

Dr Beverley Hunt, Medical Director of Lifeblood, said: “the surgeons do not see the consequences the patients have, the problems after they have been discharged or when they are admitted to another unit. I think that there is a lack of education generally about this area.”⁵²

33. Many surgeons and physicians are not aware of the incidence of VTE, especially in recently discharged patients and, therefore, are not administering thromboprophylaxis. We recommend that when a patient who has recently been discharged from hospital develops VTE the original surgeon and/or physician should be notified by letter of the incident. Notification should be made by either the primary care physician treating the recently discharged patient, or if the patient is re-admitted to hospital, by the secondary care physician. Notification should also be made in the case of death through PE of a recently discharged patient.

Concerns about bleeding

34. One reason often cited for not using pharmacological prophylaxis is the increased risk of bleeding in patients undergoing surgery. A postal survey carried out to determine the attitudes to the use of LMWH in joint replacement among two groups of orthopaedic surgeons practising in the UK found that 72% of hip surgeons and 51% of knee surgeons replying had used LMWHs for thromboprophylaxis. Of these, 48% had discontinued LMWH use due to bleeding complications. A conclusion of the survey was that although LMWHs had been shown to reduce post-operative thromboembolism in these groups, clinical experience had revealed an increased incidence of bleeding complications associated with their use.⁵³

35. Countering the argument of the perception of a higher risk of bleeding Dr Keeling, representing the RCP, quoted from the 7th ACCP guidelines the following: “Abundant data for an analysis and placebo controlled blinded randomised clinical trials have demonstrated little or no increase in the rates of clinically important bleeding with a low dose heparin or LMWH.” He continued by telling us: “I think the problem is that if someone is using prophylaxis and the patient bleeds, they will automatically say, ‘Oh this patient is bleeding because they are on heparin, I wish I hadn’t used it’ but in fact they may well have bled anyway.”⁵⁴ Mr Warwick, representing the Royal College of Surgeons, added:

..there is a substantial body of UK orthopaedic surgeons who do value the problem of bleeding more than they value the problem of thrombosis and I think a lot of that is

⁵¹ Q 7 (Mr Warwick)

⁵² Q 2

⁵³ “Attitudes to, and utilization of, low molecular weight heparins in joint replacement surgery”, *J. R. Coll. Surg. Edinb.*, Vol 42, December 1997, pp 407–409

⁵⁴ Q 44 (Dr Keeling)

due to a perception bias, in fact they attribute bleeding to a drug if you can because it is easier than blaming yourself.⁵⁵

Belief that VTE is no longer a problem

36. The concern about bleeding is compounded by the fact that many doctors believe that the incidence of VTE has declined in recent years. They frequently site retrospective surveys of their own experience. It may be true that VTE has declined recently due to more widespread use of prophylaxis as well as improved operative and perioperative management but the rate is still high. Moreover, demographic considerations indicate that there are now more extensive operations being performed on older patients, more cancer operations and more patients with obesity than in the past. These would suggest an increasing risk for thrombosis in contemporary general surgical populations.⁵⁶

Inconsistent guidelines

37. Another problem is that the guidelines are inconsistent. We were told that the SIGN guidelines consider aspirin a reasonable prophylactic agent, but the ACCP guidelines specifically state: “we recommend against the use of aspirin alone as thromboprophylaxis for any patient group”.⁵⁷ There still exists some disagreement between the producers of guidelines as to the most effective and efficacious treatment for the prevention of VTE. The introduction of a nationally agreed set of guidelines for use in English NHS hospitals would eliminate some of this confusion.

Problems of funding

38. Dr Keeling told us that thromboprophylaxis is not being administered in some instances because of the allocation of costs throughout the NHS. He told us:

..you ... have a problem where an individual is not allowed to prescribe the drug because he is spending his money but saving money somewhere else. This is a common thing in the Health Service which is a real problem. A simple example: there is a blood test called a D-dimer when you investigate these people for DVT which costs £2.50. My department does hundreds of them and our budget has gone up; people have got very cross about that. However, doing that test saves a lot of money because you do not have to do different investigations; you do not have to do tests in the radiology department. It costs my department money but the radiology department is saving money. No one can look at the bigger picture; no one can get round the bureaucracy of people telling me off for doing D-dimer tests or telling him off for trying to prescribe thromboprophylaxis. The message should be clear: it may cost money to actually write the drug prescription but overall proper implementation would save money; it maybe somebody else's money, but it will save money.⁵⁸

⁵⁵ Q 44 (Mr Warwick)

⁵⁶ Ev 10

⁵⁷ Ev 13

⁵⁸ Q 40 (Dr Keeling)

Dr Beverley Hunt agreed that funding was an issue in the amount of thromboprophylaxis administered. She stated:

A number of factors have been identified to the under use of thromboprophylaxis, including the perception that VTE was not a significant problem or that prophylaxis was ineffective; physicians lack of awareness of guidelines, concerns about possible side-effects and a lack of funding and infrastructure to adhere to recommendations.⁵⁹

39. A further obstacle to the use of prophylaxis is the operation of the common tariff, which does not include anti-DVT products. When we inquired further into the subject of tariffs Mrs de Cossart informed us that: “The tariff is cut to the bone in what it actually covers. Certainly for the extended treatments you would have to look at re-negotiating the tariff in order to introduce this...”⁶⁰ **We recommend a review of the tariffs to ensure that they do not act as a barrier to the appropriate use of thromboprophylaxis.**

Department of Health

40. The Department now sees VTE as a major public health problem. Dr Roger Boyle, National Director of Heart Disease at the Department of Health, told us that “the numbers that die from this condition are sufficient for us to take note of this and this is one reason why we have joined in the commissioning process to commission a guideline within the NICE framework...to try to make it clearer and more explicit to the NHS at large as to what action should be taken”, adding that patients’ safety “needs to be improved”.⁶¹ We welcome Dr Boyle’s statement, but we are astonished that the Department waited until 2004 before commissioning NICE to develop limited guidelines. We wholeheartedly agree with Dr Boyle that this situation is to be regretted.⁶² **We note that the ACCP has recently produced its seventh revision of guidelines and SIGN introduced their guidelines in 1995. It is astonishing that there has been no development of national guidelines in England and Wales.**

What should be done to improve the situation?

Education and awareness

41. The evidence we heard during the inquiry was clear: **the current variations in the administration of thromboprophylaxis indicate that surgeons and physicians are unaware of the extent of VTE and how readily and safely it can be prevented.** As we have seen, despite convincing scientific evidence fewer than 50% of surgeons routinely assess their patients for this condition and apply adequate prophylaxis. Education can play a part in remedying this situation. Dr Beverley Hunt, of Lifeblood told us that “It is not

⁵⁹ Ev 15

⁶⁰ Q 36

⁶¹ Q 58

⁶² Q 63

considered to be an important issue because of the lack of education among the junior staff in particular.”⁶³ We were also advised that the Royal Colleges should ensure that awareness of VTE is made apparent to their members through education and Continuing Professional Development (CPD). Mrs Linda de Cossart, representing the Royal College of Surgeons, told us that “I think it is a matter of priorities and I do not think that DVT prophylaxis is a priority but it should be.”⁶⁴ A joint exercise might be held between the Department, NICE and the Royal Colleges to raise awareness of the problem and the effectiveness of thromboprophylaxis. The specialist thrombosis teams we discuss below would also have an educational role.

42. The Royal Colleges can also bring different disciplines together to discuss the risks of VTE and its prevention. Dr Beverley Hunt told us that in hospitals specialities such as obstetrics, general surgery and orthopaedics each operate in an environment similar to a village and that these “villages” do not often communicate with each other. Dr Hunt continued: “What we really need is for someone from outside to say here is the issue and to remind everybody of the size of the issue and the need for patients’ safety and to produce some guidance to the trust on how to take it forward.”⁶⁵

43. We recommend that VTE and its prevention, including the implementation of, and adherence to, guidelines relating to thromboprophylaxis, counselling and risk assessment, be given more prominence in undergraduate medical education, Continuing Professional Development (CPD), and other relevant aspects of medical and paramedical training. We further recommend that the Royal Colleges bring forward proposals to this end as well as to raise awareness of the problems of VTE. In addition, NHS Trusts should ensure that all physicians and surgeons receive training about the subject. We make recommendations about the role of the Healthcare Commission in audit and implementation below.

Establishing guidelines

44. Improving medical education will help, but by itself is not sufficient. A key ingredient for ensuring the better treatment of VTE has to be national guidelines. As we have seen, the Department of Health has finally commissioned NICE to develop such guidelines. The draft remit is as follows:

Groups that will be covered

Adults (age 18 and older) undergoing:

- orthopaedic surgery (including total hip or knee replacement, surgery for hip fracture, knee arthroscopy)
- major general surgery
- major gynaecological surgery
- urological surgery (including major or open urological procedures)

⁶³ Q13 (Dr Hunt)

⁶⁴ Q14 (Mrs de Cossart)

⁶⁵ Q 13 (Dr Hunt)

- cardiothoracic surgery
- major peripheral vascular surgery.

Groups that will not be covered

Patients under the age of 18

Adult patients who are at a high risk of developing venous thromboembolism but are not undergoing surgery will not be covered. For example, the following circumstances will be excluded from the guideline:

- acute myocardial infarction
- acute stroke
- cancer, including patients being treated with chemotherapy
- pregnancy and the puerperium⁶⁶
- use of oral contraceptives and hormone replacement therapy
- long-distance travel

The guidelines will offer guidance for use in secondary and tertiary care.⁶⁷ The guidelines currently being prepared by NICE will be published in May 2007.⁶⁸

45. Unsurprisingly, witnesses welcomed the fact that the Department had commissioned NICE to establish guidelines. However, they were disappointed that the guidelines would take over two years to agree even though the procedures for preventing VTE are well-established and there are well regarded existing guidelines such as those issued by the ACCP. They also thought that the scope of the proposed guidelines was too limited: medical patients, who make up the majority of those patients at risk of developing VTE, are excluded. NICE is considering a single risk factor (the surgical procedure itself) rather than the multifactorial aspects of risk for VTE; for instance the current NICE scope does not include those who might be having low risk procedures but who are themselves at high risk of VTE, such as those who have experienced VTE before, have one or more inherited or acquired thrombophilia traits or are on hormone treatments.

46. Professor Sir Michael Rawlins, the chairman of NICE, explained the reasons for the length of the study: “We need our own guidelines to accommodate our own particular circumstances, to accommodate the patterns of medical practice and surgical practice in the UK.”⁶⁹ He added that there were a number of limitations to the existing guidelines – that none of them took into account cost-effectiveness; that the duration of the application of the prophylaxis is also not addressed; that different patient risk categories are not

⁶⁶ Puerperium - the 6 week period following birth

⁶⁷ *Venous thrombo-embolism - Scope*, National Institute of Clinical Excellence, 2005, www.nice.org.uk/page.aspx?o=231773

⁶⁸ *Venous Thrombo-embolism*, National Institute of Clinical Excellence, 2005, www.nice.org.uk/page.aspx?o=235874

⁶⁹ Q 68

considered; and that they are weak on medical prophylaxis.⁷⁰ While we accept some of these arguments for not immediately adopting existing guidelines and for NICE to develop guidelines we are concerned about the time that will be taken to develop and implement them. Furthermore, the current scope of the NICE guidelines will not remedy many of Sir Michael's own criticisms of the existing guidelines.

47. However, Professor Rawlins did agree that the scope ought to be expanded. "I would very much hope we would get a referral soon for medical patients because the issues are somewhat different and I think we need to address them."⁷¹ The problem is that expanding the scope of the existing study might further delay the publication of guidelines. One way of dealing with this conundrum is would be if NICE were to set up a separate study in parallel to establish guidelines in respect of the excluded groups.

48. The scope of the guidelines for VTE which NICE is preparing are too limited. Many groups of patients who are at considerable risk of VTE are excluded. We recommend that NICE extend the scope of the current project to include both medical patients and patients undergoing low risk procedures who are themselves at high risk from VTE. If NICE considers that surgical and other patients should not be covered by the same set of guidelines, we recommend that the Department commission NICE to develop guidelines for the excluded groups in parallel with its current work.

49. In view of the urgency of the situation that leads to more than 25,000 deaths, many of them avoidable, it is unacceptable to wait until 2007 for any attempts to reduce deaths from VTE. We therefore recommend that the currently accepted consensus guidelines are circulated by the relevant bodies including the Royal Colleges, the British Orthopaedic Association, hospital specialist thrombosis teams and Trust Drug and Therapeutics Committees to clinicians so that they can seriously consider whether to implement them immediately.

Counselling and risk assessment

50. Witnesses argued that guidelines must address two important issues: counselling about the risk of VTE and risk assessment. Lifeblood compared the counselling a patient receives about blood transfusion before an operation, and the counselling provided about the risks of VTE. For a patient undergoing a hip replacement — a standard and common operation in the NHS — when the patient is admitted they will be counselled on, and be asked to consent to, the risks of the operation. They will probably also receive counselling about the risks of blood transfusion. These are small nowadays. The risk of contracting a major infection through a blood transfusion is about 1 in 500,000.⁷² In contrast, the patient is unlikely to be counselled about the risks of venous thromboembolism although they are far greater. Dr David Keeling, representing the RCP, told us:

⁷⁰ For example, "British Thoracic Society guidelines for the management of suspected acute pulmonary embolism", *Thorax*, 2003, Vol 58, pp 470-484 and "Suspected Acute Pulmonary Embolism", *Thorax*, 1997, Vol 52, Supp 3 pp s2-s24, "The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy: Evidence-Based Guidelines", *Chest*, 2004, Vol:126, Supplement 3, pp 338S-400S and Prophylaxis of Venous Thromboembolism, <http://www.sign.ac.uk/guidelines/fulltext/62/index.html>

⁷¹ Q 64

⁷² Ev 15

We live in a society where people are scared of travelling by train but not by car and I receive hundreds of phone calls from GPs about patients who are going on long haul air flights and are worried about getting a DVT. These are the same patients coming into hospital where the risk is vastly greater. When people are consented for operations they are informed of all sorts of very small risks, especially with regard to blood transfusions. However, I am not sure how patients are informed of the risks of venous thromboembolism when they are consented for their operation. I think there is an issue of informing the public about this.⁷³

51. Dr Roger Boyle, of the Department, acknowledged the deficiencies in the current system:

I think that it is an area that needs to be improved very substantially. I think it needs to be improved in the context of the policy of choice for patients so that they fully understand what they are letting themselves in for. I think it requires closer attention. It is certainly in the interests of the Department of Health to improve those processes...I think there should be more consultant involvement in the process because it may be a routine event for the surgeon but it is certainly not a routine event for the patient.⁷⁴

52. Many of the hospital patients who suffer from VTE are medical patients who are not required to give written consent to treatment, as those who undergo surgery do. Often the risk of thrombosis is not communicated to this, the largest group of patients within hospitals. **We recommend that procedures for counselling both medical and surgical patients be supported by hospital specialist thrombosis teams and included in the VTE guidelines developed by NICE.**

53. Risk assessment is another key component in combating the high incidence of VTE. Although not all patients who are admitted to hospital will require prophylaxis for VTE, many patients in the medium to high risk categories are currently not being identified and, therefore, are being exposed to unnecessary risk of VTE. By identifying those patients most at risk, preventative measures can be used to reduce the incidence of VTE. As Mr Warwick pointed out: “Every patient must have his risk factors ticked off on a box as they come in because only at that point can you judge if this is low risk, medium risk or high risk.”⁷⁵ **We recommend that all patients, both medical and surgical, who are admitted to hospital undergo a risk assessment for venous thrombosis.**

Implementation of the guidelines

54. Witnesses stressed the importance of putting in place systems to ensure that the NICE guidelines will be followed. Sir Michael Rawlins informed us that: “there is about a 50% uptake for full implementation. That is not good enough.”⁷⁶ Professor David Cousins, Head of Safe Medication Practice at the National Patient Safety Agency (NPSA), also highlighted the problem:

⁷³ Q 19 (Dr Keeling)

⁷⁴ Q 94 (Dr Boyle)

⁷⁵ Q 53 (Mr Warwick)

⁷⁶ Q 87 (Sir Michael Rawlins)

We are finding through all our work that we are encountering patient harm because of the failure of the NHS to implement effectively, so often times there are plenty of guidelines out there but because of the volume of traffic, the business that everyone is facing, they have difficulties implementing. Actually trusts and the NHS desperately need methodology given to them to implement effectively.⁷⁷

55. Various proposals were made for better implementation. Sir Michael noted how effectively the guidance about VTE from the Royal College of Obstetricians and Gynaecologists had been implemented. Mr Warwick thought that this was, as we have discussed above, because the practitioners had been involved in the preparation of, and support for, the guidelines: “I think the Colleges or the British Orthopaedic Association is the correct sort of level to promulgate that so people feel they are being supported by their own rather than it being imposed from above.”⁷⁸

56. Professor Cousins emphasised that systems and safeguards should be built into protocols to make it easier for physicians and surgeons to follow agreed guidelines. Computer reminders can be a useful aid. Their use, during electronic prescribing, combined with the guidelines of the ACCP had a significant impact on the prescribing of anticoagulants in the United States. When the computer reminders were removed physicians “went back to the original poor rates of compliance”.⁷⁹

57. Witnesses also pointed to the importance of clinical governance and audit in ensuring that guidelines are implemented. We were told that there needs to be a person at each trust responsible for clinical governance, a recommendation we had made in our report into NICE in 2002. As Sir Michael Rawlins told us, chief executives of trusts have a legal responsibility for clinical governance, similar to corporate governance. He proposed that the Healthcare Commission be asked to “look at practices for prophylaxis and DVT and ask trusts what arrangements they have in place, ask trusts what figures they are getting in terms of in-patient mortality and so on.”⁸⁰ Dr Roger Boyle added that the Healthcare Commission should be inspecting organisations on clinical excellence and that VTE “is a high risk area with a major impact on mortality and morbidity and should therefore be high up their list of priorities.”⁸¹

58. Systems must be put in place to ensure that the NICE VTE guidelines are implemented. We reiterate the recommendations we made in our inquiry into the National Institute of Clinical Excellence in 2001-02 that the Government should: a) institute practical systems and structures to improve the NHS’s capacity to implement NICE guidance, including the possibility of designated individuals within the NHS trusts and strategic health authorities to liaise with NICE to facilitate implementation of the guidelines; and b) ensure the systematic monitoring of the implementation of NICE guidance. We also recommend that computer reminders are built into the electronic prescribing system of the National Programme for Information Technology to aid physicians in the prescription of thromboprophylaxis and to remind them of

⁷⁷ Q 78

⁷⁸ Q 14 (Mr Warwick)

⁷⁹ Q 78

⁸⁰ Q 77

⁸¹ Q 62

guidelines for the prevention of VTE. We further recommend that the Healthcare Commission undertake, as part of its audit process, an investigation into the availability and use of venous thromboembolism prevention protocols in each hospital, including appropriate counselling and risk assessment. It should also audit the training for and awareness of thromboprophylaxis and venous thrombosis in hospitals.

Thrombosis committees and thrombosis teams

59. In addition to the publication of NICE guidelines and the establishment of systems to ensure their implementation, our witnesses' other main recommendation was that each hospital trust establish a Thrombosis Committee and a Thrombosis Team. Dr Boyle, of the Department, supported their introduction: "having specialist skills available to run and fund hospital programmes would be a very useful way forward."⁸² So did Professor David Barnett, of NICE: "a senior champion is a good idea... you do need a senior champion and I think the idea of a protocol driven but appropriately constructed team to run and make sure that these processes are put in place."⁸³ Dr Hunt thought that the teams would "reduce mortality and morbidity from VTE at very little cost when compared with both the economic and health costs of the consequences."⁸⁴ The model would be the blood transfusion teams and committees, which were set under two Departmental directives issued in 1998⁸⁵ and 2002⁸⁶ entitled "*Better Blood Transfusion*".

60. Lifeblood told us that since the introduction of teams the use of blood is more considered; practices have improved and changed; and healthcare professionals have been educated about the use of blood. It argued that the establishment of similar teams would have similar success in ensuring effective implementation and monitoring adherence to protocols for the prevention of thrombosis in hospitalised patients.

61. The Thrombosis Committee in each trust should include representatives from all interested parties, including haematologists, surgeons, physicians, anaesthetists, obstetricians, nursing staff and pharmacists. It would ensure clinical governance and provide a local audit of thromboprophylactic procedures in each hospital.

62. A potential draft remit of such a committee would be to:

- promote best practice through local protocols based on national guidelines
- lead multi-professional audit of the use of thromboprophylaxis within the NHS Trust, focusing on specialties where risk is high
- promote the education and training of all clinical and support staff
- have the authority to modify existing VTE and risk assessment protocols and to introduce appropriate changes to practice

⁸² Q 88 (Dr Boyle)

⁸³ Q 90 (Professor Barnett)

⁸⁴ Ev 15

⁸⁵ Department of Health, *Better Blood Transfusion*, HSC 1998/224, December 1998

⁸⁶ Department of Health, *Better Blood Transfusion: appropriate use of blood*, HSC 2002/009, July 2002

- consult with local patient representative groups where appropriate
- contribute to the development of clinical governance

A remit for the thrombosis teams would be to:

- assist in the implementation of the Thrombosis Committee's objectives
- promote and provide advice and support to clinical teams on the appropriate thromboprophylaxis and risk assessment
- actively promote the implementation of good thromboprophylaxis practice
- be a source for training all hospital staff involved in the dealing with patients at risk of VTE

63. We recommend that a thrombosis committee be established in each hospital, with a specialist thrombosis team. They should be modelled on the existing Blood Transfusion teams and committees. So that these teams are established and operate effectively a basic standard of expectation (skeleton) should be issued by the Department pending the publication of NICE guidelines.

List of abbreviations used in the report

ACCP	American College of Chest Physicians
CPD	Continuing Professional Development
DVT	Deep Vein Thrombosis
LDUH	Low dose unfractionated heparin
LMWH	Low molecular weight heparin
MRSA	Methicillin-Resistant Staphylococcus Aureus
NICE	National Institute of Clinical Excellence
NPSA	National Patient Safety Agency
PE	Pulmonary Embolism
RCOG	Royal College of Obstetricians and Gynaecologists
RCP	Royal College of Physicians
RCS	Royal College of Surgeons
SIGN	Scottish Intercollegiate Guidelines Network
VT	Venous Thrombosis
VTE	Venous Thromboembolism

Conclusions and recommendations

1. We are concerned that the number of post-mortems being performed has decreased since Alder Hey. As a result the true cause of death is not being determined in many cases. We recommend that the Department encourage the increased use of post-mortems where appropriate. This would enable accurate identification of the cause of death in more patients and more reliable assessment of the current incidence of death through VTE, thereby providing a base from which to monitor progress. (Paragraph 14)
2. Many surgeons and physicians are not aware of the incidence of VTE, especially in recently discharged patients and, therefore, are not administering thromboprophylaxis. We recommend that when a patient who has recently been discharged from hospital develops VTE the original surgeon and/or physician should be notified by letter of the incident. Notification should be made by either the primary care physician treating the recently discharged patient, or if the patient is re-admitted to hospital, by the secondary care physician. Notification should also be made in the case of death through PE of a recently discharged patient.. (Paragraph 33)
3. We recommend a review of the tariffs to ensure that they do not act as a barrier to the appropriate use of thromboprophylaxis. (Paragraph 39)
4. We note that the ACCP has recently produced its seventh revision of guidelines and SIGN introduced their guidelines in 1995. It is astonishing that there has been no development of national guidelines in England and Wales. (Paragraph 40)
5. The current variations in the administration of thromboprophylaxis indicate that surgeons and physicians are unaware of the extent of VTE and how readily and safely it can be prevented. (Paragraph 41)
6. We recommend that VTE and its prevention, including the implementation of, and adherence to, guidelines relating to thromboprophylaxis, counselling and risk assessment, be given more prominence in undergraduate medical education, Continuing Professional Development (CPD), and other relevant aspects of medical and paramedical training. We further recommend that the Royal Colleges bring forward proposals to this end as well as to raise awareness of the problems of VTE. In addition, NHS Trusts should ensure that all physicians and surgeons receive training about the subject. We make recommendations about the role of the Healthcare Commission in audit and implementation below. (Paragraph 43)
7. The scope of the guidelines for VTE which NICE is preparing are too limited. Many groups of patients who are at considerable risk of VTE are excluded. We recommend that NICE extend the scope of the current project to include both medical patients and patients undergoing low risk procedures who are themselves at high risk from VTE. If NICE considers that surgical and other patients should not be covered by the same set of guidelines, we recommend that the Department commission NICE to

develop guidelines for the excluded groups in parallel with its current work.. (Paragraph 48)

8. In view of the urgency of the situation that leads to more than 25,000 deaths, many of them avoidable, it is unacceptable to wait until 2007 for any attempts to reduce deaths from VTE. We therefore recommend that the currently accepted consensus guidelines are circulated by the relevant bodies including the Royal Colleges, the British Orthopaedic Association, hospital specialist thrombosis teams and Trust Drug and Therapeutics Committees to clinicians so that they can seriously consider whether to implement them immediately. (Paragraph 49)
9. We recommend that procedures for counselling both medical and surgical patients be supported by hospital specialist thrombosis teams and included in the VTE guidelines developed by NICE. (Paragraph 52)
10. We recommend that all patients, both medical and surgical, who are admitted to hospital undergo a risk assessment for venous thrombosis. (Paragraph 53)
11. Systems must be put in place to ensure that the NICE VTE guidelines are implemented. We reiterate the recommendations we made in our inquiry into the National Institute of Clinical Excellence in 2001-02 that the Government should: a) institute practical systems and structures to improve the NHS's capacity to implement NICE guidance, including the possibility of designated individuals within the NHS trusts and strategic health authorities to liaise with NICE to facilitate implementation of the guidelines; and b) ensure the systematic monitoring of the implementation of NICE guidance. We also recommend that computer reminders are built into the electronic prescribing system of the National Programme for Information Technology to aid physicians in the prescription of thromboprophylaxis and to remind them of guidelines for the prevention of VTE. We further recommend that the Healthcare Commission undertake, as part of its audit process, an investigation into the availability and use of venous thromboembolism prevention protocols in each hospital, including appropriate counselling and risk assessment. It should also audit the training for and awareness of thromboprophylaxis and venous thrombosis in hospitals. (Paragraph 58)
12. We recommend that a thrombosis committee be established in each hospital, with a specialist thrombosis team. They should be modelled on the existing Blood Transfusion teams and committees. So that these teams are established and operate effectively a basic standard of expectation (skeleton) should be issued by the Department pending the publication of NICE guidelines. (Paragraph 63)

Formal Minutes

Wednesday 23 February 2005

Members present:

Mr David Hinchliffe, in the Chair

John Austin

Mr Keith Bradley

Mr Jon Owen Jones

Dr Doug Naysmith

Dr Richard Taylor

The Committee deliberated.

Draft Report (The Prevention of Venous Thromboembolism in Hospitalised Patients), proposed by the Chairman, brought up and read.

Ordered, That the Chairman's draft Report be read a second time, paragraph by paragraph.

Paragraphs 1 to 63 read and agreed to.

Summary agreed to.

Resolved, That the Report be the Second Report of the Committee to the House.

Ordered, That the Chairman do make the Report to the House.

Ordered, That the Provisions of Standing Order No. 134 (Select Committee (Reports)) be applied to the Report.

Ordered, That the Appendices to the Minutes of Evidence taken before the Committee be reported to the House.

Several Memoranda were ordered to be reported to the House. — (*The Chairman*)

* * *

[Adjourned till Thursday 3 March at 10.00 am.]

Witnesses

Thursday 9 December 2004

Mrs Linda de Cossart, Royal College of Surgeons; **Mr David Warwick**, Royal College of Surgeons; **Professor Ajay Kakkar**, Professor of Surgical Science and Consultant Surgeon, Barts and the London Medical School; **Dr David Keeling**, Royal College of Physicians; **Dr Beverley Hunt**, Lifeblood: the Thrombosis Charity

Ev 1

Dr Roger Boyle, National Director of Heart Disease, Department of Health; **Professor Sir Michael Rawlins**, Chair, National Institute of Clinical Excellence; **Professor David Barnett**, Chair of Appraisals Committee, National Institute of Clinical Excellence; **Professor David Cousins**, Head of Safe Medication Practice, National Patient Safety Agency.

Ev 31

List of Written evidence

1	Mr David Warwick (VT 1)	Ev 1
2	Professor Ajay Kakkar (VT 13)	Ev 9
3	Royal College of Physicians (VT 15)	Ev 12
4	Lifeblood: the Thrombosis Charity (VT 6)	Ev 14
5	Mrs Linda de Cossart (VT17)	Ev 16
6	Department of Health (VT 14)	Ev 31
7	National Patient Safety Agency (AL58)	Ev 33
8	National Institute of Clinical Excellence (VT 16)	Ev 41
9	Dr Ricky Autar (VT 2)	Ev 55
10	Mr J H Scurr (VT 3)	Ev 58
11	Huntleigh Healthcare PLC (VT 5)	Ev 59
12	Tyco Healthcare (UK) Commercial Ltd (VT 7)	Ev 60
13	sanofi-avetis (VT8)	Ev 65
14	Alexander T Cohen (VT 9)	Ev 68
15	DR S K Kakkos and Mr G Geroulakos (VT 10)	Ev 70

List of unprinted written evidence

Additional papers have been received from the following and have been reported to the House but to save printing costs they have not been printed and copies have been placed in the House of Commons library where they may be inspected by members. Other copies are in the Record Office, House of Lords and are available to the public for inspection. Requests for inspection should be addressed to the Record Office, House of Lords, London SW1. (Tel 020 7219 3074) hours of inspection are from 9:30am to 5:00pm on Mondays to Fridays.

Orthofix Vascular Novamedix (VT 4)

Royal College of Physicians of Edinburgh (VT 12)

Reports from the Health Committee since 2001

The following reports have been produced by the Committee since the start of the 2001 Parliament. The reference number of the Government's response to the Report is printed in brackets after the HC printing number.

Session 2004-05

First Report	The Work of the Health Committee	HC 284
--------------	----------------------------------	--------

Session 2003-04

First Report	The Work of the Health Committee	HC 95
Second Report	Elder Abuse	HC 111 (Cm 6270)
Third Report	Obesity	HC 23 (Cm 6438)
Fourth Report	Palliative Care	HC 454 (Cm 6327)
Fifth Report	GP Out-of-Hours Services	HC 697 (Cm 6352)
Sixth Report	The Provision of Allergy Services	HC 696 (Cm 6433)

Session 2002-03

First Report	The Work of the Health Committee	HC 261
Second Report	Foundation Trusts	HC 395 (Cm 5876)
Third Report	Sexual Health	HC 69 (Cm 5959)
Fourth Report	Provision of Maternity Services	HC 464 (Cm 6140)
Fifth Report	The Control of Entry Regulations and Retail Pharmacy Services in the UK	HC 571 (Cm 5896)
Sixth Report	The Victoria Climbié Inquiry Report	HC 570 (Cm 5992)
Seventh Report	Patient and Public Involvement in the NHS	HC 697 (Cm 6005)
Eight Report	Inequalities in Access to Maternity Services	HC 696 (Cm 6140)
Ninth Report	Choice in Maternity Services	HC 796 (Cm 6140)

Session 2001-02

First Report	The Role of the Private Sector in the NHS	HC 308 (Cm 5567)
Second Report	National Institute for Clinical Excellence	HC 515 (Cm 5611)
Third Report	Delayed Discharges	HC 617 (Cm 5645)

Oral evidence

Taken before the Health Committee

on Thursday 9 December 2004

Members present:

Mr David Hinchliffe, in the Chair

John Austin
Mr Keith Bradley
Mr Simon Burns

Mrs Patsy Calton
Dr Doug Naysmith
Dr Richard Taylor

Memorandum by Mr David Warwick (VT 1)

A SYNTHESIS OF RECENT RESEARCH CONCERNING THE PREVENTION OF VENOUS THROMBOEMBOLISM IN ORTHOPAEDIC SURGERY

Thromboprophylaxis is a controversial and changing topic. Some new concepts are presented in this submission.

WHY PROPHYLAXIS REALLY IS NECESSARY

Some have questioned the very need for thromboprophylaxis. Various reasons are given to include the relatively low frequency of symptomatic thromboembolic events, the risk of bleeding, the possibility of late infection, the reliance on surrogate endpoints such as venography and finally “no evidence of effect” (the beta error misinterpreted as “evidence of no effect”). However, in our current environment of risk management it would be wise to remember that the weight of evidence supports the view that thromboembolism is a potentially serious complication and that on the balance of probability the risk can be diminished (The THRIFT Group 1998, International Consensus Statement 2001 Geerts *et al* 2002). Anecdote aside, there is no evidence that *careful* prophylaxis causes major wound bleeding, infection, implant loosening or death.

WHY THROMBOEMBOLISM REALLY IS IMPORTANT

The **fatal PE rate** without prophylaxis after hip and knee replacement is probably in the region of 0.4%. One might say that 0.4% is a rare and therefore unimportant event rate. However, the individual who dies is 100% dead. With 1.25 million hip and knee replacements in Europe each year, 0.4% represents 5,000 fatalities annually or the capacity of an Airbus each month . . . Even very low death rates are important.

Symptomatic venous thromboembolism (VTE) is the most common complication after arthroplasty (around 4%). This makes it more common than dislocation and infection combined. Every orthopaedic surgeon accepts the need for antibiotic prophylaxis to avoid infection and a meticulous surgical approach to avoid dislocation. Why not accept the need for safe and effective thromboprophylaxis?

THROMBOPROPHYLAXIS REALLY DOES WORK

Fatal PE. John Charnley (Crawford *et al* 1968) showed, by comparing phenindione with control in a randomised trial of 900 patients, that extreme anticoagulation merely exchanges a reduction in fatal PE for an increase in fatal bleeding. However, more judicious anticoagulation can probably reduce death. Fatal PE is very rare indeed in patients taking prophylactic warfarin at adequate levels (for example, no fatalities in 3,000 consecutive hip arthroplasty patients (Amstutz *et al* 1989)). There is fairly good evidence that death rates can be reduced by heparin. A meta-analysis (Collins *et al* 1988) of all the early randomised trials of heparin in orthopaedic surgery and showed that the fatal PE rate was reduced by 66% in those receiving heparin rather than placebo or nothing. The overall death rate, as well as the fatal PE rate, was reduced by heparin. However, there was an increase in bleeding of two-thirds in those taking heparin (2% absolute increase) (Figure 1). Death rates are now so low even without prophylaxis that a randomised study is unlikely to be large enough (about 90,000 patients) to study death as an end point (Warwick *et al* 1995). We will have to rely upon surrogate endpoints.

Symptomatic VTE. It has been argued (Warwick and Samama 2000) that the evidence for thromboprophylaxis is based upon a surrogate outcome—usually venography—rather than a clinical outcome. However, there is in fact evidence that reduced DVT rates correspond with reduced symptomatic event rates.

The heparin meta-analysis paper (Collins *et al* 1988) showed a similar risk reduction for *both asymptomatic DVT* (scintigraphy or venography) of 67% (60.5% to 20.3%) and *fatal PE* of 68% (1.9% to 0.6%). (Figure 1). However, this paper was weakened because it was based upon a rather heterogeneous group of small studies of various orthopaedic patients diagnosed primarily with iodinated fibrinogen.

More robust data are now available. A meta-analysis (Hull *et al* 2001a) shows that extending the duration of LMWH for about five weeks after hip replacement will reduce the venographic DVT rate from 21% to 8.2% (risk reduction 61%). These studies were large enough to show that the frequency of symptomatic VTE was reduced by the same proportion from 4.5% to 1.7%, (risk reduction 62%). (Figure 2). Similarly, when placebo was compared with pentasaccharide in a double blind RCT for 4 weeks after hip fracture surgery, the venographic DVT risk was reduced by 95.9% (77/220 or 35% vs 3/208 or 1.4%) and the symptomatic event rate by a similar 88.8% (9/330 or 2.7% vs 1/326 or 0.3% (Eriksson *et al* 2003). (Figure 3).

Thus we can now be confident that venographic surrogates do reflect clinical reality.

Chronic venous insufficiency. Whether joint replacement predisposes to chronic venous insufficiency, and whether this risk can be reduced by prophylaxis, is not yet known.

EXTENDED PROPHYLAXIS SHOULD BE CONSIDERED

Until recently, most clinical trials studied the use of prophylaxis in arthroplasty for only seven to 10 days—whilst the patient was in hospital. With this strategy, LMWH would reduce the venographic DVT rate by 60% (2). However, there is consistent evidence from several sources that half of symptomatic VTE after knee replacement and two-thirds after hip replacement occur beyond the second week—usually when the patient has been discharged from hospital (White *et al* 1998, Colwell *et al* 1999, Dahl *et al* 2000). The Total Hip Replacement Outcome Study (Gregg *et al* 2000) shows that venous thromboembolism is the commonest cause of readmission after hip replacement. As described above, several recent randomised trials have consistently shown that the risk of thrombosis (both venographic and symptomatic) after hospital discharge in *hip surgery* can be reduced by two-thirds if low molecular weight heparin or pentasaccharide is continued for at least four weeks after surgery (Hull *et al* 2001a, Cohen *et al* 2001, Eikelboom 2001, Eriksson 2003). (Figure 3,4). The advantage for extended prophylaxis in *knee replacement* is not so clear.

These studies show that the number-needed-to-treat (NNT) to prevent one symptomatic DVT or PE after hip replacement is 37; from this figure, one can calculate cost effectiveness. Because the cost of LMWH is relatively low, and the cost of investigation or treatment of thromboembolism relatively high, this is likely to be a cost effective approach (Friedman and Dunsworth 2000, Sarasin and Bounameaux 2000).

Even if these statistics are not thought compelling enough to extend prophylaxis for five weeks, it should be remembered hospital stays after arthroplasty are falling. Discharge at four days after surgery is not uncommon and minimally invasive day case hip surgery is on the horizon. Even the most sceptical may realise that prophylaxis for only one day is probably too short. Thus the practical issue of administering prophylaxis after discharge is real—when do you need to stop it, who gives it, who will pay for it . . .

THE RISE AND FALL OF ASPIRIN

Aspirin is superficially attractive. It is a cheap, readily available, familiar tablet. Surely if aspirin is given, the surgeon won't have to worry, the patient will be fine and the lawyers will be out of work. Initial meta-analysis suggested that aspirin might reduce the frequency of DVT and PE (ATC 1994). However, the recent PEP study (PEP 2000) showed aspirin is not as helpful as might have been hoped. (Figure 4) Over 13,000 hip fracture patients were randomised to have either aspirin or placebo. The death rate was identical in each group. The risk reduction for symptomatic VTE from 2.5% to 1.6% was only about 30%—half what one would expect from LMWH and one-third from pentasaccharide) (Figure 5). This reduced risk of VTE was matched by an increased risk of transfusion, gastro-intestinal bleeding and wound bleeding (Fig 5). In the supplementary group of 4,000 hip and knee replacement patients, there was an insignificant difference in symptomatic VTE (Cohen and Quinlan 2000). In other words, aspirin has a relatively weak thromboprophylactic effect, carries an alternative complication rate and its use might deprive patients of safer or more effective prophylaxis. It is not recommended by the two largest evidence-based Consensus groups (Geerts *et al* 2001, ICC 2001). Furthermore, it is not licensed for thromboprophylaxis in the United Kingdom.

IS WARFARIN MORE TROUBLE THAN IT IS WORTH?

Warfarin has been widely used in North America and the United Kingdom for prophylaxis. Used carefully, death is exceedingly rare and it is as effective as LMWH in reducing venographic DVT. Its use is supported by the main Consensus Groups. It can be delivered beyond hospital discharge to protect against the risk of late onset VTE. However it has many drawbacks and for this reason is regarded as more or less obsolete by many in Western Europe and Scandinavia. It requires regular monitoring, which is expensive and time consuming. If started too close to surgery or at too high a dose, there will be a risk of bleeding. If started judiciously—later and at a lower dose—there will be an interval of several days during which the

patient will be unprotected—at their most thrombogenic time. Warfarin interacts with many drugs and alcohol. On objective comparison, it is difficult to see an advantage for Warfarin over LMWH or pentasaccharide, except that (arguably) it is more convenient to continue beyond discharge.

PENTASACCHARIDE

Fondaparinux (Arixtra, Sanofi-Synthelabo, Guildford UK) is a pentasaccharide which offers a new, effective and relatively safe pharmacological approach. It precisely inhibits factor Xa, which is a key component of coagulation. It has been meticulously compared with LMWH in over 7,300 hip replacement, knee replacement and hip fracture patients (Turpie *et al* 2002). The overall VTE rate at 11 days after surgery (venographic DVT plus symptomatic DVT or PE) was reduced from 13.7% with Enoxaparin to 6.8% with Arixtra (odds reduction 55.2%; 95% confidence interval 45.8 to 63.1%, $p < 0.001$) (Figure 6). Some of this advantage in VTE (and disadvantage in bleeding) may be explained by a different timing schedule than LMWH—rather closer to surgery. With respect to bleeding, it is as well to remember that an omelette cannot be made without cracking an egg. Fondaparinux appeared to have some increased minor bleeding (so called bleeding index) but no major bleeding side effects in comparison with LMWH. It must be given *at least* six hours after surgery and after removal of the spinal/epidural catheter to avoid the risk of surgical or neuraxial (ie spinal) bleeding. The case for pentasaccharide has been critically analysed (Lowe *et al* 2003) with some discussion about cost, the choice of endpoint, the relevance of the bleeding and the means of reversal. Nevertheless, the risk reductions presented for DVT are enticing.

CHEMICAL PROPHYLAXIS WITH NEURAXIAL ANAESTHESIA

Neuraxial (ie spinal or epidural) anaesthesia conveys many benefits to orthopaedic patients (Rodgers *et al* 2000). The mortality after surgery is reduced by 30%, post-operative analgesia is enhanced and it is even weakly thromboprophylactic (Prins and Hirsh 1990). Initial European experience suggested that neuraxial anaesthesia could be safely used in the presence of prophylactic anticoagulants (Bergqvist 1992). However, more recently the American Food and Drug Administration has raised concerns that on occasions a spinal haematoma may develop. It is therefore prudent to avoid giving neuraxial anaesthesia and chemical prophylaxis within at least six hours of each other (Horlocker 2001).

ORAL THROMBIN INHIBITORS

The ideal chemical agent would be taken orally. This would overcome the difficulty of reconciling the clear need for extended prophylaxis with the pragmatic issue of who will administer it. *Aspirin* (anti-platelet rather than anti-thrombotic) may fulfil this, but the efficacy is weak and there is no good evidence for its extended use. *Warfarin* has many disadvantages described above. *Melagatran* (AstraZeneca, UK) is a recently-developed direct oral thrombin inhibitor which has a number of important advantages over warfarin. There is a wide therapeutic and safety window; no monitoring is needed; it is not known to interact with other medications. Recent trials show equivalence with LMWH in prophylaxis after arthroplasty (Eriksson 2001, Heit 2001, Eriksson 2002). Future trials may show its efficacy for extended prophylaxis in which case a pragmatic solution to this important problem would be available.

JUST-IN-TIME PROPHYLAXIS

There is a dilemma with chemical prophylaxis: the closer to surgery that it is administered, the better the thromboprophylaxis but the greater chance of bleeding complications. If LMWH is given before surgery (as recommended in Europe), then because of a relatively short half life, serum levels will be too low for any prophylactic effect. If LMWH is delayed until after surgery (as recommended in North America), then thrombi may have already begun to form during the very thrombogenic operation. Prophylaxis needs to be given close, but not too close, to surgery—so called “just in time prophylaxis” (Hull *et al* 2001b). The optimum moment to administer LMWH or Fondaparinux is probably around six to eight hours after surgery.

COMBINED MECHANICAL AND CHEMICAL PROPHYLAXIS

The Art, rather than Science, of clinical medicine is to apply knowledge in a balanced way, tailored to the needs of the individual patient.

Thromboprophylaxis has been often regarded as a dichotomy- *either* chemical *or* mechanical. This risks throwing the baby out with the bathwater. The advantages of chemicals (ease of use, relative cheapness and efficacy) must be weighed against the potential for bleeding both into the surgical wound and into the spinal cord following neuraxial anaesthesia. The advantages of mechanical prophylaxis such as the Foot Pump (no bleeding side effects, no interactions, reasonable efficacy) must be weighed against the disadvantages (compliance, refitting when mobilising, impracticality of extended use). A sensible approach would be to use the Foot Pump as soon as possible after injury or surgery and then to switch to chemical prophylaxis once the risk of bleeding has subsided and for as long as the risk of thromboembolism pertains. For patients

with a particularly risk of thrombosis, the two can be combined in the hope of a synergistic effect (although this has not yet been studied). There are no clinical trials which have directly addressed this approach and perhaps there will not be.

CAN WE DESIGN A SENSIBLE, SAFE, EVIDENCED BASED APPROACH?

Care pathways and guidelines are becoming endemic. They should ensure the routine and automatic provision of important care, yet allow flexibility when individual patient circumstances require. This should give the patient the benefit of best practice and give the hospital protection against risk.

It is wise for each orthopaedic Department to combine common sense with evidence and then publish guidelines for thromboprophylaxis. These guidelines can then be incorporated into care pathways. The author (hopefully not tainted by wild speculation or subconscious prejudice) suggests that the following would not be unreasonable:

Risk assessment: all patients should have a risk assessment to detect particularly high risk (previous VTE, family history, malignancy, likely prolonged immobility or poor mobilisation).

Hip replacement: regional anaesthesia and early mobilisation should be encouraged. For those surgeons who are comfortable with chemical prophylaxis (reassured by the literature and their experience) then they should start LMWH or pentasaccharide no less than six to eight hours after surgery and regional block. For those surgeons who are concerned about peri-operative bleeding, a mechanical device such as a Foot Pump should be started in the recovery room. It should be continued for the entire hospital stay for those thought to have a particularly high risk of VTE. Otherwise it could be stopped once the patient begins to mobilise. Chemical prophylaxis should be started once the surgeon feels that the risk of bleeding has subsided and at least six hours after any indwelling epidural catheter has been removed. In an ideal world it should be continued for five weeks (notwithstanding the logistical issues of funding and administration).

Hip fracture: In some patients, medical and social co-morbidity may occasionally suggest a more holistic approach. Otherwise, a mechanical device should be applied as soon after injury as possible (ie in the Emergency Department). The device should be used, and chemical prophylaxis instigated in the same way and for the same duration as hip replacement.

Knee replacement: The risk of soft tissue side effects is higher in knee replacement, yet VTE is more resistant to prophylaxis. Regional anaesthesia should be encouraged. A mechanical device should be started in recovery and continued, if tolerated, for as long as the patient is in hospital. Chemical prophylaxis should be started as soon after surgery/regional block as the surgeon feels is safe and continued for the entire hospital stay. For those going home in less than 10 days, or for those with other risk factors, chemical prophylaxis should be considered beyond discharge.

Other orthopaedic operations: There are so few data on both epidemiology and prophylaxis that one has to resort to common sense. If the risk assessment suggests a minimal risk of VTE then the cost and potential side-effects of peri-operative chemical prophylaxis may not be justified. However, if there is a potential risk, then a sensibly-timed combination of mechanical and chemical prophylaxis should be devised. *Major lower limb trauma and spinal surgery* certainly carry a risk of symptomatic thromboembolism yet carry a greater threat of bleeding. A longer period of mechanical prophylaxis, followed by extended chemical prophylaxis when safe, seems sensible. *Day case arthroscopy* causes very occasional VTE problems yet practical prophylaxis is difficult (the patient will have gone home before it is safe to give chemicals). The best one can do is to carry out a careful risk assessment and provide anyone with a higher risk with an injection prior to discharge and follow with home-prophylaxis until fully mobile.

Updating: Scientific knowledge, clinical experience and attitudes to risk change with time. It takes effort to get new medications on to a hospital formulary. It takes persuasion to change habits. A group of interested individuals in a department or hospital can keep the local guidelines acceptable and current.

CONCLUSION

Opinions about and options for thromboprophylaxis are continuously developing; perhaps this article helps surgeons to think about this important aspect of surgical care.

REFERENCES

- Amstutz H, Friscia D A, Dorey F, Carney BT (1989). Warfarin prophylaxis to prevent mortality from pulmonary embolism after total hip replacement. *J Bone Joint Surg*; 71A:321–6.
- Anti-platelet Trialists Collaboration, (1994) Collaborative overview of randomised trials of antiplatelet therapy; reduction in venous thrombosis and pulmonary embolism by anti platelet prophylaxis amongst surgical and medical patients. *British Medical Journal*: 308:235-246.
- Bergqvist D, Lindblad B, Matsch T. Low molecular weight heparin for thromboprophylaxis and epidural/regional anaesthesia—is there a risk? *Acta Anaesthesiol Scand* 1992; 36:605–609.

-
- Cohen A, Bailey C S, Alikhan R, Cooper D J. (2001) Extended thromboprophylaxis with low molecular weight heparin reduces symptomatic venous thromboembolism following lower limb arthroplasty. *Thrombosis and Haemostasis*; 85:940–941.
 - Cohen A, Quinlan D. (2000) PEP trial (letter). *Lancet*: 356:247.
 - Collins R, Scrimgeour A, Yusuf S, Peto R (1988). Reduction in fatal pulmonary embolism and venous thrombosis by perioperative administration of subcutaneous heparin. *N Eng J Med*; 318:1162–73.
 - Colwell C W, Collis D K, Paulson R, McCutchen J W, Bigler GT, Lutz S, Hardwick M E (1998). Comparison of enoxaparin and warfarin for the prevention of venous thromboembolic disease after total hip arthroplasty. Evaluation during hospitalisation and three months after discharge. *JBJS (A)* 1999; 81A:932–939.
 - Crawford W J, Hillman F, Charnley J (1968). A clinical trial of prophylactic anticoagulant therapy in elective hip surgery. *Internal Publication* 14, Centre for Hip Surgery, Wrightington Hospital.
 - Dahl O E, Gudmunsen T E, Haukeland L. Late occurring clinical deep vein thrombosis in joint-operated patients. *Acta Orthop Scand* 2000; 71:47–50.
 - Eikelboom J W, Quinlan D J, Douketis J D. (2001) Extended duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of the randomised trials. *Lancet*: 358:9–15.
 - Eriksson B I, Arfwidsson A C, Frison L *et al.* (2002). A dose ranging study of the oral direct thrombin inhibitor ximelagatran and its subcutaneous form Melagatran compared with dalteparin in the prophylaxis of thromboembolism after hip or knee replacement :METHRO I. *Thromb Haem*; 87:231–237.
 - Eriksson B I, Lassen M R. Duration of prophylaxis against venous thromboembolism with fondaparinux after hip fracture surgery: a multicentre, randomized, placebo-controlled, double blind study. *Arch Int Med* 2003; 163:1337–1342.
 - Eriksson B I, Ogren M, Agnelli G *et al* (2001). The oral direct thrombin inhibitor ximelagatran and its subcutaneous form Melagatran compared with enoxaparin as thromboprophylaxis after total hip or knee replacement (METHRO III). *Thromb Haem* 86S; OC46.
 - Friedman R J, Dunsworth G A. (2000) Cost analysis of extended prophylaxis with enoxaparin after hip arthroplasty. *Clinical Orthopaedics and Related Research*: 370:171–182.
 - Geerts *et al.* (2001) Prevention of venous thromboembolism. *Chest*; 119:132–175S.
 - Gregg P J, Devlin H B National Total Hip Replacement Outcome Study 2000. www.rcseng.ac.uk
 - Heit J A, Colwell C W, Francis C W *et al* (2001). Comparison of the oral direct thrombin inhibitor, ximelagatran compared with dalteparin in the prophylaxis of venous thromboembolism after knee replacement. *Arch Int Med*; 161:2215–21.
 - Horlocker T T (2001). Low molecular weight heparin and neuraxial anesthesia. *Thrombosis Research* 101:141–154.
 - Hull R D, Pineo G F, Stein P D, Mah A F, MacIsaac S M, Dahl OE, Butcher M, Brant R F, Ghali W A, Bergqvist D, Raskob G E. (2001a), Extended out of hospital low-molecular weight heparin prophylaxis against deep venous thrombosis in patients after elective hip arthroplasty: a systematic review. *Ann Intern Med.* 2001 Nov 20; 135(10):858–69.
 - Hull R D, Pineo G F, Stein P D, Mah A F *et al* (2001b) Timing of low molecular weight heparin prophylaxis against deep venous thrombosis in patients following elective hip arthroplasty. *Arch Int Med*; 161:1952–1960.
 - International Consensus Statement. *International Angiology*, 20:1–37 2001.
 - Lowe G D, Sandercock P A, Rosendaal F R. Prevention of venous thromboembolism after major orthopaedic surgery: is Fondaparinux an advance? *Lancet*; 362:504–5.
 - PEP. Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention trial. *Lancet* 2000;355:1295–1302.
 - Pre-operative vs postoperative initiation of low molecular weight heparin prophylaxis against venous thromboembolism in patients undergoing elective hip replacement. *Arch Int Med* 159:137–141.
 - Prins M, Hirsh J. A comparison of general anesthesia and regional anesthesia as a risk factor for deep vein thrombosis following hip surgery: a critical review. *Thromb Haemost* 1990; 64:497–500 Prins and Hirsh.
 - Rodgers A, Walker N, Schug S, McKee A, Kehlet H, van Zundeert A, Sage D, Futter M, Saville G, Clark T, MacMahon S. (2000). Reduction of post-operative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. *B Med J*; 321:1493–7.

- Sarasin F P, Bounameaux H. Out of hospital anti-thrombotic prophylaxis after total hip replacement: low molecular weight heparin, warfarin, aspirin or nothing. (2002) *Thrombosis and Haemostasis*: 87:586–92.
- THRIFT Consensus Group. (1998) Risk of and prophylaxis for venous thromboembolism in hospital patients. *Phlebology* 13:87–97.
- Turpie A G G, Bauer K A, Eriksson B I, Lassen MR. (2002). Fondaparinux vs Enoxaparin for the prevention of venous thromboembolism in major orthopaedic surgery. *Arch Int Med*; 162:1833–1840.
- Warwick D J, Samama M M. (2000) The contrast between radiological and clinical outcomes in orthopaedic thromboembolism. *J Bone Joint Surg* 2000.
- White R H, Romano P S, Zhou H, Rodrigo J, Bargar W (1998) Incidence and time course of thromboembolic outcomes following total hip or knee arthroplasty *Arch Intern Med*; 158:1525–1531 1998.

Figure 1

REDUCTION IN ASYMPTOMATIC DVT IN ORTHOPAEDIC SURGERY CORRELATES WITH REDUCTION IN FATAL PE

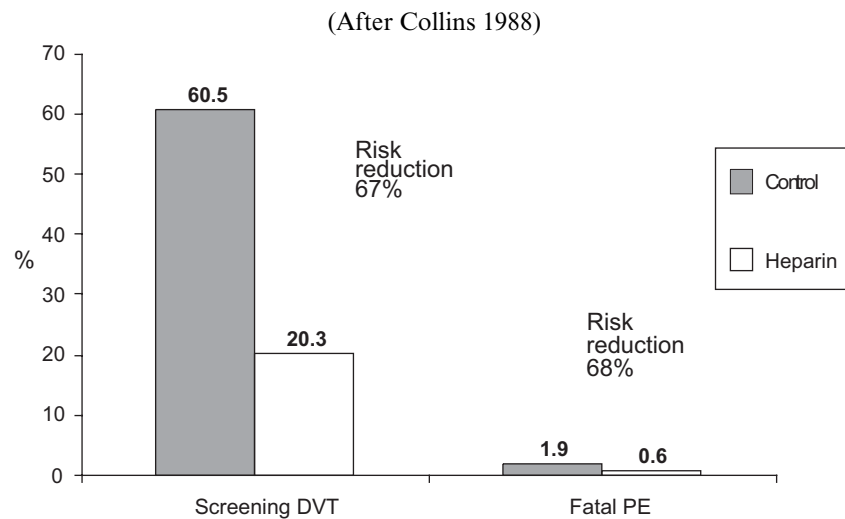


Figure 2

RISK REDUCTION WITH EXTENDED PROPHYLAXIS: VENOGRAPHIC DVT CORRELATES WITH SYMPTOMATIC VTE

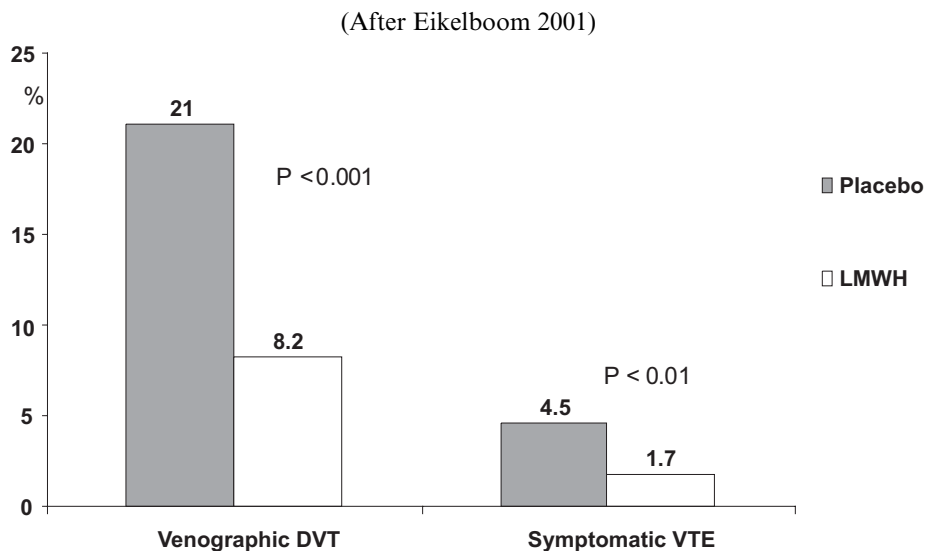


Figure 3
ARIXTRA EXTENDED FOR FIVE WEEKS AFTER HIP FRACTURE
 (After Eriksson 2003)

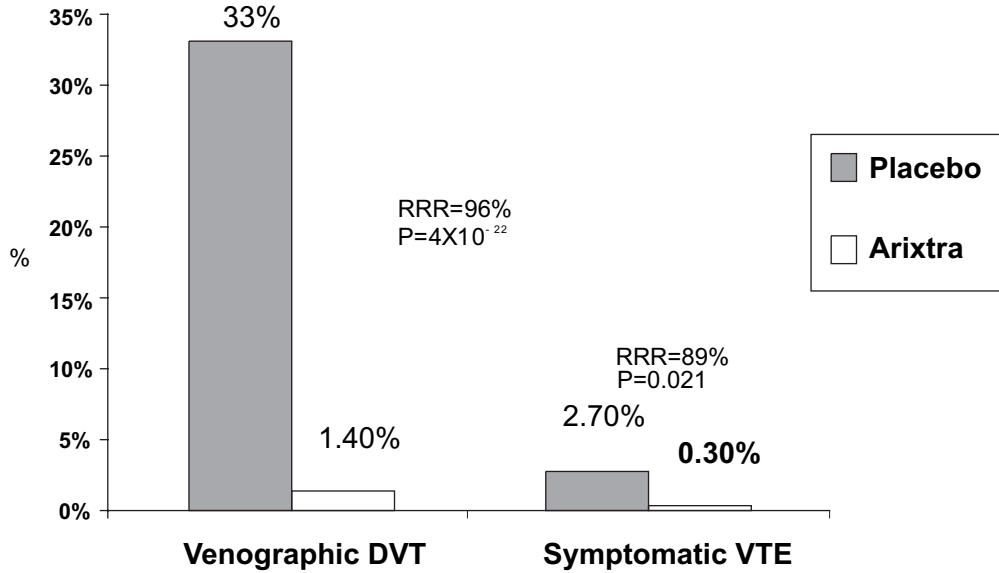
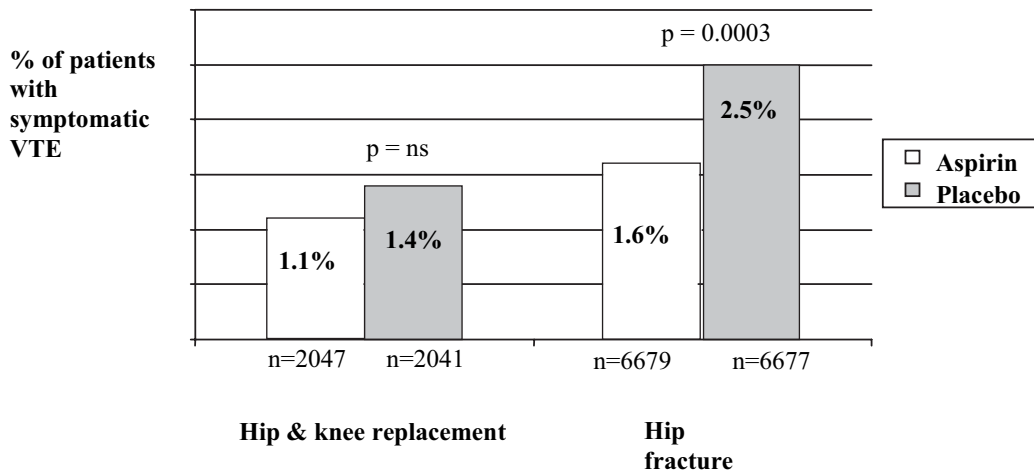


Figure 4:
FREQUENCIES OF DVT AND PE WITH ASPIRIN
 (after PEP study 2000)



Death Rate 447/6679 aspirin, 461/6677 placebo (hip fracture)
 17/2047 aspirin, 22/2041 placebo (hip and knee replacement)

Figure 5

SIDE EFFECTS WITH ASPIRIN—EVENTS PER 1,000 PATIENTS TREATED WITH ASPIRIN COMPARED WITH PLACEBO

(overall death rate unchanged)

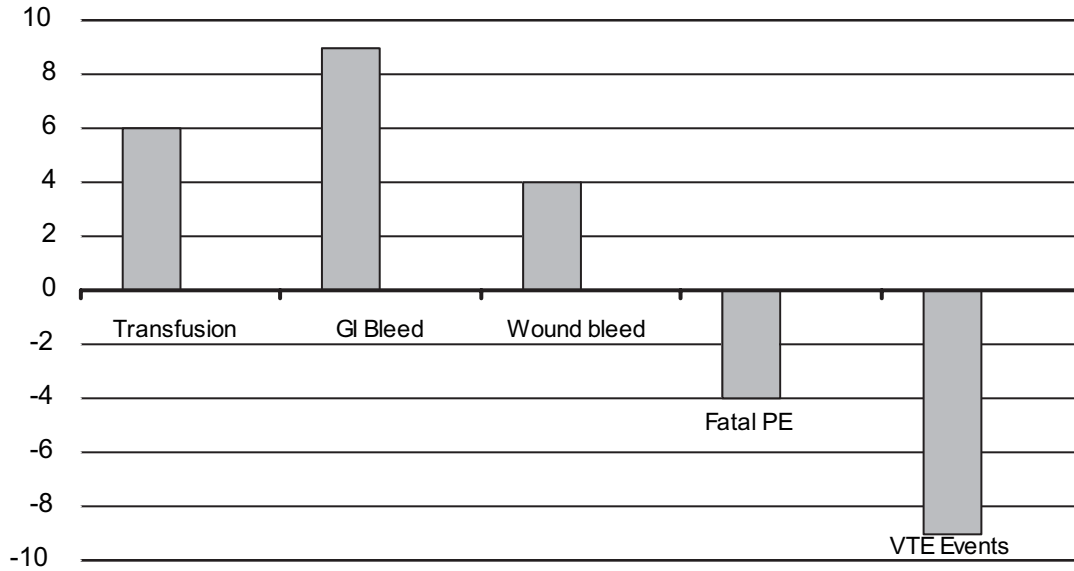
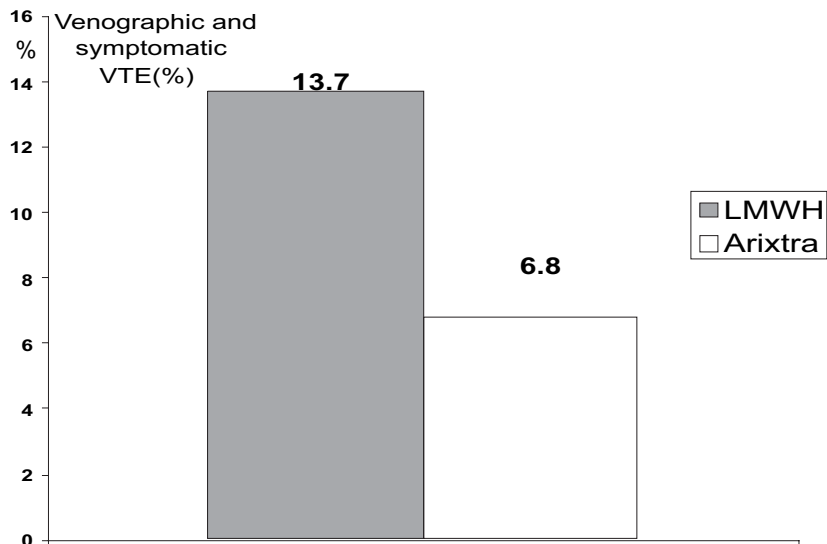


Figure 6

PENTASACCHARIDE VS LMWH. VTE RATES AFTER 11 DAYS

(after Turpie *et al* 2002)

($p = 10^{-17}$) Overall odds reduction 55.3%, (CI 45.8 to 63.2%)



Memorandum by Professor Ajay Kakkar (VT 13)

1. WHAT IS VENOUS THROMBOEMBOLISM (VTE)

Venous thromboembolism is a spectrum of disease ranging from (small) deep vein thrombosis (DVT), most frequently occurring in the deep venous system of the lower limbs to pulmonary embolism (PE), a potentially fatal disease resulting when thrombus enters the pulmonary arterial circulation and occludes blood flow to the lungs. Thrombosis in the venous circulation may be asymptomatic (no clinical symptoms) whether a DVT or a PE, or symptomatic (clinically apparent). Both asymptomatic and symptomatic VTE may be associated with acute morbidity or may be fatal.

2. WHAT IS THE RATIONALE FOR PREVENTING VENOUS THROMBOEMBOLIC DISEASE (THROMBOPROPHYLAXIS) FOR HOSPITALISED SURGICAL AND MEDICAL PATIENTS

2.1 The rationale for providing thromboprophylaxis is based upon (1) the high prevalence of VTE amongst hospitalised patients in certain defined risk groups; (2) the adverse consequences of unprevented VTE; (3) the proven efficacy and cost effectiveness of thromboprophylaxis.

2.2 Without thromboprophylaxis the reported frequency of hospital acquired DVT is approximately 10–30% for medical and general surgical patients and 40–60% for orthopaedic surgical patients. About $\frac{1}{4}$ to $\frac{1}{3}$ of these thrombi form in the proximal deep veins. The proximal vein thrombi may be associated with potentially fatal pulmonary embolism (PE).

2.3 VTE is the most common serious complication experienced by certain groups of hospitalised patients, with a reported frequency of PE at autopsy of about 30% for patients dying within 30 days of operation, in whom about $\frac{1}{3}$ it was the cause of death. 10% of hospital deaths may be attributed to PE.

2.4 Since VTE is often silent when acquired in hospital, reliance on clinical diagnosis is not appropriate, since the first manifestation of this disease may be fatal PE.

2.5 If VTE is not prevented, the consequences include the risk of fatal PE, the morbidity associated with acute symptomatic VTE, bleeding associated with long-term anticoagulation, need for monitoring of long-term anticoagulant therapy, increased risk for future episodes of VTE, need for re-admission/increased lengths of stay to treat the thrombosis as well as the considerable healthcare and wider associated costs, and the pain and disability associated with the post-thrombotic syndrome many years after the acute thrombosis.

2.6 Thromboprophylaxis has been shown to be effective in preventing both DVT and PE, for which such strategies have also been shown to be cost effective in high-risk hospitalised patients.

3. REPORTED FREQUENCY OF VTE FOR SPECIFIC HOSPITALISED POPULATIONS

3.1 The rate of DVT in hospitalised patients, not receiving thromboprophylaxis using objective diagnostic methods for screening both asymptomatic (not clinically overt) and symptomatic (clinical) disease are:

general surgical	15–30%
hip and knee	40–60%
medical	10–20%
stroke	20–50%

3.2 Identification of high-risk patient groups (eg above) is possible but predicting which individual patient will develop a hospital acquired VTE is not. Fatal PE frequently occurs without warning, and thus strategies based upon diagnosing VTE once it occurs and treating it will not be successful. Frequently, (70–80% of cases) when fatal PE occurs it was not considered as a potential diagnosis prior to death.

3.3 Numerous clinical trials over the past 30 years have confirmed that thromboprophylaxis reduces the frequency of both asymptomatic and symptomatic VTE and fatal PE.

3.4 Pulmonary embolism is the most common preventable cause of hospital death. In the report “Making healthcare safer: a critical analysis of patient safety practices” by the United States Agency for Healthcare research and quality, a 79 patient safety intervention was reviewed. The highest ranked safety practice was the “appropriate use of prophylaxis to prevent VTE in patients at risk”. This conclusion was based upon evidence that thromboprophylaxis reduced adverse patient outcome and at the same time decreased overall cost.

4. INTERPRETING THE RESULTS OF CLINICAL TRIALS IN THE FIELD OF THROMBOPROPHYLAXIS

4.1 Numerous studies have evaluated the efficacy and safety of various methods for thromboprophylaxis over the past three decades. These studies have utilised different endpoints including asymptomatic thrombosis, detected by objective screening methods, symptomatic DVT and PE, fatal PE and all cause mortality.

4.2 Safety endpoints in such studies have included minor and major bleeding events associated with pharmacological therapy.

4.3 For both efficacy and safety, well-designed trials have used independent blinded adjudication of events to maintain objectivity.

4.4 Although the priority of thromboprophylaxis is to prevent fatal PE, this event is uncommon. Beyond prevention of fatal PE, avoidance of symptomatic DVT or PE are also very important objectives, since these events occur more frequently than fatal PE and are associated with a significant morbidity, increased consumption of healthcare resources and long-term clinical consequences as manifest by the post phlebotic syndrome and chronic pulmonary hypertension.

4.5 There are differing views as to which endpoints are appropriate for clinical trials assessing thromboprophylaxis. Some argue that the demonstration that a specific method of prophylaxis can prevent fatal PE is the only endpoint suitable to validate its use in specific high-risk populations. Others argue that endpoints that screen for all thrombosis, even if the disease is asymptomatic are valid, since although most asymptomatic disease is not clinically relevant, there is a strong correlation between the surrogate marker of asymptomatic thrombosis, and symptomatic clinical disease.

4.6 Studies evaluating pharmacological methods of thromboprophylaxis utilising low dose unfractionated heparin (LDUH) or low molecular weight heparin (LMWH) have been shown to reduce the frequency of asymptomatic DVT, symptomatic disease and fatal PE for general surgical patients.

5. GENERAL SURGICAL PATIENTS

5.1 The observed rate for DVT in general surgical patients not receiving thromboprophylaxis is 15–30% with a fatal PE rate of 0.2% to 0.9%. Many factors may influence the risk of thrombosis in this patient group including age, previous history of DVT, obesity, cancer, oestrogen use.

5.2 Some argue that these reported rates are historic and the frequency of VTE may be falling. This is not possible to test since it would be unethical to perform trials without thromboprophylaxis in this population. However, demographic considerations indicate that there are now more extensive operations being performed on older patients, more cancer operations and more patients with obesity than in the past. These would suggest an increasing risk for thrombosis in contemporary general surgical populations.

5.3 For surgical patients, patients may be allocated to one of four potential risk groups low, moderate, high and highest based upon patient age, presence of absence of VTE risk factors, and type of operation. Not all patients require active pharmacological prophylaxis. For low risk patients eg under the age of 40 with no other risk factors and a duration of operation less than 30 minutes, no specific thromboprophylaxis is required apart from mobilisation. But for highest risk patients, where the VTE risk is substantial (proximal DVT rate 10–25%; fatal PE rate 0.2–5%), eg age over 40 years, with other VTE risk factors present, having an operation for cancer or an orthopaedic procedure, pharmacological prophylaxis would be indicated.

5.4 The landmark study that heralded the modern era of thromboprophylaxis was the International Multicentre trial (Lancet 1975) published from the United Kingdom. This study in over 4,000 patients undergoing major surgery, with an endpoint of autopsy proven fatal PE, demonstrated that the use of perioperative low dose heparin reduced the frequency of fatal PE from eight per 1,000 to one per 1,000 operated patients—saving seven lives per 1,000 operated patients.

5.5 In a meta-analysis of 46 studies evaluating low dose heparin against placebo/control in general surgical patients, the rate of DVT was reduced from 22% to 9% (OR 0.3, number of patients needed to treat to avoid one DVT was seven); fatal PE was reduced from 0.8% to 0.3% (OR 0.4, number of patients needed to treat to avoid one fatality 182). This was associated with a small increase in bleeding 3.8% to 5.9% (number needed to harm 47).

5.6 An alternative option for pharmacological thromboprophylaxis in general surgical patients is low molecular weight heparin (LMWH) administered once daily subcutaneously. A meta-analysis of randomised trials in general surgical patients comparing LDUH with LMWH involving 44,000 patients demonstrated LMWH administered once daily to be as effective as LDUH, which is usually administered twice or three times daily.

5.7 Mechanical methods of thromboprophylaxis (pneumatic calf compression, compression stockings) have been evaluated in general surgical patients. A systematic review of trials using such methods indicated that mechanical methods did reduce the frequency of DVT, but these methods have not been as extensively investigated as pharmacological methods of thromboprophylaxis, and have not been shown to reduce the frequency of fatal pulmonary embolism (PE). They may be considered in general surgical patients at high-risk for bleeding.

5.8 Thromboprophylaxis for moderate to high-risk general surgical patients is usually recommended for the duration of hospital stay. The question of extended thromboprophylaxis beyond hospital discharge has recently been considered, since although the risk of developing VTE is greatest in the first week or so after

surgery, certain patients including those having undergone operation for cancer have a persistent VTE risk beyond hospital discharge. There is no consensus as to whether thromboprophylaxis should be extended out of hospital for this population.

5.9 Routine thromboprophylaxis appears to be well accepted among general surgical practitioners in the UK.

6. ORTHOPAEDIC PATIENTS

6.1 Elective joint arthroplasty is a common procedure. Without thromboprophylaxis the frequency of asymptomatic (non-clinical) DVT is 40–60%, symptomatic clinical VTE is 2.5% and fatal PE is about 0.5% in elective hip joint replacements.

6.2 The great fear of orthopaedic surgeons with regard to the use of pharmacological thromboprophylaxis is the risk of bleeding complications, which may result in an increased risk for bleeding around the replaced joint cavity with risk of prosthesis infection or loosening.

6.3 Mechanical methods of thromboprophylaxis have been evaluated in orthopaedic patients but have not been as extensively tested as pharmacological methods. Although they do not increase bleeding risk, they are not as effective as pharmacological methods in the prevention of potentially serious proximal vein thrombi, nor have they been shown to reduce the frequency of fatal PE.

6.4 Pharmacological methods have been extensively studied in this population. The available recommended options include LMWH and the oral anticoagulant Vitamin K antagonists. Low dose heparin is not as effective an agent for thromboprophylaxis in orthopaedic patients as other methods available, and is not recommended. Vitamin K antagonists are used in North America, but not Europe. Rates of DVT are reduced to around 15–20% with LMWH prophylaxis, with reported rates of bleeding around 5%, compared to bleeding rates in historic placebo controlled studies of about 4% (ie 1% increase).

6.5 The recommended thromboprophylaxis for orthopaedic hip surgical patients in Europe is LMWH. The duration is for at least the duration of hospital stay. Recent studies indicate that for hip replacement patients, the duration of risk for VTE extends into the post discharge period for up to 5 weeks after operation, where continuing LMWH prophylaxis into the post discharge is associated with a significant reduction in both asymptomatic and symptomatic VTE.

6.6 Use of thromboprophylaxis among orthopaedic practitioners is less well established. This may be driven by concern about the adverse consequences of bleeding.

7. MEDICAL PATIENTS

7.1 Acutely ill hospitalised medical patients are at risk for the development of VTE. 50–70% of symptomatic VTE and 70–80% of fatal PEs occur in hospitalised medical patients. The reported rate of all thrombosis (asymptomatic disease), screened using venography in hospitalised medical patients, is 15% indicating these patients have a low to moderate risk for hospital acquired VTE.

7.2 Patients at particular risk for the development of VTE in an acute medical illness include those with severe heart failure, chronic respiratory disease, sepsis and cancer.

7.3 Both LDUH and LMWH have been shown to provide effective and safe thromboprophylaxis in hospitalised acutely ill medical patients who are at risk for VTE. These interventions have also been shown to be cost effective if applied to appropriate populations with acute illness.

8. RECOMMENDATIONS

8.1 Appropriate use of pharmacological prophylaxis has the ability to prevent potentially serious VTE. Not all hospitalised medical or surgical patients require prophylaxis. Specific patient groups at particular risk for the development of hospital acquired VTE are recognised. In these specific groups application of validated methods of thromboprophylaxis are both efficacious, safe, and cost effective.

8.2 Hospitals should be encouraged to have written policies for VTE prevention which may be applied to appropriate patient populations in whom a definite risk for VTE is identified. These policies may be based on internationally accepted consensus guidelines which are available.

REFERENCE

Prevention of Venous Thromboembolism

The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy

Geerts W H, Pineo G F, Heit J A, Bergqvist D, Lassen M R, Colwell C W, Ray J G

Chest 2004;126:338S-4002S

Memorandum by The Royal College of Physicians (VT 15)

THE PROBLEM

1. Thrombosis in the veins usually occurs in the deep veins of the lower limb or pelvis (deep vein thrombosis, DVT). The main danger is that a clot can break free (embolise), and be carried in the blood stream into the right atrium of the heart. From there it will usually pass with the blood into the right ventricle of the heart and then out of the heart in the pulmonary artery. As the pulmonary arterial system divides into smaller vessels the clot will come to rest and block the flow of blood through the lungs. This is called a pulmonary embolism (PE) and a large PE can be fatal. DVT and PE are collectively referred to as venous thromboembolism (VTE).

2. The incidence of DVT is approximately 100 per 100,000 and for PE 50 per 100,000. The risk factors are increasing age, surgery and trauma, immobilisation and paresis, malignancy, and changes in the blood (the inherited thrombophilias and antiphospholipid antibodies). In women they would also include pregnancy and the puerperium, the combined oral contraceptive pill and hormone replacement therapy.

3. Most hospitalised patients have risk factors for VTE and DVT is common in hospitalised patients. The condition is often at first clinically silent but symptomatic DVT and PE are common in patients who do not receive prophylaxis. The in-hospital case-fatality rate of VTE is often underestimated—it is 12%¹. Approximately 10% of hospital deaths may be due to PE^{2, 3}. Investigating and treating symptomatic patients is costly. Patients are at increased risk of future VTE and may develop post-thrombotic syndrome. Post thrombotic syndrome is chronic pain, swelling, and occasional ulceration of the skin of the leg and it occurs in up to one third of patients who have a DVT^{4, 5}. It can occur early or have a latency of up to 10 years, the cumulative frequency has been estimated as 23% at two years and 28% at five years⁴.

4. Thromboprophylaxis is highly effective and cost effective. PE is the most common preventable cause of hospital death. The Agency for Healthcare Research and Quality has published a report entitled “Making Health Care Safer: a Critical Analysis of Patient Safety Practices”⁶. This systematic review ranked 79 patient safety interventions based on the strength of the evidence supporting more widespread implementation of these procedures. The highest ranked safety practice was the “appropriate use of prophylaxis to prevent VTE in patients at risk.”

DO WE NEED GUIDELINES?

5. No, we already have them. I think the best are the ACCP guidelines⁷ available at http://www.chestjournal.org/cgi/content/full/126/3_suppl/338S. These have just been updated and are evidenced based with 794 references.

WHAT DO THE GUIDELINES RECOMMEND?

6. A summary of the ACCP advice is:

“For moderate-risk general surgery patients, we recommend prophylaxis with low-dose unfractionated heparin (LDUH) (5,000 U bid) or low-molecular-weight heparin (LMWH) (< 3,400 U once daily) (both Grade IA). For higher risk general surgery patients, we recommend thromboprophylaxis with LDUH (5,000 U tid) or LMWH (> 3,400 U daily) (both Grade IA). For high-risk general surgery patients with multiple risk factors, we recommend combining pharmacologic methods (LDUH three times daily or LMWH, > 3,400 U daily) with the use of graduated compression stockings and/or intermittent pneumatic compression devices (Grade 1C). We recommend that thromboprophylaxis be used in all patients undergoing major gynecologic surgery (Grade IA) or major, open urologic procedures, and we recommend prophylaxis with LDUH two times or three times daily (Grade IA). For patients undergoing elective total hip or knee arthroplasty, we recommend one of the following three anticoagulant agents: LMWH, fondaparinux, or adjusted-dose vitamin K antagonist (VKA) (international normalized ratio (INR) target, 2.5; range, 2.0 to 3.0) (all Grade IA). For patients undergoing hip fracture surgery (HFS), we recommend the routine use of fondaparinux (Grade IA), LMWH (Grade 1C), VKA (target INR, 2.5; range, 2.0 to 3.0) (Grade 2B), or LDUH (Grade 1B). We recommend that patients undergoing hip or knee arthroplasty, or HFS receive thromboprophylaxis for at least 10 days (Grade IA). We recommend that all trauma patients with at least one risk factor for VTE receive thromboprophylaxis (Grade IA). We recommend, on admission to the intensive care unit, all patients be assessed for their risk of VTE. Accordingly, most patients should receive thromboprophylaxis (Grade IA).”

THE ADVICE FOR MEDICAL PATIENTS

7. 70 to 80% of fatal PEs occur in non-surgical patients. Hospitalised medical patients account for one quarter of all VTE in the population⁸. LDUH and LMWH lower the risk of VTE by at least 50% in medical patients. The advice for medical patients is:

“In acutely ill medical patients who have been admitted to the hospital with congestive heart failure or severe respiratory disease, or who are confined to bed and have one or more additional risk factors, including active cancer, previous VTE, sepsis, acute neurological disease, or inflammatory bowel disease, we recommend prophylaxis with LDUH (Grade 1A) or LMWH (Grade 1A).”

WHY IS PROPHYLAXIS NOT GIVEN PROPERLY?

8. Many doctors believe that the incidence of VTE has declined in recent years. They frequently site retrospective surveys of their own experience. It may be true that VTE has declined recently due to more widespread use of prophylaxis as well as improved operative and peri-operative management but the rate is still high. The low post-mortem rate in the UK means that many cases of fatal PE will not be known.

9. Another reason for not giving prophylaxis is the perceived risk of bleeding. However, abundant data from meta-analyses and placebo-controlled, blinded, randomized clinical trials have demonstrated little or no increase in the rates of clinically important bleeding with LDUH or LMWH. In practice bleeding may be mistakenly attributed to prophylaxis whilst its benefit (say a reduction in fatal PE from 0.7 to 0.2%) may not be appreciated by the individual practitioner.

10. Finally it should be emphasised that although the SIGN guidelines⁹ consider aspirin a reasonable prophylactic agent, the ACCP guidelines specifically state that “we recommend against the use of aspirin alone as thromboprophylaxis for any patient group (Grade 1A)”. The oft quoted PEP trial¹⁰ supporting aspirin has been heavily criticised, eg¹¹.

WHAT DO WE NEED TO DO?

11. We have excellent guidelines but need to ensure they are implemented.

12. Every patient admitted to hospital should have their risk of VTE assessed. All clinical areas should have protocols for VTE prophylaxis based on authoritative guidelines. It should be clearly recorded either that the patient does not require prophylaxis or if they do the regimen should be recorded in the notes and implemented.

References:

1. Anderson, F J, *et al*, *A population-based perspective of the hospital incidence and case fatality rates of deep vein thrombosis and pulmonary embolism. The Worcester DVT Study*. Arch Intern Med, 1991. 151(5): p 933–8.
 2. Lindblad, B, A Eriksson, and D Bergqvist, *Autopsy-verified pulmonary embolism in a surgical department: analysis of the period from 1951 to 1988*. Br J Surg, 1991. 78(7): p 849–52.
 3. Stein, P D and J W Henry, *Prevalence of acute pulmonary embolism among patients in a general hospital and at autopsy*. Chest, 1995. 108(4): p 978–81.
 4. Prandoni, P, *et al*, *The long-term clinical course of acute deep venous thrombosis [see comments]*. Ann Intern Med, 1996. 125(1): p 1–7.
 5. Prandoni, P, *et al*, *Which is the outcome of the post-thrombotic syndrome? [letter]*. Thromb Haemost, 1999. 82(4): p 1358.
 6. Shojania, K G, *et al*, *Making health care safer: a critical analysis of patient safety practices*. Evid Rep Technol Assess (SunuP), 2001(43): p i–x, 1–668.
 7. Geerts, W H, *et al*, *Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy*. Chest, 2004. 126(3 Suppl): p 338S–400S.
 8. Heit, J A, *et al*, *Relative impact of risk factors for deep vein thrombosis and pulmonary embolism: a population-based study*. Arch Intern Med, 2002. 162(11): p 1245–8.
 9. *Prophylaxis of Venous Thromboembolism*. SIGN Publication No 62 ISBN 1899893 03 2www.sign.ac.uk/guidelines/fulltext/62/index.html, 2002.
 10. *Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial*. Lancet, 2000.355(9212): p 1295–302.
 11. Cohen, A and D Quinlan, *PEP trial. Pulmonary Embolism Prevention*. Lancet, 2000. 356(9225): p 247; author reply 250–1.
-

Memorandum by Lifeblood: the Thrombosis Charity (VT 6)

Lifeblood: the thrombosis charity was born out of frustration caused by the lack of awareness of thrombosis, especially venous thromboembolism (VTE). VTE is a life-threatening disorder and is the commonest preventable cause of hospital mortality. VTE is easily prevented, but prevention depends on both patients and health professionals being aware of this condition. Thus it is critical to heighten this awareness.

We are extremely grateful to the members of the Health Select committee for organising this enquiry, which we in Lifeblood believe is much needed.

THE FACTS

Explanatory terms

Deep vein thrombosis (DVT)—development of a clot (thrombus) in the leg

Pulmonary embolism (PE)—when clot in the leg breaks off and travels round the circulation through the right side of the heart to block the pulmonary arteries. Large ones can be fatal. Small ones can cause chest pain and breathlessness.

Venous thromboembolism (VTE)—a term that encompasses deep vein thrombosis and pulmonary embolism.

Post-phlebotic syndrome—chronic venous insufficiency after deep vein thrombosis characterised by swelling, pain, dermatitis, cellulites, varicose veins, pigmentation of the skin and eventually chronic ulceration of the lower leg.

IN THE UK VTE CAUSES AROUND 32,000 DEATHS EACH YEAR

Risk factors for VTE are well defined¹—immobility, acute illness, major surgery especially long operations and orthopaedic surgery, malignancy, pregnancy, increasing age and obesity. The risk is increased further where the patient has several risk factors.

Deep vein thrombosis is common in hospital in-patients, both in medical and surgical patients, for example prior to specific prevention measures being introduced, around 30% of surgical patients developed a DVT. Furthermore the patient often had no signs or symptoms of this serious complication.

The condition can lead to sudden death due to pulmonary embolism. Pulmonary embolism following deep vein thrombosis is the immediate cause of death in 10% of all patients who die in hospital.

VTE has a high recurrence rate. The estimated recurrence rate over 10 years is estimated to 30%.²

Doctors often forget and patients often don't appreciate that deep vein thrombosis can lead to long term health problems due to post-thrombotic limb and venous ulceration. **Around 100,000 people in England and Wales are estimated to suffer from venous leg ulcers often arising following a DVT.** Various methods are used to promote healing but some ulcers are resistant, resulting in severe distress and often prolonged periods of hospitalisation. The NHS cost of treating venous leg ulcers is as high as £400 million per year.

There is a huge body of research showing that use of specific treatments to prevent clots (thromboprophylaxis) reduces the frequency of death and post phlebotic syndrome substantially if given at times of high risk such as after surgery or during an in-patient stay.

Guidelines do exist to provide advice on thromboprophylaxis. The most widely quoted are the Scottish Intercollegiate Guidelines Network (SIGN)³.

In hospital medicine we are reaching the stage where the question should not be “Does this patient need thromboprophylaxis”, but a clinical assumption should be that all adult patients need thromboprophylaxis unless there are contraindications and so the question should be “Is there any reason for this patient not to receive thromboprophylaxis?”

ARE WE IMPLEMENTING THROMBOPROPHYLAXIS APPROPRIATELY IN THE UK?

In the UK we should congratulate ourselves on leading the world in prevention of venous thromboembolism in pregnancy. We have good data collection: The Confidential Enquiry into Maternal Deaths⁴ in the UK has highlighted that venous thromboembolism remains the commonest cause of maternal death. We have many of the international leaders in the field: they produce superb research. The medical

community has responded well: the Royal College of Obstetricians has produced a series of guidelines to highlight the risks and preventative measures⁵, which are followed by the obstetric community.

However practice in other fields is not so good. Although the risks of deep vein thrombosis are in the order of one in two in orthopaedic surgery, we know that clinical practice is enormously variable. Indeed last year the Department of Health estimated that four out of every 10 orthopaedic patients do not receive any thromboprophylaxis at all⁶. A recent audit of 2,000 in-patients from around England showed that 35% of surgical patients and 45% of medical patients who are eligible for thromboprophylaxis are not receiving it⁷.

A number of factors have been identified to the under use of thromboprophylaxis, including the perception that VTE was not a significant problem or that prophylaxis was ineffective; physicians lack of awareness of guidelines, concerns about possible side-effects and a lack of funding and infrastructure to adhere to recommendations⁸.

To highlight the problems, let us imagine that each one of us needs a hip replacement—a standard and common operation in the NHS. We are all going to be cared for by different orthopaedic surgeons. When we are admitted, we will be counselled and asked to consent about the risks of the operation and perhaps blood transfusion. The risks of blood transfusion are small nowadays. The risk of contracting a major infection through a blood transfusion is about one in half a million. Contrast this with the very real risk of VTE, yet few, if any health professionals will counsel the patient about the risks of venous thromboembolism. Surgery has long been recognised as a major risk factor for VTE, and, after hip surgery, clinical (detectable by a doctor) DVT develop in about 8% of cases. However, if one looks at patients with special scans, up to 60% develop a deep vein thrombosis if they do not receive thromboprophylaxis. About 1–2% of these patients will develop pulmonary emboli.

IF NO THROMBOPROPHYLAXIS IS GIVEN DURING HIP REPLACEMENTS OPERATIONS ABOUT 0.4% RESULT IN DEATH, AND WITHIN FIVE YEARS 16% OF PATIENTS WILL HAVE POST PHLEBITIC SYNDROME WITH NEARLY 4% GETTING LEG ULCERS IN THE LONG-TERM

Now it may be that your surgeon uses thromboprophylaxis and you will receive daily injections of some form of heparin to reduce the risk. But for many patients they receive inadequate prevention. Why is it that we are receiving counselling about Blood Transfusion, when most of us will receive none at all about the most common complication after surgery—deep vein thrombosis? Currently this is considered acceptable practice in the UK.

HOW CAN WE MAXIMISE THE USE OF THROMBOPROPHYLAXIS?

Recently the French Government has set a target to reduce the incidence of deep vein thrombosis by 15%⁹.

In the UK “The prevention of venous thromboembolism in patients undergoing orthopaedic surgery and other high risk surgical procedures” is listed on the eighth NICE work programme⁶. However at Lifeblood: the thrombosis charity we hold major concerns that the production of guidelines will take several years to develop, that they will be limited to a group of hospitalised patients and more importantly that there will be failure to implement them appropriately.

We suggest that there needs to be more active intervention from the Department of Health. Perhaps the best model of how the situation can be improved is that of Blood Transfusion. The Dept of Health issued two directives in 1998 (HSC 1998/224)¹⁰ and 2002 (HSC 2002/009)¹¹ entitled “Better blood transfusion” that set out a number of requirements for improvement in the clinical practice of blood transfusion. These included the appointment of Blood Transfusion specialists within each Trust, and a committee within each trust to supervise the use of blood within the Trust. What has happened? The use of blood is more considered. Practices have improved and changed. Health care professionals have been educated about the use of blood.

Perhaps such a model might be applicable to thromboprophylaxis. Ideally each trust could be directed to have a committee to oversee the production and adherence to thromboprophylaxis protocols in all area. This would be a win-win situation. For increasing the use of thromboprophylaxis would reduce the mortality and morbidity from VTE at very little cost when compared with both the economic and health costs of the consequences. This is not a difficult project. We understand the disease, we can identify those at risk, we can prevent the problem with simple effective and cheap interventions, but we lack awareness and thereby the will to effect change.

THE POLICY IS CLEAR, INCREASE AWARENESS OF VTE AND REDUCE DEATH AND DISABILITY FROM THE COMMON CONDITION

References:

1. Heit J A. Risk factors for venous thromboembolism. Clin Chest Med 2003.
2. Heit *et al.* Predictors of recurrence after deep vein thrombosis and pulmonary embolism: a population-based cohort study. Arch Intern Med 2000; 160: 761–8.
3. Scottish Intercollegiate Guidelines Network (SIGN). www.sign.ac.uk
4. The Confidential Enquiry into Maternal and Child Health (CEMACH). www.cemach.org.uk
5. Royal College of Obstetricians. www.rcog.org.uk
6. Department of Health. Further action to tackle post-code lottery in care [press release]. <http://www.dh.gov.uk>
7. Preliminary pooled data from a national audit. Unpublished data from Sanofi-Aventis
8. Kakkar AK *et al.* Compliance with recommended prophylaxis for venous thromboembolism: improving the use and rate of uptake of clinical practice guidelines. J Thromb Haemost 2004; 2: 221–7.
9. French government. Loi de Sante Publique 2004–08- prevention des TVP: une nouvelle priorite (p 79).
10. Health Service circular HSC 2002/009. Better Blood Transfusion. Date of issue 4 July 2002. <http://www.doh.gov.uk/publications/coinh.html>
11. Health Service Circular HSC 1998/224. Better Blood Transfusion.

Memorandum by Linda de Cossart (VT 17)

What is a deep vein thrombosis?

For the purpose of this paper a deep vein thrombosis is defined as a clot within the deep veins of the lower limb or pelvis. This may occur spontaneously but more commonly is a result of an illness or operation requiring the person to be confined to bed. It may be related to a person's acquired or genetic predisposition.

What are the complications of DVT disease?

The complications are:

- The requirement to be on drug therapy with either Heparin and Warfarin for period which may be as long as six months.
- Chronic Venous Insufficiency which is a life long problem and may lead to leg ulcer formation.
- Pulmonary embolism (where the clot in the lower extremity breaks off and travels into the lungs causing occlusion of the inflow into the lungs) which is potentially lethal.

Epidemiology

Some of the best figures for the incidence and complications of DVT disease come from the USA. Population based studies suggest that in the USA:

- two million people are affected per year;
- 56 per 100,000 are subject to DVT; and
- 23 per 100,000 to pulmonary embolism and in this last group a 12% mortality is recorded.

These figures must however be taken with some degree of scepticism with respect to the fact that they are not complete data sets from national registries and may therefore be an under representation of the problem.

The key for clinicals is to have a high index of suspicion in for the diagnosis of DVT and pursuing the most appropriate method to exclude the condition. Prevention of DVT in hospitalised patients is key.

Aetiology

Hypercoagulability is created by a genetic predisposition, increasing age and many clinical events/ conditions eg cancer, operations, bed rest, pregnancy (until recently PE was the highest cause of perinatal mortality) and trauma. The body's natural fibrinolytic system attempts to minimise the risk of thrombosis and in the steady state these two system probably work in equilibrium.

The diagnosis of DVT and pulmonary embolism relies on:

- clinical suspicion;
- screening if appropriate;
- Colour Flow Duplex Imaging;
- Venography; and
- CT angiography.

Increases in the demand for imaging has put great strain on imaging departments through the UK in the past 10 years.

The management of DVT disease

Once deep vein thrombosis has been diagnosed then it must be treated by anti-coagulation to prevent further extension of the thrombosis and contain the problem therefore ideally minimising the risk of complications. The two treatment modalities that are most commonly used are subcutaneous Heparin therapy and Warfarin therapy. The time of each of these treatments will depend on the extent of the disease at the initial diagnosis. New drugs are being currently investigated and although not yet introduced in clinical practice will compete with Warfarin for oral therapy for this condition. It is recognised that about a 1% risk per year of a serious bleed on Warfarin is a current risk of patients on this treatment.

If PE has occurred or there is a risk of one because of free floating clot a vena caval filter may be needed.

Preventing DVT: Thrombo-prophylaxis

There are groups of patients that are clearly at risk of developing DVT disease. This has been well recognised in the surgical domain where operation predisposes people immediately and the thrift assessment for categorising risk is well known. (see Figure I)

These patients of course can then be managed by an anti-DVT prophylaxis regime in order to minimise the risk. Failure to implement this are shown in the classification of risk enclosed on the previous chart. (see Figure II)

Two modalities of prophylactic treatment increase the effectiveness of the prevention of DVT and may be combinations of, subcutaneous heparin and graduated support stockings beginning prior to surgery. Intra-operative treatment with calf compression firstly increases the fibrolytic systemic effects of the compression as well as a mechanical relationship to squeezing the calf during a time of stasis of the veins and blood flow in the limbs because of operation.

THE KEY THINGS THAT ARE CALLED TO THE PUBLIC'S MIND WITH RESPECT TO DVT DISEASE

1. *Varicose veins*

In every textbook it is identified that varicose veins are a predisposing factor to DVT disease but this theory has very little evidence in fact. What is clear is the complications of varicose veins such as thrombophlebitis (where the varicose vein becomes thrombosed with clot) do have a higher incidence of extension into the deep veins and pulmonary embolism. There needs to be further investigation of phlebitis nationally with respect to risk of DVT. Much work needs to be considered to investigate this as a serious community risk.

2. *Oral contraceptive and HRT*

The oral contraceptive and hormone replacement therapy are known to increase the population risk of DVT disease but of course this is different for every individual. The management of this condition as far as patients who are subjected to a context of risk within an illness event (for example they are confined to bed or have an acute illness) are not really clearly understood. This is evidenced by the dilemma about whether the oral contraceptive pill is stopped for surgical procedures or whether HRT is also stopped under such circumstances. There is a great need to understand this more clearly.

3. *Do all Surgeons and Physicians obey the rules with respect to prophylaxis?*

No they do not.

4. *Patients need to be proactive in asking for the prophylaxis*

VISIONS FOR THE FUTURE

The condition ought at best to be able to be predicted and prevented. Our understanding of the predisposing causes still remain very unclear. Whilst significant understanding has been achieved there is a clear lack of use of this information in order to prevent patients being subject to this very unpleasant and life threatening conditions. These particular things are related:

- The use of anti-DVT prophylaxis on a routine basis in hospital practice (whilst this has become increasingly established in surgical practice it remains a significantly poor resourced care of patients in medical practice).
- The understanding of those at risk of the disease needs to be clearly clarified and would benefit from a national register.
- The complications of the condition are poorly recorded in particular at present post-mortem is rarely carried out in hospital practice (the effects of Bristol and workload are not insignificant in this area).

All of these things need to be considered very carefully with respect to future development and understanding of this condition which is a significant national threat.

Figure I

<i>Congenital</i>	<i>Acquired</i>
Antithrombin deficiency	Prolonged surgery and trauma
Protein C deficiency	Immobilisation
Protein S deficiency	Stroke, cardiac failure
Resistance to activated protein C	Pregnancy, HRT, oral contraceptive
Dysfibrinogenaemias	Antiphospholipid syndrome
Increased plasma levels of tissue plasminogen activator inhibitor 1(PAI-1)	Hyperviscosity syndrome
Plasminogen deficiency	Inflammatory bowel disease
Factor VII deficiency	Malignancy
Factor XII deficiency	Behcet's disease
Tissue plasminogen activator (tPA) deficiency	Nephrotic syndrome
Thrombomodulin deficiency	Paroxysmal nocturnal haemoglobinuria
Heparin cofactor II deficiency	Sepsis
Homocysteinaemia	Chronic inflammatory disorders
Hypercholesterolaemia	Diabetes
Haemoglobinopathies	Haemolytic uraemic syndrome
Disorders of histidine-rich glycoprotein (HRG)	Thrombotic thrombocytopenic purura
	Heparin-induced thrombocytopenia

Source: Thrift Consensus Group, BMJ 1992; 305: 567–574

Figure II

<i>Risk category</i>	<i>Incidence of DVT (%)</i>		<i>Incidence of pulmonary embolism (%)</i>	
	<i>Calf</i>	<i>Proximal</i>	<i>Clinical</i>	<i>Fatal</i>
Highest risk Major surgery in >40 years of age + prior venous thromboembolism, malignancy or hypercoagulable state Elective hip or knee surgery Hip fracture Stroke, multiple trauma, spinal cord injury	40–80	10–30	4–10	1–5

<i>Risk category</i>	<i>Incidence of DVT (%)</i>		<i>Incidence of pulmonary embolism (%)</i>	
	<i>Calf</i>	<i>Proximal</i>	<i>Clinical</i>	<i>Fatal</i>
High risk Major surgery in > 60 years of age + no additional risk factors Major surgery in 40–60 years of age + additional risk factors Myocardial infarction or medical patients + risk factors	20–40	4–8	2–4	0.4–1.0
Moderate risk Major or minor surgery in 40–60 year old + no additional risk factors Major surgery in < 40 years of age + no additional risk factors Minor surgery (any age) + risk factors	10–20	2–4	1–2	0.1–0.4
Low risk Minor or uncomplicated surgery in < 40 years of age + no risk factors	2	0.4	0.2	0.002

Source: Clagett *et al*, Chest 1998; 114: S 51–60

Witnesses: **Mrs Linda de Cossart**, Royal College of Surgeons, **Mr David Warwick**, Consultant Orthopaedic Surgeon, Southampton University Hospital, **Professor Ajay Kakkar**, Professor, Surgical Science and Consultant Surgeon, Barts and the London Medical Schools, **Dr David Keeling**, Royal College of Physicians and **Dr Beverley Hunt**, Medical Director, Lifeblood: the Thrombosis Society, examined.

Q1 Chairman: Good morning, and could I welcome you to this session of the Committee and particularly our witnesses. We are very grateful for your participation in this inquiry. I wonder if you would each introduce yourselves to the Committee, starting with you, Dr Hunt.

Dr Hunt: My name is Dr Beverley Hunt. I am Medical Director of a new national charity called Lifeblood: The Thrombosis Society.

Mr Warwick: I am David Warwick. I am a consultant orthopaedic surgeon from Southampton. I have been researching DVTs in orthopaedics for the past 12 years.

Dr Keeling: I am David Keeling. I am a consultant haematologist at the Oxford Haemophilia Centre and Thrombosis Unit. I am here representing the Royal College of Physicians.

Mrs de Cossart: I am Linda de Cossart. I am a vascular surgeon from Chester and I am here representing the Royal College of Surgeons.

Professor Kakkar: I am Ajay Kakkar, professor of Surgical Sciences at Barts and the London Medical schools and consultant general surgeon at the Barts and London NHS Trust.

Q2 Chairman: Can I just make the point before we start that this is a very specialised area of investigation about which you know a great deal and we know not a great deal. There is only one member of our Committee who is medically qualified so if you could take that into account in your answers we would be very grateful. If one or two of us get our DVTs mixed up with our DVDs perhaps you will forgive us. Can I begin by saying that I have been very interested in the evidence that we have received in this inquiry and I think many of us are grateful to

our colleague Dr Richard Taylor for suggesting we, as a Committee, have a look at this whole area because when you do look at it it does raise some serious concerns about the problems that we are facing. We appear to have a major public health problem but there is not a lot of awareness about it, certainly among politicians and people like ourselves. It seems to be a preventable cause of death in many instances that we are not seriously addressing. I want to start by asking a general point about the reasons for this apparent lack of awareness and lack of understanding of VTE and appropriate treatment within the medical profession. Is this the case and, if so, why is it the case? Dr Hunt, you have obviously been expressing concerns about this, would you like to comment on it?

Dr Hunt: The Charity was born out of the frustrations and the lack of awareness in the public and in the health profession about thrombosis—especially venous thrombosis—and its consequences. Our aim is to increase this awareness and also increase funds for research and development. The Charity was started two years ago and it is fantastic that we are sitting here today and discussing it. It is very difficult to say why this is a problem. I think there are multiple reasons. I think that in many of the causes of venous thromboembolism—quite often surgery—the surgeons do not see the consequences the patients have, the problems after they have been discharged or when they are admitted to another unit. I think that there is a lack of education generally about this area. I do not think this problem is confined at all to this country. I have just come back—as has Dr Keeling—from the American Society for

9 December 2004 Mrs Linda de Cossart, Mr David Warwick, Professor Ajay Kakkar, Dr David Keeling and Dr Beverley Hunt

Haematology and there are a number of papers there suggesting that thromboprophylaxis—prevention of venous thromboembolism—is an international problem and there is a registry which typifies this called IMPROVE, it is taken from the International Medical Prophylaxis of Venous Embolism registry. They quote figures of failure of uptake of about 30 to 40% across Europe and the States.

Q3 Chairman: Can I just press you on the international comparisons because one point that has struck me that I do not think I was aware of is that in recent times in the UK we have had fewer post mortems, the consequences of Alder Hey et cetera. Therefore, the figures that we are aware of may well be much lower than the real figure. How accurate are our figures in terms of international comparison?

Dr Hunt: I think you have hit the nail on the head there. Where we lead the world—and we really do—is in obstetrics where we do have the figures because we have the national confidential inquiry into maternal death and there we know that venous thromboembolism is the biggest killer. What have we done? We have had a lot of superb research out of the UK and the Royal College of Obstetricians has responded with fantastic guidelines. The prevalence of venous thromboembolism is going down. It is a superb model of how we can work in other areas. So it is not all bad.

Q4 Chairman: Do any of the other witnesses want to comment on that?

Professor Kakkar: I think that one of the most important issues about venous thromboembolism is that it is frequently a silent disease and the first manifestation may be the fatal event which is a pulmonary embolism. The problem about that is that if you do not do post mortems then a pulmonary embolism can be designated as some other cause of death—an acute respiratory problem or a heart attack—rather than identifying the fact that it was indeed a blood clot that had formed in the deep veins of the leg and had ended up in the lungs. The real challenge we face is this problem between a low frequency of recognised symptoms of the disease but a very high frequency of the silent disease lurking in the deep veins of the leg, potentially resulting in the first manifestation which will be the fatal disease or many years after the patient's hospital stay for acute medical illness or after acute surgical intervention with the development of an ulcer in the leg or swelling in the leg (the so-called post thrombotic syndrome). That is the real disconnect between a true, silent disease affecting potentially very large proportions of patients going into hospital, but only a few of them providing us with clinical manifestation. The problem is that the silent disease can still be deadly and it is bridging that gap between the silence of the disease and the low frequency of the clinical symptoms that I think has been the great problem in persuading large numbers of clinicians about the seriousness of the disease.

Q5 Chairman: Can you put on the record why we are not doing the post mortems? Obviously we have had anecdotal information, but what are your views as to why there has been this major dip and what are the consequences of that?

Dr Keeling: I would like to make one comment on that because the organ retention scandal has made matters very much worse. People think a post mortem is unimportant but quite often when you do post mortems you find the cause of death was not what the doctor looking after the patient thought it was in a frightening number of cases. I think it has been eloquently explained that many people who die after a time in hospital their death is put down to something such as a myocardial infarction or their previous illness whereas in fact they may well have died of pulmonary embolism which remains undiagnosed. I think it is a very important issue to somehow increase the post mortem rate in this country.

Q6 Chairman: What do you think could be done about? We are looking at a specific possible cause of death here but the comments you are making have a much wider implication on other areas of medicine.

Dr Keeling: They are much wider and your initial question actually applies to huge tracts of medicine. Why do doctors continue to use treatment that has been proven to be ineffective and why do doctors not use treatment that has been proven to be effective? Education is one thing, obviously, but to some extent there has to be more than that.

Mrs de Cossart: Speaking as a general and vascular surgeon we have seen the decline in post mortems for two reasons. One is the issues of Alder Hey and of organ retention but the other is actually a workload issue. There has been a dearth of pathologists and the opportunities to actually do this as part of their clinical work is considerable and with the consent issues—as a consequence of Alder Hey—I think that has compounded their workload so I think there is a real workload issue apart from perhaps the need to think about it from investigating disease. Could I just say one thing about the patient's perception? I think one of the useful things to come out of unusual presentations and certainly patients in my clinics know what DVT is because of long haul flight deep vein thrombosis and that has brought an awareness of a condition that they were completely unaware of before. What that lacks is an understanding and a consensus from clinicians about how it is managed. I think that is the crux, really.

Q7 Chairman: That answer takes me on to why do we see variations in the use of prophylaxis for venous thrombosis even within the same region in indeed the same hospital? That does seem to raise some questions.

Mrs de Cossart: I think it comes back to the general comment which is actually that there is a lot of evidence but people sometimes choose not to take note of it. The facts are that every patient is

9 December 2004 Mrs Linda de Cossart, Mr David Warwick, Professor Ajay Kakkar, Dr David Keeling and Dr Beverley Hunt

different and every condition is different, but then unfortunately every doctor is different too and they all have their own opinions about what might happen. I think what we have to do is find a way forward to make it sensible so that patients and their doctors talk about the condition with relation to each individual and use the evidence to build on that conversation and a decision for individual patient care.

Mr Warwick: I would just like to take Ajay Kakkar's point forward about the perception of disease, if you are an orthopaedic surgeon about four in a thousand hip replacement patients will die from a pulmonary embolism if you do not use prophylaxis. That, I suppose is quite a small number in as much as if you are a busy hip surgeon and you do a hundred hip replacements a year you will not see a pulmonary embolism for three or four years and when you do it may have happened at home. So for you individually it is not a problem, but the thing is that we do 90,000 hip and knee replacements per annum in the United Kingdom, so 90,000 times 0.4% is 360 deaths per year. That is an airbus or a jumbo jet per year. It causes a huge problem when you have a small percentage multiplied big. The orthopaedic surgeon then has the problem looking through this mountain of evidence that shows that prophylaxis works, but they worry about bleeding. You cannot make an omelette without breaking an egg and if you use prophylaxis poorly you can get bleeding. Then of course the surgeon is faced with a patient with a bleed in their wound and that is an error of his commission whereas if you do not do anything it never gets noticed. That is now changing because people do notice if they are bleeding and did not have prophylaxis. If you do use chemicals properly they will be safe. It is that balance that the surgeon is trying to make.

Professor Kakkar: In terms of the question you have just put, the issue is about how we present the evidence with regard to the efficacy of preventing thrombosis. It comes down to the end points that you use in the clinical studies. The field of thromboprophylaxis has been very much driven by research in the United Kingdom over the last three decades and initially when this research began it was considered quite ethical to do studies where you randomised patients to receive some form of active thromboprophylaxis in one arm or a placebo or no anti-thrombotic therapy in the other arm. Those studies required thousands of patients but they could use the end point of autopsy proven fatal pulmonary embolism. I think doctors are very, very convinced across the board by evidence which shows that the method of preventing thrombosis can reduce the frequency of the fatal event of pulmonary embolism. More recently, we have started to compare different types of intervention to prevent thrombosis in different populations of hospitalised patients—the original trials were done in general surgical patients—an end point which screens for all thrombosis that occurs (that is asymptomatic disease, non-clinical

disease) allows smaller numbers of patients to be involved because the frequency of the asymptomatic clots is greater than a symptomatic thrombosis or a fatal event. I think some clinicians argue that the asymptomatic disease is not of importance and that has been one of the problems in the education message amongst clinicians. For those of us who have a lot of experience of the thromboprophylaxis field the evidence is very clear that it the asymptomatic sub-clinical blood clots are the first stage of the clinical blood clots and for every clinical clot that you will see symptomatically in a patient there will be about 10 asymptomatic clots. This is all part of a pathway that leads eventually to the fatal pulmonary embolism. I think it is getting across that message as well that the end points that have been used in the trials are indeed valid in determining that the methods which have been shown to be effective should be used for patients across the board; that is part of the challenge.

Q8 John Austin: I think you have answered some of my next question which is why thromboprophylaxis is not being used widely when the evidence we have before us suggests that about 40% of patients should be receiving it but are not. Would you agree with those figures?

Professor Kakkar: If you look at a population for instance of general surgical patients, looking for all thrombosis—even the smallest blood clots that occur in the veins in the calf right through to the symptomatic disease, the more proximal vein thrombosis—the rate of thrombosis is about 30% without prophylaxis. If you look at orthopaedic patients it is about 40 to 60%; if you look at acutely ill non-surgical patients in hospital, it is about 15 to 30%. The question you have to ask yourself when you are providing prophylaxis is: is the method that I am going to offer the patients validated in terms of being effective in reducing the frequency of thrombosis on the one hand, and safe in terms of not increasing the bleeding risk on the other? Those trials need to be done by patient population because in each individual population you will put a certain value on reducing the risk of thrombosis on the one hand versus the risk of bleeding on the other. If I take two extremes in surgical practice, the general surgical patient—for instance those undergoing an operation for abdominal cancer—the rate of thrombosis would be very high and the risk of fatal pulmonary embolism without prophylaxis probably approaches 0.8 to 1% from historic literature. There, as a cancer surgeon, I would be concerned that nearly 1% of my patients might die of a pulmonary embolism if I did not provide prophylaxis where the added risk of bleeding (it may be a small bruise in the wound or a bleed post-operatively) is about 1 to 2% extra if I give prophylaxis. Under those circumstances I would put a greater value on preventing thrombosis against the potential bleeding complication. However, for a neurosurgeon operating on a small

9 December 2004 Mrs Linda de Cossart, Mr David Warwick, Professor Ajay Kakkar, Dr David Keeling and Dr Beverley Hunt

brain tumour the risk of a small bleed into the brain after surgery would put a much greater value on the risk of bleeding than the risk of thrombosis, even though the thrombosis risk is very high in those patients. The debate is by patient population and it is by looking at this efficacy/benefit analysis for each group where there is now excellent data.

Q9 John Austin: If it is down to the clinical judgment of the doctor given the patient, given the operation, given all these factors, does it appear to you that in general doctors have the balance right?

Dr Keeling: No.

Q10 John Austin: Why?

Dr Keeling: We are back to a question that was asked earlier: we do have very good guidelines and I do not think there is any need for further development of guidelines, but they are not implemented.

Q11 John Austin: Whose responsibility is it to see that guidelines are implemented? Is it the Royal College's?

Dr Keeling: As I say, we are back to the question that was asked originally: when there is good evidence for a treatment why is it not widely used and that is a difficult question to answer. I think the phrase that often strikes dread into you when you are looking down an agenda for hospital meetings is "clinical governance". Often it is there as a token; it is on the agenda because you are told it has to be on the agenda, but there is a real issue for clinical governance, and this is a real issue for clinical governance. If there is good evidence—which there is—and treatment is being underused and as a consequence people are dying, that is a clinical governance issue. It does need to be taken forward in some way. We get risks out of proportion as you know. For example, I have just been involved in a huge exercise about the risk of variant CJD in haemophilia patients who are given pooled blood products. I personally think their risk is minimal and yet there are other patients in our hospitals with very significant risks—maybe up to a 1% chance of dying of pulmonary embolism—who are not necessarily getting thromboprophylaxis. There needs to be a person at each trust responsible for clinical governance. I am sure there is, if only by name, but it is an issue that needs to be taken more seriously.

John Austin: Whose job is it to ensure the implementation? Everybody says the Government ought to do something about it; is the Government capable of doing something about it or is this something that needs to be done within the profession?

Q12 Chairman: Can I just ask, does the Health Care Commission have a role to play in ensuring what is done at a local level?

Professor Kakkar: I think it may be a question that the Health Care Commission could ask. There are a number of groups around the world that write guidelines based upon the evidence available in the

field of thrombosis. Probably the most authoritative of those is the American College of Chest Physicians who have been writing guidelines in this area since the late 1980s and they have their seventh revision just published on a consensus on anti-thrombotic therapy. One of the clear recommendations they make in general is that every hospital should have a written protocol for prevention of venous thromboembolic disease of hospitalised patients. I think it comes down potentially to an individual trust basis in terms of having a protocol available. In terms of the individual patient it is very important; in terms of the health care system it is also very important because in that same report—and others in the United States—there is a view that probably the most common preventable cause of hospital mortality remains pulmonary embolism. I think that is important when you put into context a view that we want to make the patient's experience in hospital safer. The United States Agency for Health Care Research and Quality has actually ranked 79 safety practices in hospitals and based upon the effectiveness of the intervention and the cost-effectiveness of applying that intervention routine thromboprophylaxis for appropriate patient groups in hospital was ranked the number one most important safety practice. I think taking into context the fact that we have evidence based guidelines, taking into context the fact that we have an analysis to show that the number one safety measure to be taken in hospitals is to introduce protocols for prevention of venous thromboembolism I think it becomes a health trust issue.

Q13 John Austin: Given the seriousness of the issue, why has it only just hit the radar screens?

Dr Hunt: It is just hitting the radar screens now internationally; I do not think that we are behind here. No-one has looked at the global problem across all of the patients within a hospital. If you think how a hospital functions, it is like a little series of villages—we have the orthopaedic village, the surgical village, the obstetric village—and the villages do not often talk between each other. What we really need is for someone from outside to say here is the issue and to remind everybody of the size of the issue and the need for patients' safety and to produce some guidance to the trust on how to take it forward. We are all very aware of clinical governance within my trust where I work. Everyone has guidelines but they need to be pulled together so there is coherence. Also, it needs to be higher up in the health care agenda so that it is considered to be an important issue. It is not considered to be an important issue because of the lack of education among the junior staff in particular.

Mrs de Cossart: Beverley has said some of the things I wanted to say, but just looking at this group here we are actually from different disciplines in medicine and I think that is one of the issues because in surgery particularly where this is a major position the surgeon takes final responsibility for the patient

9 December 2004 Mrs Linda de Cossart, Mr David Warwick, Professor Ajay Kakkar, Dr David Keeling and Dr Beverley Hunt

and actually may have some difficulties with the issues about implementing even what might be very important guidelines in particular situations.

Q14 John Austin: Do the Royal Colleges talk to each other?

Mrs de Cossart: I think it is fair to say that probably the Royal Colleges do not talk to each other enough on this particular issue. They talk to each other about an awful lot of things and there are an awful lot of things in the air at the present time. I think it is a matter of priorities and I do not think that DVT prophylaxis is a priority but it should be, particularly if you look at the issues of death and limb complications as Ajay has already alluded to. It is not just death; people can have significant complications from thrombosis disease. I would argue that in many patients that you did not suspect before that they might get DVT disease, certainly my experience in the databases that we have built up they are actually more likely to occur in benign disease and in patients who are actually non-surgical.

Mr Warwick: Traditionally in British medicine the individual doctor has taken his own judgment as to what he does. It has been very much that personal level so one orthopaedic surgeon may say, "Well, I've always used aspirin and that's that" and he will go on and do something else. The other end of the spectrum would be that the Government says: "You must do this". In France everybody gets low molecular heparin after a joint replacement. Full stop. It happens. No question; it is. In the UK medical fraternity society I think a top-imposed thing does not necessarily work because there are clinical objections. One individual surgeon may put more value on bleeding whereas another one may, having just had a patient die of pulmonary embolism, put a lot more value on thrombosis prevention. My view would be that these new guidelines—particularly from the American College of Chest Physicians which have just come out—are a superb assimilation of all the data and a very sensible balanced judgment on how to apply them. I think the Colleges or the British Orthopaedic Association is the correct sort of level to promulgate that so people feel they are being supported by their own rather than it being imposed from above.

Q15 John Austin: Can I move away from the personal tragedy of patients and the life saving that might go on and talk about money. Dr Cohen, in his written evidence, says that VTE is costing the UK approximately £640 million each year to manage. He estimates that 60 to 80% of those costs could be saved through preventative measures. Are they reasonable estimates that you would agree with?

Professor Kakkar: I think there is now work taking place to try to look at the frequency of thromboembolic disease over the population. There are two issues. One issue is the one we are discussing today and that is hospital acquired thromboembolic disease. Probably half to two-thirds of patients get spontaneous thrombosis in the community and then

present to hospital for its treatment. For those who develop spontaneous thrombosis in the community the opportunity for prevention of that disease is very limited so it is the hospital population that one is looking at. I think, however, we have to be careful because not every patient coming into hospital for every procedure is going to be at risk from thrombosis. Younger patients, those having less serious surgical interventions, those with less extensive medical disease are going to be at much lower risk and may not be considered for active thromboprophylaxis. There will be higher risk populations clearly and those are very important proportions of patients in our hospitals where thromboprophylaxis is validated. In terms of the cost estimates, I think there is work that others are doing at the moment to try to look at the frequency of disease and how, if you prevented that disease, you would reduce health care costs. However, I think in general, beyond the figures that you quote, if you look at evidence from trials that have assessed the cost effectiveness of routine thromboprophylaxis in well-defined, high-risk surgical or medical populations of patients, there is no doubt that the cost effectiveness is very well established. Beyond the figures that you quote in terms of the cost of treating an established thrombosis, if you weigh the cost of primary prophylaxis against the thrombosis that you would prevent there is no doubt that intervention is cost effective and also efficacious in terms of preventing the disease for the patient.

Q16 Dr Naysmith: We have already touched on all the questions I was going to ask, but if we could just tease one or two of them out a little bit more, particularly this question of awareness and understanding amongst the professions and possibly amongst a wider audience. Dr Hunt and Mr Warwick have commented about the incidence looking as if it is relatively low because sometimes it happens outside of hospital when it is not perceived by the people who actually do the high risk surgery to start with, and yet there is still very clearly—as you have pointed out—a very significant number of deaths from this condition. How would you suggest that we should raise awareness and understanding more? There have already been some attempts to say that, but if we were to embark on a campaign to make sure that everyone knew about it in the profession and did something about it, what would you do?

Dr Hunt: I think we have a fantastic opportunity here to really lead the world in this area. We need the Department of Health to come out with some form of directive to tell trusts that we need to make thromboprophylaxis a bigger issue and I did suggest in my written statement that we follow the model of better blood transfusion. We have had two health directives in 1998 and 2002 which put blood transfusion high up on the trust's agenda as far as risk management was concerned. Each trust has had to establish a committee and have a specialist in

blood transfusion. They run protocols and they audit the use of blood. There is no doubt that it has improved the way in which we use blood.

Q17 Dr Naysmith: I am interested in you bringing it down to the level of the trust and say that the trust has to implement guidelines. I have come across some orthopaedic surgeons and some other surgeons in my time—I used to work in the Department of Surgical Science once—and nobody would have told them what to do. As Mr Warwick said earlier on one surgeon will say an aspirin and then someone will use a totally different method. Do you think that instituting guidelines at the trust level is enough?

Mrs de Cossart: I think that is a start. I think one of the problems is actually auditing whether or not any guideline that is there is actually used. There is certainly one aspect where I think this is emerging and will come out very well, which is electronic prescribing. There are some emerging papers in surgical practice about the use of anti-DVT prophylaxis because you can now audit it very carefully.

Q18 Chairman: Who should do that?

Mrs de Cossart: If you have electronic prescribing then it is actually on a database and that is very easily audited by scrutinising and querying the database. The trouble with a lot of hospitals is that they do not have that level of sophistication for collecting data. It is a very arduous task and in-built into the problems people have of getting the work done at the moment, actually spending days trawling through notes is quite hard work. I think the key thing in looking at it would be perhaps to go to units where they are using electronic prescribing, look at the use of anti-DVT prophylaxis and begin to see whether the guidelines they have there are actually utilised rather than perhaps starting audit in other places. I do think hospitals should be pushed to make clear to patients what their guidelines on this problem actually are.

Q19 Dr Naysmith: So we are saying that it is not enough just to raise awareness. That is the first step but then you have to make sure that something happens afterwards. I know the medical profession are not all that keen on having more auditing and more tests.

Mr Warwick: I think it is right that you ask each trust to explain its guidelines but I do not think at trust level the individual departments could necessarily generate their guidelines. That sounds patronising so I want to be careful. If a small department of three or four orthopaedic surgeons get together on a Friday lunchtime and say, “That is what we are going to do” and that is it, and that is your guideline, I do not think that is valid. I think it is valid for each trust to be asked “What are your guidelines?” but I think the guidelines they use probably have to be based upon a slightly higher network, in other words the professional association for example comes up with those guidelines then the

trust has to say they have implemented them. I do not think each individual trust can come up with its own guidelines necessarily; it is too dependant upon the particular interest and knowledge base of the small number of individuals in each department then.

Dr Keeling: I think everyone of us has endorsed the ACCP guidelines so I think there are guidelines there. The issue, as has been teased out, is how we implement them. I want to come back to your question of how we raise awareness. We live in a society where people are scared of travelling by train but not by car and I receive hundreds of phone calls from GPs about patients who are going on long haul air flights and are worried about getting a DVT. These are the same patients coming into hospital where the risk is vastly greater. When people are consented for operations they are told all sorts of very small risks, especially with regard to blood transfusions. However, I am not sure how patients are informed of the risks of venous thromboembolism when they are consented for their operation. I think there is an issue of informing the public about this.

Q20 Dr Naysmith: We will come onto that in a minute. I am interested in what you were saying about people outside of the hospital. Often DVT does occur after patients have gone home. How do we raise awareness of primary care trusts and GPs and so on? Are they aware of the situation or do they need to be reminded as well?

Dr Keeling: I suppose that one thing I am guilty of to some extent is that I see a lot of patients with deep vein thrombosis because I run a DVT service and quite a few of those have had an operation six weeks previously. Maybe every time that happens I should be writing a big letter in bold to the surgeon letting them know what has happened.

Mrs de Cossart: I think that is a big issue really. I would find that patients have been admitted under physicians into the hospital who have had a venous complication from their surgery.

Q21 Dr Naysmith: So there is nothing like the yellow card system or anything like that?

Mrs de Cossart: No. Again I think it is people paying attention to detail and how they manage things. I think the general practitioners are aware of it and if you do run a good screening service for querying DVT disease in your hospital—I am sure what we are hearing from David and it is similar in our place—they do send them in with a very low threshold. They send them in for a screen or a scan and they are looked at, so there is reasonable awareness. There is an issue there, of course, which is workload. Certainly since introducing duplex scanning in our hospital we have increased the workload five or six times what it was before which puts an immense strain on the services that we can offer. We are managing but there is a workload issue. I think awareness will create more work.

9 December 2004 Mrs Linda de Cossart, Mr David Warwick, Professor Ajay Kakkar, Dr David Keeling and Dr Beverley Hunt

Q22 Dr Naysmith: I do not want to be political about this but since the Government has been in there are a fair number more consultants and doctors in the service than there were in 1997 so presumably they are doing a bit more work.

Mrs de Cossart: It depends where they are.

Q23 Dr Naysmith: Yes, it depends which speciality they are in and where they are. We will not go down that road.

Mrs de Cossart: They do not have to be doctors; some of this work can be done by technologists.

Q24 Dr Naysmith: The other thing I was going to explore a little bit more with you was this question of counselling because people are counselled before they have operations about transfusions and that sort of thing, but probably not very often about the risks of DVT. Is that right? Are people counselled about that?

Mr Warwick: The new consent forms which have only just come out actually do have a section that says: "The probable risks for this procedure include:" and I think most people would put down thrombosis, but there is no reason why you should not have a standard consent form for things like hip and knee replacement which would include that.

Q25 Dr Naysmith: Presumably if you are doing an orthopaedic operation like that the risk is higher than it is for other operations.

Mr Warwick: It is, yes.

Q26 Dr Naysmith: Therefore you should take your patient into your confidence. Does that not happen?

Mrs de Cossart: It does happen. I counsel patients quite regularly about the risks of DVT but the question is, what risks do you put to them because you obviously have to customise it to the operation, to the patient and to their previous history. Certainly if there is a significant risk it should be discussed with them.

Q27 Dr Naysmith: In some of the written evidence we have had it has been suggested that counselling is not too widespread.

Mrs de Cossart: It is back to this issue of who takes consent and actually the authority and knowledge of those particular people and we are struggling with that with the new consent issues and dictacts of governance in trusts at the moment where certain sectors of the population of doctors are now prevented from doing these jobs. Again it is an issue of education and making sure that people are actually able to consent people appropriately.

Q28 Dr Naysmith: Why would people be prevented from doing this job?

Mrs de Cossart: Traditionally—rightly or wrongly, I am not arguing the case one way or the other—house officers and senior house officers in hospitals and surgical units would consent the patients for their surgery and now that has all changed. The person doing the operation—and I think there are

good reasons for this—consent the patient so they are fully educated and aware of the complications. That has therefore driven the need for consent to be done by more senior staff, almost de-skilling the people at the bottom end because we have not invested enough time in educating them to make sure they are comfortable in doing the job.

Q29 Dr Naysmith: We are beginning to cover all sorts of issues then, are we not?

Mrs de Cossart: That is the case, I think.

Professor Kakkar: Coming back to your original point about how we make this happen, if one goes for a strategy where one recommends that each individual trust has a written protocol for the prevention of thromboembolic disease, then I think the point has been made very clearly that we have to help those trusts to adopt the best evidence. Otherwise one might get slightly awkward differences in the views of individual groups of clinicians as to what basis these protocols should be made upon. I think if we are going to have a strategy to implement it we have to provide the best evidence that we have validated centrally made available to trusts so that they can then tailor that to individual protocols written for practice in their hospitals. I think then the point of auditing is very important and that may be achieved in part. The Royal College of Surgeons has done that very successfully in the national confidential inquiry into perioperative deaths. For instance, when they looked at surgery for patients undergoing hip fracture operations as an emergency they found some years ago—I think in the early 1990s—that about 40% of patients dying after hip fracture had evidence of pulmonary embolism. There are those types of audits and the confidential inquiry into maternal deaths has done the same in obstetric practice. That is one route forward of auditing. A second route for auditing could be that in the audits that the Commission of Health Audit and Improvement undertake in one of their audit rounds they could look at both the availability of the venous thromboembolism, deep vein thrombosis prevention and protocol in the hospital and its uptake across that hospital emphasising again that it is not all patients but appropriately selected patients who require prophylaxis in hospital. Then I think it is very important that we do not ignore the importance of continuing professional education in this area because the thrombosis field is very active in research and there continues to be the generation of new data, much more elegant research in terms of the impact and outcome long-term of hidden thrombosis on populations of patients and that needs to be communicated to clinicians I think through the educational and CPD activities of the Royal Colleges. So it is a combination of things I think that would help us to get the game up, but primarily if we look at the recommendations that are published by, for instance, the American College of Chest Physicians and other authoritative guideline groups, the one important thing that we can do to raise awareness in hospitals is to encourage those

9 December 2004 Mrs Linda de Cossart, Mr David Warwick, Professor Ajay Kakkar, Dr David Keeling and Dr Beverley Hunt

hospitals to have a written protocol. Once a written protocol exists in the hospitals clinicians think about it more. With regard to the patient consent issue I think it is very important as an abdominal and cancer surgeon. When I consent patients I always raise the issue of thromboembolic risk with them because I personally think it is an important problem in cancer surgery. I describe to them my preferred intervention which is to use pharmacological prophylaxis to prevent that thrombosis. I think Mr Warwick has said the same, that most orthopaedic surgeons now consenting their patients would raise that issue and in general, using the new NHS consent form, we are obliged to complete a section where we make it clear to patients the important and common risks associated with their procedure. For a number of surgical procedures it would be very clear that thrombosis is a common and important risk. If we turn away briefly from the surgical to the medical patients, I think that is where we have a big problem because often they come in for medical therapy for their disease where there is not written consent and communicating the thrombosis risk for that group—the largest number of patients in our hospitals—I think is more difficult.

Q30 Dr Naysmith: What would you say if someone said, “I don’t want pharmaceutical intervention; I want a mechanical one”?

Professor Kakkar: I think that is very reasonable. I think if you discuss with the patient the benefit in terms of preventing thrombosis and the risk of bleeding—and they had a real fear of bleeding risk—there is evidence in the literature for many hospitalised populations that suggests that mechanical prophylaxis will work. It is not always as effective as pharmacological but evidence, no doubt, that it will work and that should not be denied as part of the discussion with the patient.

Q31 Dr Naysmith: Where does clinical judgment come into this and the fact that you might know what is best for the patient even against their wishes?

Mrs de Cossart: Could I say one thing with respect to the patient here? I still think you have to remember what sort of population we are actually looking after. They are still very cowed about the idea of asking or challenging doctors’ management plans.

Q32 Chairman: That is changing.

Mrs de Cossart: Absolutely, and rightly so. I think we should encourage and if we did nothing more it would be to ask your doctor about what their anti-DVT plans for you actually are. If we simply did that—in the same way as we have successfully done, “Do you wash your hands between patients in the critical care unit?”—these very small things would begin to raise awareness in everybody’s mind and should not be underestimated in the effect that they might have with driving the education, the clinical governance and the whole profession’s attitude to this very complicated problem.

Mr Warwick: I think we do need some help also on implementation of protocol. In our hospital we have designed a protocol which uses foot pumps early on after hip fracture or hip or knee replacement because we place a value on potential bleeding. We also use spinal anaesthetics. The foot pump allows us to use pretty effective prophylaxis for a short period of time. We now also recognise the evidence that we should be using low molecular heparins, for example, for five weeks after hip replacement. That evidence is crystal clear now; clinical prophylaxis needs to be used at least after hip replacement and hip fracture for at least five weeks. However we have hit a brick wall at both ends of that spectrum of prophylaxis. To try to buy foot pumps you have to have a business case: where is the money coming from, can you prove you are going to save money?

Q33 Chairman: What is the cost of a foot pump?

Mr Warwick: Say £2,000, but we rotated them round the patients, and so on. There are processes in which just to try to get something new goes on forever. I then tried to get extended duration prophylaxis for hip fractures and hip replacement and that was just impossible. The trust is already £15 million over spent this year; they are not interested. The PCT tell us they have set up their costs for hip replacement and that is not going to include five weeks of prophylaxis. You hit brick walls all the time. There is a new drug come out which looks quite effective. We looked at introducing that to our Therapeutics Committee but when we submitted the evidence it just got thrown back to us and that was that. I think we need help actually in getting this stuff on board.

Q34 Chairman: This new tariff system in terms of costs or individual interventions, does the common tariff reflect?

Mr Warwick: No.

Q35 Chairman: That is very interesting. Are you sure about that?

Mrs de Cossart: Absolutely. The common tariff probably does not include anti-DVT products.

Q36 Chairman: Which interventions are we talking about here?

Mrs de Cossart: The tariff is cut to the bone in what it actually covers. Certainly for the extended treatments you would have to look at re-negotiating the tariff in order to introduce this and it certainly will not include, I think, the acquisition capital for the new recruitment that you might use in order to do things.

Q37 Dr Taylor: We were told very clearly the Secretary of State himself yesterday that the common tariffs, if you are talking about hip replacements, would be varied from one tariff for the cheaper, absolutely ordinary low risk ones and a different tariff for the more complicated ones. Should we be making a point very strongly that prophylaxis should be included in that tariff?

9 December 2004 Mrs Linda de Cossart, Mr David Warwick, Professor Ajay Kakkar, Dr David Keeling and Dr Beverley Hunt

Mrs de Cossart: That should probably also be covered by the comment that David has just made about how long you should give the prophylaxis for. That, of course, introduces a whole new ball game with respect to educating the patient because obviously if they are having it for five weeks they give it to themselves and there is a management issue about looking after them while that is going on.

Q38 Dr Taylor: But that has got to be included in the tariff for the cost of the operation.

Mrs de Cossart: Yes.

Q39 Chairman: We have also heard that different clinicians have different views in the approach they take. This is a very complex area where I am not sure we will be able to come up with any easy answers.

Mrs de Cossart: I think the individual clinicians who might not want to do it would play into the hands of having the low tariff.

Q40 John Austin: On the question of clinicians' preferences, Mr Warwick was saying earlier that some surgeons may like to rely on aspirin and my understanding was that although there are certain prophylactic benefits from aspirin it is not particularly preventative in terms of DVT.

Mr Warwick: For orthopaedic thromboprophylaxis it is second rate without a doubt. It is just not adequate. That view is supported by, for example, the American College of Chest Physicians which has looked at it all and it does not work well enough. You may say it only costs two pence a tablet and that is that; we are cheap on tariff and that is what we are going to do.

Dr Keeling: I would like to raise an issue about cost because, as was said earlier, thromboprophylaxis is cost effective. This, if implemented properly, will save money; it will not cost money. However, you then have a problem where an individual is not allowed to prescribe the drug because he is spending his money but saving money somewhere else. This is a common thing in the Health Service which is a real problem. A simple example: there is a blood test called a D-dimer when you investigate these people for DVT which costs £2.50. My department does hundreds of them and our budget has gone up; people have got very cross about that. However, doing that test saves a lot of money because you do not have to do different investigations; you do not have to do tests in the radiology department. It costs my department money but the radiology department is saving money. No-one can look at the bigger picture; no-one can get round the bureaucracy of people telling me off for doing D-dimer tests or telling him off for trying to prescribe thromboprophylaxis. The message should be clear: it may cost money to actually write the drug prescription but overall proper implementation would save money; it maybe somebody else's money, but it will save money.

Professor Kakkar: If one goes back to this research in the United States that shows that implementation of an appropriate protocol is the number one safety

practice available to hospitals, then I think it becomes a hospital-wide issue rather than an individual patient group issue. I think that part of the debate has to be to allow these important hospital-wide practices to be implemented in trusts without the need maybe to provide it by individual tariffs.

Q41 Mrs Calton: Can I just pick up on consent? It seems to me from a certain amount of personal experience but also listening to yourselves, when consent is done well and it seems to go through all of the details and give the patients the pros and the cons, and it is not just a matter of looking at a form that has had thromboembolism written on it which the patient may well feel they have put that on to cover themselves legally but actually it is not going to happen to me. I am just concerned that the consent form is not necessarily the best point at which the patient can be educated and be fully informed about the risks. Can you give me some idea yourselves as to whether this is the right time? The consent form is widely viewed by patients, I would have thought, as being the medical profession covering itself rather than actually a point where they are going to give the patient any real assistance.

Professor Kakkar: My own personal view in terms of consent in general is that it is probably the most important thing we do because patients undergoing surgical intervention must understand the benefit and risk of what we are going to do for them. You have to judge the individual risks of what patients are going to be offered and I think a lot of us now do our consent through a variety of procedures in the pre-admission clinic and provide patients with an opportunity to discuss it a few weeks before their operation and come back with any questions. I think that is the best form of consent, to see patients in pre-admission, discuss with them both the benefits of their procedure, the risks of the complications of that procedure. I think thrombosis for many procedures should be discussed as a risk. They should be given a second opportunity when they are admitted to hospital to discuss that again and as part of that providing written literature for patients is important. One of the things trusts may do is to provide simplified written information with regard to the thrombosis problem for the individual procedures that patients may be experiencing which would help them decide the benefits versus the risks of prophylaxis.

Mrs de Cossart: Can I come back to you on the comment about surgeons particularly protecting themselves. I think that is an interesting and perceptive comment which is worthy of some investigation because I think we have been made to feel that we do it for that very reason. That actually is the worse reason to do it. I think the consent form is a sham and is a myth with respect to protecting the whole system about good medical practice. Good medical practice requires the clinician talking to the patient to develop a good relationship with them and talk appropriately about what is going to happen to them. Nothing and no paperwork can take away—I

9 December 2004 Mrs Linda de Cossart, Mr David Warwick, Professor Ajay Kakkar, Dr David Keeling and Dr Beverley Hunt

do not believe, but correct me if I am wrong in your experience—that rapport and understanding that can be created between clinician and patient. I think the paperwork we have introduced as a short-term measure to cover these issues is clouding the need for clinicians to get up to speed with it. If I may make an example of that, I have already alluded to the fact that the lower, less experienced doctors are being almost excluded or the understanding is prevalent now. I had a conversation with a SHO who said that pre-registration house officers cannot take consent; they are not allowed. My comment was that that is not true; the actual requirement is that when they take consent they have been taught to do it and they understand how they do it, but the mindset that is coming through by this paperwork is creating a different attitude to the process. The educational mountain in front of us is huge. I think the consent form can be very good or extremely bad and in a lot of cases it is probably not worth the paper it is written on.

Q42 Mrs Calton: Particularly given this condition where it seems to appear very often after the patient has left hospital and so if the patient has not had a full discussion presumably they have no idea about what might happen and what the symptoms might be.

Mrs de Cossart: That is right.

Q43 Dr Naysmith: Should the paperwork not be filled in by the physician? It should be a means of eliciting the discussion that you think should happen.

Mrs de Cossart: Absolutely and I think done well it does go very well but I think the issue is that sometimes people do not pay attention to detail and there is still a problem for people filling in that first part of the consent form to a standard which most of us would aspire to.

Q44 Mrs Calton: Could I just a little bit more about the increased incidents of bleeding? I think Professor Kakkar mentioned that it was 1 to 2% or something like that and clearly will be of more consequence in some patient groups than in others. We have had the guidelines that exist described as excellent. Do the guidelines actually go into all the different patient groups and the information that is available there?

Professor Kakkar: They do, yes. The American College of Chest Physicians' latest version published in September of this year has a chapter on prevention of thrombosis which has reviewed about 800 articles on prophylaxis, its efficacy and the risks of bleeding. It breaks down its recommendations by individual groups: general surgical patients, orthopaedic surgical patients, medical patients, vascular patients, neurosurgical patients and so on. In the discussion where they reach their final recommendations for each of those patient groups they review both pharmacological methods of prophylaxis, mechanical methods of prophylaxis, the evidence or the efficacy of those individual methods of prophylaxis, the bleeding risks

associated with those, the balance for the individual patient group and then they reach a recommendation which is graded on the basis of the quality of the published literature. That grading is determined by the methodology that has been used for the individual clinical trials so: was there an appropriate end point? Was there independent blinded adjudication of the results for efficacy and blinded adjudication of the results with regard to bleeding? Was the study appropriately statistically sample size adopted? I think there is information for individual groups, but there are some groups of hospitalised patients where the data still does not exist to the extent that it does for other groups.

Dr Keeling: I would like bleeding to be kept into perspective. Let me give you a very short quote from the ACCP guidelines when it is talking about why prophylaxis is not widely used. It says, "Abundant data from meta-analysis and placebo controlled blinded randomised clinical trials have demonstrated little or no increase in the rates of clinically important bleeding with a low dose heparin or low molecular weight heparin". That is the statement and I think the problem is that if someone is using prophylaxis and the patient bleeds, they will automatically say, "Oh this patient is bleeding because they are on heparin, I wish I hadn't used it" but in fact they may well have bled anyway. We go right back to the beginning when Mr Warwick said that they see that but what they do not see a reduction in fatal pulmonary embolism from 0.7% to 0.2% on a day to day basis.

Mr Warwick: Orthopaedic surgeons believe it is an issue and there is a substantial body of UK orthopaedic surgeons who do value the problem of bleeding more than the value the problem of thrombosis and I think a lot of that is due to a perception bias, in fact they attribute bleeding to a drug if you can because it is easier than blaming yourself. It is also an issue of how much they understand the literature; they may not have realised that the literature has been assimilated, for example, in the American College of Chest Physicians work. I think that any sort of guideline that is imposed on surgeons without taking account of that fear would be so fiercely resisted it would not be taken on board, hence our local guidelines, for example in Southampton where we have a mechanical bias earlier on but very much recognise the strengths of chemicals in the longer term. I think that has to be recognised to be appreciated and taken on.

Q45 Mrs Calton: Can we go on to infection risk. Is there any evidence of an association between thromboprophylaxis and increased post-operative infection rates?

Professor Kakkar: I think in general surgical patients one or two very large trials have looked at whether prophylaxis or different methods of prophylaxis actually have an impact on the overall outcome of surgery in terms of bleeding and potentially wound dehiscence or wound infection and so on. As far as I am aware it is not clear to me

9 December 2004 Mrs Linda de Cossart, Mr David Warwick, Professor Ajay Kakkar, Dr David Keeling and Dr Beverley Hunt

that there has been any evidence of a substantial increase in infection associated with pharmacological prophylaxis.

Mrs de Cossart: I would agree with that. There is no evidence of it but we all know from clinical experience that if you get a haematoma in a wound then your risks of getting it secondarily infected are higher than if you do not get a haematoma. If you do have a wound haematoma which is known to occur and is the most common complication of subcutaneous heparin therapy then you do increase the potential. Whether that potential is a real risk is another matter.

Q46 Mrs Calton: We now hear that venous thrombosis is common—or at least some of us now hear—in patients with cancer. What special considerations need to be made for the care of patients suffering from cancer to prevent venous thromboembolism and does having venous thromboembolism when already suffering from cancer adversely affect outcome? Why are we not prophylaxing everybody with cancer?

Professor Kakkar: That is my own particular area of research interest. It is a difficult area for patients undergoing surgical intervention for their cancers—laparotomies for abdominal or pelvic cancer—and it very clear that post-operative thrombosis is an important problem. All the guidelines do in fact indicate that for abdominal and pelvic cancer surgery that prophylaxis should be provided at least for the duration of hospital stay. For hospitalised non-surgical cancer patients—those who come in because of complications of their chemotherapy or because they have an infection or they are dehydrated—they are then confined to a hospital bed and immobile and those too should receive thromboprophylaxis. I think the big problem is in advocating routine thromboprophylaxis to the large numbers of cancer patients who are treated outside hospital with chemotherapy or radiotherapy where there are only very few trials at the moment in limited numbers of cancer patients and only really investigated in breast cancer patients. It is difficult to make recommendations about routine thromboprophylaxis for that large group of ambulant patients but there are a large number of trials looking at those patient groups at the moment. The problem is, of course, once a cancer patient develops a thrombosis they are at a much greater risk—three times greater risk—than a non-cancer patient of getting a recurrent thrombosis and they are twice as likely to get significant bleeding complications while receiving treatment for their thrombosis than a non-cancer patient. It has a devastating impact on their quality of life. There are some very early suggestions which I think need to be taken with caution to suggest that developing a thrombosis in cancer has an important potential impact on the outcome of that cancer. That is a very complex molecular question at the moment about how the activated blood clotting system changes the behaviour of the tumour and that again is an area of active research consideration.

Q47 Dr Taylor: The crucial thing to me is implementation. We have talked a little bit about it; we have gathered there are a lot of guidelines, there are a lot of protocols and they are not being implemented. Dr Hunt, how have the obstetricians implemented the guidelines which you obviously imply they have?

Dr Hunt: They have worked very clearly on a set of data. They have an internal confidential inquiry. There is quite a strong cohort of research people in this country, particularly in Scotland; we probably lead the field. They have been very influential in the Royal College of Obstetricians in highlighting the problem and the Royal College of Obstetricians have numerous guidelines for the different types of thromboprophylaxis we can apply and also for the treatment of venous thromboembolism. If you go to an obstetric meeting quite often there is a discussion about the management of venous thromboprophylaxis or venous thromboembolism. It is high up in their agenda; they are very, very aware of it. I think because of the maternal inquiries they have a very strong database.

Chairman: That is a very important point you are making. We were discussing privately about the fact that here we have some definite evidence whereas in other areas the information is much vaguer. This is a very key element of the evidence, I think.

Q48 Dr Taylor: I was going to ask how we can translate this from the College of Obstetricians to the other Colleges.

Dr Hunt: There is evidence it is occurring but in obstetrics there are not actually very good trials looking at the efficacy of thromboprophylaxis but everyone is doing it because they think it is a good thing, whereas if you look at the medical and surgical areas there are superb trials that show that thromboprophylaxis works. There are six in medical thromboprophylaxis which are of outstanding quality, and it is not happening. It is a bit of a paradox really.

Mrs de Cossart: We have to remember that every group of patients is different. The obstetric patients are young women with a lot of children involved and carries a huge emotional and important impact with respect to the group of people who may die from pulmonary embolism. Of course, until recently pulmonary embolism was the highest cause of perinatal mortality in women. That is improving; whether it is improving through prophylaxis we do not know, but it is a big issue. I think the drive to actually make it happen there is because of the young group of people and the attitudes around that. The rest of it, the patients are elderly, there is a more heterogeneous group and a more heterogeneous group of doctors as well.

Q49 Chairman: You are implying basically that the change in obstetrics has not been through the fact that there is clear factual evidence, more the client group.

9 December 2004 Mrs Linda de Cossart, Mr David Warwick, Professor Ajay Kakkar, Dr David Keeling and Dr Beverley Hunt

Mrs de Cossart: The client group in combination with their clinicians, to be fair. The medical group—the haematologists and obstetricians—have taken very seriously the problem they have and it has driven them because it is in the public domain. The perinatal mortality figures have been available for a long time now; we stare them in the face. This is what is happening in your practice and that staring them in the face has actually driven them to do something about it. I do not think the evidence for death and complications of thromboembolic disease in the wider surgical and medical community stares us in the face.

Q50 Dr Taylor: The ACCP guidelines divide patients up into moderate risk, high risk and low risk. Are there well-known guidelines for assessing risks and are those implemented? If there was an absolute rule that every patient, when they went in, had to have their risk assessed, would that be one way forward?

Professor Kakkar: If you look at it for surgical patients where that ACCP analysis is made it does it on the broad group of patients so, for instance, low risk surgical patients are those under the age of 40, having a procedure lasting less than 30 minutes with no other risk factor for thrombosis. The risk factors are well recognised: obesity, previous history of thrombosis et cetera. Then you have moderate risk patients: those over the age of 40, having a procedure lasting greater than 30 minutes, an abdominal operation, or those with a single risk factor for thrombosis. You have the highest risk patients: those undergoing major orthopaedic surgery, cancer surgery, over the age of 40 or anyone with multiple risk factors for the development of thrombosis. Those are very simple categories which are well validated that a clinician can quickly apply to determine whether a patient falls into a certain risk group and based upon which risk group the patient falls into—low, intermediate or high—he or she can then turn round and say, “Well, this patient requires no prophylaxis; this patient requires medium risk prophylaxis and this person requires high risk”. If one tries to go into very complex risk assessment models the problem is selecting patients on the basis of those risk assessment models has not been validated in terms of appropriately defining which patients require prophylaxis and often they are very complex. If they are very complex, clinicians will not do them and so it is far better to look at the individual populations of patients rather than the individual risk for a patient. We do not know how the individual risk factors for the single patient interact to give you a numerical risk for DVT.

Q51 Dr Taylor: Should junior doctors be taught to include in their checking an assessment of this risk? Or do they?

Mrs de Cossart: They are taught about it. They will have a lecture on it in medical school. The question is whether it is forefront in their mind when they are talking to patients. I think forefront in their mind very often is what is the percentage risk of wound

infection, of failure of the graft put in or some other thing rather than DVT risk. You asked about implementation of these things and Ajay has pointed out the three category risk formula which I think is what most people would adopt as the most sensible way forward, but in even broader terms than that there is the question of whether one should have a blanket position for an anti-DVT process or a selective one. My experience is that when you do it selectively patients get missed. If you have it on an elect-out basis rather than an elect-in basis you do actually catch more patients who require the prophylaxis so in broad terms I would suggest that we should perhaps be advising that an anti-DVT prophylaxis is given to all patients in this category unless the doctor decides it is too dangerous.

Q52 Dr Taylor: To all patients in which category?

Mrs de Cossart: Certainly in the moderate and high risk categories in the consensus documents that are available.

Q53 Chairman: I notice one or two nodding and one or two shaking their heads. Do you disagree with that, Mr Warwick?

Mr Warwick: I agree with it to some extent. If you said that all hip replacements and all knee replacements should have something then I think that is fine. However, the problem is that moderate and low risk—as Ajay said—is defined by the risk factors so you have got yourself into a circular argument there because you only know if you are at moderate risk or high risk if you have already assessed a list of risk factors. If you gave a prophylaxis to every single person who came into hospital and every toe nail avulsion was given five weeks of prophylaxis you have strayed way beyond cost effectiveness and you have probably strayed beyond the risk benefit thing as well and you will have more problems.

Mrs de Cossart: To be fair I did leave out the low risk one and I said that that is the one where maybe you would have a problem.

Mr Warwick: We only know they are low risk if we look at the list of risk factors. Every patient must have his risk factors ticked off on a box as they come in because only at that point can you judge if this is low risk, medium risk or high risk.

Mrs de Cossart: But there would still be some who would fall out of that category; you will not have all the factors and you will have to make a clinical judgment about whether you use it or you do not use it.

Q54 Dr Taylor: Should we go so far as to recommend that all people on the highest risk level should have prophylaxis regardless?

Mrs de Cossart: Or should have a conversation with somebody who says: “Because of your particular problem I think that is unwise”?

9 December 2004 Mrs Linda de Cossart, Mr David Warwick, Professor Ajay Kakkar, Dr David Keeling
and Dr Beverley Hunt

Dr Taylor: One of the most frequent complaints about the Health Service I get—and I get an awful lot of them—is because of poor communication between doctors and patients. I very much welcome your comments on that.

Q55 Chairman: We hear a lot about MRSA; how does the problem we have been talking about this morning rank alongside MRSA in terms of seriousness?

Mrs de Cossart: It is much more serious.

Professor Kakkar: I agree with that. I saw a report that maybe 5,000 deaths were associated with MRSA. If you look at the epidemiological calculations—bearing in mind we no longer do an autopsy on patients who die in hospital—there is a suggestion that something between 20,000 and 30,000 patients a year may be dying of pulmonary embolism. One must be cautious because we do not

have the autopsy driven evidence for that statement but it appears to be in a much greater ball park and therefore I think that a lot of these reports still put pulmonary embolism as the most—or one of the most—important avoidable causes of hospital mortality.

Q56 Chairman: Asking as a lay person—and forgive the question if it is extremely naïve, which it probably is—presumably it is much easier to determine a MRSA cause of death. Am I right in assuming that?

Mrs de Cossart: Yes. There is a trail of infection analysis which will lead up to that death.

Chairman: Thank you for that. Can I express on behalf of the Committee our gratitude to you all for an excellent session. We really are very grateful for the evidence that you have given. Thank you very much. If you wish to remain for the remainder of the session you would be very welcome.

Memorandum by the Department of Health (VT 14)

INTRODUCTION

1. The Government welcomes this opportunity to set out the existing position on the prevention of venous thromboembolism.

2. Deep vein thrombosis (DVT) of the lower limbs is a common disease, often not noticed by the affected person, but presenting with clinical symptoms (leg pain or swelling) in about one per 1,000 people per year in the general population.

3. Deep vein thrombosis (DVT) may occur in about 30% of surgical patients and is commonly without symptoms. However, the condition can lead to sudden death due to pulmonary embolism (clot in the lung), or cause long-term effects on health due to venous ulceration and development of residual pain and/or swelling in the limb. Pulmonary embolism (PE) following lower limb deep vein thrombosis is the cause of death in 10% of patients who die in hospital.

4. Put simply, the condition is one of blood clot formation in veins of the leg (the “thrombo” part of the name). This has a risk of clot becoming detached (the “embolism” part), passing through the blood vessels to the heart and thence to the blood vessels to the lungs. Once in the blood vessels of the lung (pulmonary embolism (PE)), the clot can block blood flow, impede the output of the heart, and prevent the adequate exchange of oxygen and carbon dioxide by the lungs. It is this embolic feature of the disorder which causes the serious effects such as death.

5. Most thrombi occur in the deep veins of the legs. Formation of thrombi is associated with inactivity and high-risk surgical procedures. The risk is particularly high in patients undergoing orthopaedic surgery and lengthy operations.

6. Deep vein thrombosis (DVT) has multiple causes, but the main risk factors are: surgery; age; obesity; varicose veins; previous venous thromboembolism; genetic and other blood disorders leading to increased tendency to blood clotting (thrombophilias); acquired causes of increased clotting such as the presence of malignant tumours elsewhere in the body; hormone therapy; pregnancy; immobility; hospitalisation; prolonged travel.

7. Pulmonary embolism (PE), which in 90% of cases results from an asymptomatic deep vein thrombosis (DVT), may present as sudden death, breathlessness, faintness, collapse, or chest pain.

8. About 10% of hospital deaths (1% of all admissions) were attributable to pulmonary embolism (PE) in the UK in one study from the 1980s. More recent studies have continued to highlight the significant contribution of pulmonary embolism (PE) to in-hospital deaths, especially after emergency surgery when prophylaxis is often omitted.

9. This memorandum summarises existing NHS preventive interventions in respect of venous thromboembolism, existing and planned guidelines, and some key recent high profile issues.

MAIN PREVENTION MEASURES IN PLACE WITHIN THE NHS—FOR EXAMPLE, POST-SURGERY

General measures

Mobilisation, leg exercises and adequate hydration.

Mechanical methods

Graduated elastic compression stockings (GECS).
Intermittent pneumatic compression.

Main Pharmacological (Drug) Agents

Antiplatelet pharmacological agents (eg aspirin).
Unfractionated and low molecular weight heparins.
Oral anticoagulants.
Dextrans.

Clinical practice varies, however, and it is estimated that four out of 10 orthopaedic patients do not receive any form of prophylaxis (source NICE Guidelines Scope).

PROMOTING BEST PRACTICE: AVAILABILITY OF PROTOCOLS AND GUIDANCE

10. The National Institute for Clinical Excellence (NICE) has commissioned the National Collaborating Centre for Acute Care to develop a clinical guideline on the prevention of venous thromboembolism for use in the NHS in England and Wales. In the draft scope of this guideline, adult patients who are at a high risk of developing venous thromboembolism, but are not undergoing surgery will not be covered. However, the scope is currently out to consultation and may thus be modified. The expected date of issue of this guideline is given as May 2007.

11. The British Thoracic Society have issued authoritative guidelines on the detection and management of the pulmonary embolism¹—the main complication from venous thromboembolism. These were issued in June 2003.

12. Other Guidelines have been produced by the Scottish Intercollegiate Guidelines Network (SIGN) in 2002.

13. The National Electronic Library for Health makes these guidelines available to clinicians via their web-site.

RECENT CONCERNS AROUND THROMBOEMBOLISM

14. Although there are a wide range of risk-factors for thromboembolism, two which have been of concern recently are set out below in more detail (these details are provided from the SIGN Guideline).

Oral contraceptives

The background rate of spontaneous venous thromboembolism (VTE) in healthy women who are not pregnant and who do not use the combined oral contraceptive (COC) pill is around five cases per 100,000 women per year. The risk is increased threefold (*15/100,000 women per year*) in users of second generation contraceptives, and six fold (*30/100,000 women per year*) in users of third generation oral contraceptives.

The absolute risk of thrombosis in women taking third generation pills is small (*an excess risk of 10–25 cases of VTE per 100,000 women years*) and is less than the risk associated with pregnancy (*estimated at 100 cases per 100,000 maternities*). However, the risks are higher during the first year of use, approaching 30 per 100,000 women per year for users of third generation COC. The risk is also much higher in women with thrombophilias.

Long Distance Travel

There are many published anecdotal reports which link venous thromboembolism with prolonged travel, particularly air travel, but there are only three published case-control studies, and some studies of consecutive patients which are small, prone to bias, and gave contrasting and imprecise results.

The risk appears higher in patients with known risk factors and with flights over 3,000 miles. Possible mechanisms include: immobility; cramped position; dehydration (*augmented by drinking alcohol and coffee*); compression of calf (popliteal) veins by edge of seat; and seated posture, especially when sleeping. Research findings demonstrate that the relative risk remains to be established in further case-control studies, and the absolute risk remains to be established in large, prospective studies.

¹ British Thoracic Society guidelines for the management of suspected acute pulmonary embolism British Thoracic Society Standards of Care Committee Pulmonary Embolism Guideline Development Group. *Thorax* (2003); 58:470–484.

Small trials have observed reductions in the incidence of symptomless DVT by Graduated Elasticated Stockings (GECS). Stockings used in hospital are designed for use in recumbent patients and are not suitable for use in flight. Patients should be provided with the correct type and size of stocking, and should be instructed how to wear them correctly. Stockings also reduce leg oedema after long flights. They may precipitate superficial thrombophlebitis in people with varicose veins.

One small trial observed reduction in the incidence of symptomless DVT by a single dose of heparin two to four hours before flight, but not by aspirin (*400 mg daily for three days, starting 12 hours before flight*).

Long Distance Travel Guidelines

Recent guidelines for travellers (issued by the Scottish Intercollegiate Guidelines Network (SIGN)) include:

To minimise the risk of thrombosis when travelling long distances (eg *over four hours*), especially by air, all travellers should be advised to:

- ensure good hydration;
- restrict alcohol and coffee intake; and
- regularly carry out simple leg exercises and take occasional walks during travel.

In patients at high risk of thrombosis (eg *previous deep vein thrombosis or pulmonary embolism; known blood disorders, such as thrombophilia; recent major trauma, surgery or immobilising medical illness, pregnancy*), the following prophylactic methods should be considered:

Graduated elastic compression stockings (GECS):

- a single dose of aspirin (150 mg) before travel (\pm GECS);
- a single injection of a low molecular weight heparin before travel in prophylactic dose (\pm GECS); and
- patients already receiving warfarin should continue to take it (\pm GECS). INR should be checked one week before long-distance travel and the dose adjusted to within the target therapeutic range.

SOURCES AND WEB-LINKS

National Electronic Library for Health

<http://libraries.nelh.nhs.uk/guidelinesFinder/viewResource.asp?uri=http://libraries.nelh.nhs.uk/common/resources/?id=30462>

National Institute for Clinical Excellence

<http://www.nice.org.uk/page.aspx?o=63366>

British Thoracic Society Guidelines

<http://www.brit-thoracic.org.uk/docs/PulmonaryEmbolismJUN03.pdf>

Scottish Intercollegiate Guidelines Network

<http://www.sign.ac.uk/guidelines/62/index.html>

Memorandum by the National Patient Safety Agency (VT 11)

1. INTRODUCTION TO THE NATIONAL PATIENT SAFETY AGENCY

The National Patient Safety Agency (NPSA) was established as a Special Health Authority in the National Health Service in July 2001 following the recommendations of the Chief Medical Officer's report on patient safety, *An Organisation with a Memory*¹. The NPSA's role is to improve the safety of NHS patients by promoting a culture of reporting and learning from errors and systems failures, and to manage the national reporting system to support this function. By collecting and analysing data on patient safety problems, the Agency will be able to identify trends and patterns of avoidable incidents, provide feedback to organisations to enable them to change their working practices, help develop models of good practice and systems solutions at a national level, and support ongoing education and learning. Further information is available at www.npsa.nhs.uk

A patient safety incident is any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS funded healthcare. This is also referred to as an adverse event/incident, mistake or clinical error, and includes near misses².

2. NPSA RISK ASSESSMENT PROJECT ON THE USE OF ANTICOAGULANT MEDICINES

The NPSA is currently conducting a risk assessment project on the use of anticoagulant medicines. The risk assessment is intended to determine the extent and nature of these risks and to identify potential safety solutions that can be developed during 2005 and then introduced into the NHS IN 2006. A report on this work is planned to be published in March 2005. The NPSA wishes to inform the Parliamentary Health Committee of this work and some emerging findings in order to assist the inquiry into 'The Prevention of Venous Thromboembolism in Hospitalised Patients'.

3. EVIDENCE OF HARMS WITH ANTICOAGULANTS

3.1 In primary care, anticoagulants are one of the three classes of drugs most commonly associated with fatal medication errors.³ Case studies have been published to describe deaths associated with anticoagulant therapy.⁴⁻⁶ A coroner and the Chief Medical Officer have recently highlighted the death of a patient from a warfarin overdose caused by misinterpretation of a doctor's handwriting.⁷⁻⁹

3.2 In secondary care warfarin and heparin errors are among the most frequently reported medication errors.¹⁰⁻¹¹

3.3 Oral anticoagulants were included in the Department of Health Report, Making Medication Practice Safer (2004) as high risk medicines that require the implementation of additional safety controls.¹²

3.4 In the USA,¹³⁻¹⁴ and Australia¹⁵ anticoagulants have been identified in the top five medicine classes associated with patient safety incidents with medicine.

3.5 The NPSA contacted the medical and pharmacy defence organisations as well as the NHS Litigation Authority (Personal communications). There have been 600 patient safety incidents of harm or near harm associated with the use of anticoagulants in the UK between 1990–2002. Of these cases, 20% (120) have resulted in the death of the patient.

3.6 Death associated with the use of warfarin is responsible for 77% (92 reports) and deaths associated with heparin is responsible 23% (28 reports).

3.7 Further analysis of the data from the Medical Defence Union was possible. Fatal incident reports from this source concerning warfarin made up 88% (79 reports) of the total 92 reports.

3.8 Deaths associate with the use of warfarin in primary care were 76% (60 reports) of the total reported to the MDU (79 reports). The main types of causes for these fatal incidents were (1) inadequate laboratory monitoring and (2) clinically significant drug interactions usually involving non-steroidal anti-inflammatories.

3.9 Fatal incident reports concerning heparin in secondary care from the MDU made up 93% (26 reports) of the total of 28 reports. The main causes of these fatal incidents were (1) inadequate laboratory monitoring, (2) inappropriate cessation, (3) inappropriate use of heparin when contraindicated, (4) Dose miscalculation.

3.10 Reports concerning heparin were not usually associated with the use of low dose heparin products used for thromboprophylaxis. However, there is the risk potential for low dose heparin products to be confused with higher dose products.

3.11 Some thromboprophylaxis guidelines recommend the use of oral anticoagulants. Some other guidelines requiring thromboprophylaxis to commence in hospital and continue in the community. Although low dose injected heparin products may be the preferred treatment, oral anticoagulants may be substituted if the patients in the community are not able to make suitable arrangements for daily heparin injections.

4. EMERGING FINDINGS FROM THE NPSA RISK ASSESSMENT

A multidisciplinary healthcare team from the NHS are in the process of risk assessing systems for anticoagulant treatment in the NHS.

Anticoagulants treatments include injectable heparin products and oral anticoagulants eg warfarin. The clinical effectiveness of anticoagulants is monitored by routine blood tests; the International Normalised Ratio (INR) for Warfarin and Activated Partial Thromboplastin Test (APTT) for sodium or calcium heparin products. Anticoagulant doses are adjusted following the results of these tests. Low molecular weight heparin products do not usually require blood tests or dose adjustment.

The following are emerging as the high risk issues in the current error-prone anticoagulant system.

4.1 Failure to initiate anticoagulant therapy where indicated.

- Inadequate consideration of thrombosis in pre-operative assessment.
- Inadequate consideration of thrombosis in medical assessment.
- Misdiagnosis.

- Failure to check the requirement for anticoagulant therapy in higher risk patients.
- Service capacity issue—reluctance to increase patient numbers on anticoagulants—continue to use aspirin when patient may benefit from warfarin therapy.
- Lack of knowledge and use of treatment guidelines when therapy should be initiated.
- Conflicting treatment guidelines.
- Inadequate review of previous medical history.
- Absent or incomplete medical and medication history available.
- Wrong information or lack of information.
- Fear/reluctance to prescribe due to risk of bleeding/stroke—especially in the elderly.
- Failure of patient to seek treatment.

4.2 Lack of information and confusion over treatment plan, increasing risk of wrong or delayed treatment, dose or duration of therapy.

- Absent, incomplete or unclear record indicating reason for treatment, target INR, duration of therapy/planned cessation date and medication history.
- Failure to record and communicate plan to nurses, pharmacists, receptionist, anticoagulant clinic/GP. Discharge/handover information incomplete. Pre-screening information/treatment cessation plan missing.
- Lack of clarity over which member of the hospital medical team is responsible for recording this information and when this information should be recorded. This could be either at the same time the anticoagulant is prescribed or before or at the same time the patient is discharged from hospital.
- NHS pressures of discharge. Lack of time, lack of knowledge, inability to find template referral forms or poor documentation system, or assumption that some other member of the team is responsible or failure to understand the importance of recording this information for the safe and effective anticoagulant treatment. No treatment plan. Discussions / decisions not recorded.

4.3 Patient has appointment with anticoagulant service but long time period between discharge and clinic appointment.

- Risk to patient that dosing is incorrect due to delay between clinical review during anticoagulant induction therapy.
- Patient may be required to return to hospital ward for blood test and dosing—*ad hoc* arrangement “on duty” staff who may not know or expect the patient are required to manage care on an interim basis. Patients’ care record may no longer be on the ward. Patient may not attend due to confusion over arrangements.

4.4 Patient is discharged on loading dose.

- Loading dose may be continued in error.
- Poor inpatient documentation.
- Unclear, incomplete or wrong completion of yellow book eg, loading doses recorded in yellow book, delay in appointment for anticoagulant clinic, no further doses recorded in yellow book, patient assumes that they are to continue with previous dose until seen in the anticoagulant clinic.
- Lack of awareness of regime by junior doctor.

4.5 *Prescribe wrong dose or no dose of anticoagulant.*

- Mis-communication of intended dose of anticoagulant between members of the clinical team, the laboratory and the clinical team, the hospital and the GP surgery. Healthcare staff and the patient or carer. Doses may frequently be communicated verbally.
- Oral anticoagulants may be prescribed by the “number” of tablets to taken rather than mg dose. There are 5mg, 3mg, 1mg and 0.5mg tablets available.
- Healthcare organisations and practitioners may have standardised on the use of one or more strengths of anticoagulant product. This may cause confusion as neighbouring healthcare organisations and practitioners may have standardised on different strength products.
- Dose does not appear on prescription but held separately eg at the back of a hospital prescription care or on a separate anticoagulant prescription form.
- The laboratory results may be matched to the incorrect patient and used to determine new dose of anticoagulant.
- No baseline INR measured before commencing induction doses of oral anticoagulants. The selected doses may be inappropriate for the patients for this reason.

- The first INR test undertaken on day three, the patient may already be discharged from the hospital and this may cause difficulty in arranging the test and adjusting the dose before the patient is transferred into the care of the outpatient anticoagulant service of GP service.
- Poor dosing decisions by prescribers based on INR and other factors.
- Lack of standardisation of loading dose regimens between healthcare organisations and practitioners.
- Anticoagulant doses are prescribed on a daily basis by junior doctors in hospitals. Prescriptions for these daily doses are frequently omitted and this can lead to dose omission as nursing staff have no information as to what dose to administer.
- Heparin products are prescribed mg/kg body weight or unit/kg body weight. A body weight may not be available or may be incorrectly estimated. The dose of heparin may be miscalculated due to an arithmetic errors.
- Low molecular heparin products have different licensed clinical indications and the dose and dose frequency differs with indication. These factors can cause confusion and the wrong product, dose or frequency is prescribed for a specific indication.
- Poorly hand written prescriptions for heparin in “units” can be misinterpreted as dose zeros causing dose errors of factors of 10.

In Primary Care for oral anticoagulants.

- Repeat prescriptions for oral anticoagulants are generated via patient/carer request alongside requests for other medicines. There is no additional safety checks for oral anticoagulants.
- There are less safety checks for anticoagulants as no dose or frequency or duration information is included on prescription. It is assumed that dosing information is provided to the patient by the anticoagulant clinic.
- INR results may not be recorded in GP case record.
- Current oral anticoagulant dose information may not be recorded in GP case record.
- Routine checks of the continued appropriateness of treatment, recent and safe INR, the current dose, appropriateness of the dose or quantity requested or date of next appointment with the anticoagulant clinic may not be included in the repeat prescription process in GP’s surgeries.

4.6 *Prescription and labels for oral anticoagulants include the instruction “as directed”.*

- Prescription for discharge and repeat supplies of oral anticoagulants include the instruction “as directed”. There is a separation of responsibilities—those prescribing the “supply” of anticoagulants to those “dosing” anticoagulants.
- Once discharged from hospital, the patient held record called “the yellow book” is the only information source that provides information about the current dosage. The yellow book is not regarded as a prescription but rather “supplementary clinical information”.
- The information in the patient held record especially the dose and the latest INR result is not usually checked by the GP prescribing maintenance supplies or the pharmacist when dispensing maintenance supplies of oral anticoagulants.

4.7 *Failure to monitor anticoagulant therapy to adjust dose to effect.*

- Lack of time, or poor documentation system, or assumption that some other member of the team is responsible for monitoring and dose adjustment.
- Failure to understand the importance of communicating to the team for the safe and effective anticoagulant treatment.
- Inadequate follow-up of patients who do not attend the anticoagulant clinic to have a blood test and dose of oral anticoagulant adjusted as appropriate.

4.8 *Dose adjustment for surgery/dentistry/endoscopy/cardioversion.*

- Different guidelines, opinion and practice on how to manage patients on anticoagulants requiring surgery, dental treatment, endoscopy or cardioversion.
- Anticoagulant clinics frequently expected to manage patients therapy before and after treatment without any guidance from the surgeon or dentist or investigating clinician as to what is required.
- Blood test frequently undertaken immediately prior procedure, the operation or procedure is cancelled and delayed if INR is not correct, even when the patient an anticoagulant clinic have not been informed what was required.

4.9 *Unconsidered co-prescribing of non-steroidal anti-inflammatories and other interaction medicines with oral anticoagulants.*

- Lack of knowledge, time, professional judgement of prescriber.
- Lack of use of cytoprotective agents.
- Incomplete or unavailable medication history.

- Patients self prescribing/taking over the counter supplies of nonsteroidals

4.10 *Incorrect selection and preparation of heparin products*

- There are many different types and strength of heparin products and there may be a mis-selection error.
- Heparin products are prescribed mg/kg body weight or unit/kg body weight. A body weight may not be available or may be incorrectly estimated. The dose of heparin may be miscalculated due to an arithmetic errors.
- Sodium Heparin—supplied as concentrate that requires dilution. Mis-selection and arithmetic calculation errors.
- Incorrect physical syringe measurement of dose.
- Incorrect dilution of concentrate.
- For heparin infusions incorrect calculation of rate of administration. Confusion over mls/hour, units/hour.
- For heparin infusions incorrect operation of infusion pump when programming rate of administration to be delivered.

4.11 *Inappropriate dispensed supply of oral anticoagulants.*

- There are less safety checks for anticoagulants as no dose or frequency or duration information is included on prescription. It is assumed that dosing information is provided to the patient by the anticoagulant clinic.
- Routine checks of the continued appropriateness of treatment, recent and safe INR, the current dose, appropriateness of the dose or quantity requested or date of next appointment with the anticoagulant clinic are not usually included in the repeat dispensing process.
- A review of the patient held record is not usually included when supplies of anticoagulants are dispensed.

5. ISSUES FOR THROMBOPROPHYLAXIS OF HOSPITAL PATIENTS ARISING FROM RISK ASSESSMENT

It is important that the use of any anticoagulant products for thromboprophylaxis should be as safe as possible and forms part of an anticoagulant system that has identified and minimised risks. Identified risks in section 4 will help the NPSA develop safety solutions for the anticoagulant system during 2005. Specific risks concerning thromboprophylaxis for further discussion are included in this section.

5.1 *Failure to treat or undertreatment*

The indications for thromboprophylaxis and recommended drug regimens have been reasonably well established and there is a range of guidance available¹⁵⁻¹⁹. Failure to treat or suboptimal thromboprophylaxis has been identified during the NPSA risk assessment process. This risk has also been identified in published studies in the UK and internationally (Table 1)²⁰⁻²⁶.

Failure to use thromboprophylaxis is particularly poor in patients admitted to nonsurgical areas of the hospital. Most acutely ill medical patients are at risk for venous thromboembolism, at least 75% of fatal pulmonary emboli occur in this group. Medical patients are at significant risk of thromboembolic disease. Patients over 75 years of age, a history of venous thrombosis with chronic respiratory disease, congestive heart failure, and infectious disease and with a diagnosis of cancer are at high risk of symptomatic venous thromboembolism (VTE), particularly pulmonary embolism. Most medically ill patients in the hospital do not receive any form of venous thromboembolism prophylaxis despite evidence that their venous thromboembolism risk is similar to surgical patients. Many patients recently discharged from the hospital remain at high risk for thrombosis²⁷⁻²⁹. Recent studies have identified the risk factor profiles in this group of patients, and a risk assessment model for medical patients has been developed. Risk stratification will help to ensure that patients receive appropriate thromboprophylaxis²⁷.

In a publication concerned with the application of the American College of Chest Physicians Seventh National Guidelines on Antithrombotic and Thrombolytic Therapy recommendations for appreciable resources to be devoted to the distribution of educational materials, computer generated reminders and to patient mediated interventions as these methods are judged to be effective³⁰. The authors suggest that few resources are devoted to educational meetings, audit, feedback and educational outreach as these methods do not appear to be very effective in applying the agreed guidelines in practice.

5.2 Management of patients on oral anticoagulants for dental procedures, surgical procedures and other procedures

Another reason for patients requiring thromboprophylaxis not to be treated or undertreated is due to a widespread belief among healthcare practitioners that oral anticoagulation therapy must be discontinued before dental treatment, minor surgery and other procedures to prevent serious bleeding.

The scientific literature does not support routine discontinuation of oral anticoagulation therapy for dental patients. Use of warfarin sodium as it relates to dental or oral surgical procedures has been well-studied. Some dental studies of antiplatelet therapy are consistent with the findings in warfarin sodium studies. Dental therapy for patients with medical conditions requiring anticoagulation or antiplatelet therapy must provide for potential excess bleeding. Routine discontinuation of these drugs before dental care, however, can place these patients at unnecessary medical risk. The coagulation status—based on the International Normalized Ratio—of patients who are taking these medications must be evaluated before invasive dental procedures are performed. Any changes in anticoagulant therapy must be undertaken in collaboration with the patient's prescribing physician³¹.

In an Australian study of 70 patients who were on warfarin treatment requiring minor oral surgical procedures were treated in the Oral Surgery Department. A control group of 35 had their warfarin stopped prior to the minor oral surgical procedure. The other 35 formed the study group. Patients with an International Normalized Ratio outside the therapeutic range of two to four, or with history of liver disease or on drugs affecting liver function were excluded from the study³². Any incidences of post-operative bleeding were recorded. None of the patients in either control or study group had any serious bleeding complications.

In a systematic review peri-operative management of patients receiving oral anticoagulants 31 published studies were found. Although the quality of the identified reports was generally poor; and no randomized controlled trials have been performed and duration of follow-up was typically not stated. The reports indicated that most patients can undergo dental procedures, arthrocentesis, cataract surgery, and diagnostic endoscopy without alteration of their regimen.

For other invasive and surgical procedures, oral anticoagulation needs to be withheld, and the decision whether to pursue an aggressive strategy of peri-operative administration of intravenous heparin or subcutaneous low-molecular-weight heparin should be individualized. The reviewers emphasised that the current literature is limited and further and more rigorous studies are needed to better inform treatment with anticoagulants in these clinical situations³³.

5.3 Extended thromboprophylaxis

Prolonged thromboprophylaxis with LMWH for up to 35 days after major orthopaedic surgery has been recommended³³. The American College of Chest Physicians (ACCP) recommendation for a minimum of seven to 10 days of prophylaxis after hip and knee replacement, even if patients are discharged from the hospital within seven days of surgery. As risk of VTE persists for up to three months after surgery, patients at high risk for postoperative VTE may benefit from extended prophylaxis (eg, an additional three weeks after the first seven to 10 days). Extended prophylaxis with low-molecular-weight heparin (LMWH) reduces the frequency of post discharge VTE by approximately two thirds after hip replacement; however, the resultant absolute reduction in the frequency of fatal pulmonary embolism is small (ie, estimated at one per 2,500 patients). Indirect evidence suggests that, compared with LMWH, efficacy of extended prophylaxis after hip replacement is greater with fondaparinux, similar with warfarin, and less with aspirin. Extended prophylaxis is expected to be of less benefit after knee than after hip replacement. In keeping with current ACCP recommendations, at a minimum, extended prophylaxis should be used after major orthopaedic surgery in patients who have additional risk factors for VTE (eg, previous VTE, cancer). If anticoagulant drug therapy is stopped after seven to 10 days, an additional month of prophylaxis with aspirin should be considered^{19, 35}.

Cancer patients receiving radiotherapy. The duration of prophylaxis should usually last for the period of treatment, except in the case of pelvic or cerebral radiotherapy where it is continued for four to 12 months beyond the treatment period³⁶.

Arranging for the continuation of thromboprophylaxis after discharge from hospital can be complicated and if not arranged carefully may cause many of the risks described in section 4. Safe models of practice need to be developed and promoted to enable the safe extended thromboprophylaxis in the community using injected low dose heparin products and where appropriate oral anticoagulants.

6. SUMMARY

The NPSA has identified the use of anticoagulants in hospital and in the community as a high risk process. The NPSA is currently conducting a risk assessment project to determine the extent, nature and prioritise these risks and to identify potential safety solutions. A report is planned to be published in March 2005. The NPSA intends to develop the safety solutions during 2005 for introduction into the NHS IN 2006.

Specific issues associated with thromboprophylaxis of hospital patients have been identified as high risk issues in the emerging findings from the NPSA risk assessment. This includes failure to treat or undertreatment with anticoagulants for thromboprophylaxis, lack of clarity over how patients on oral anticoagulants should be managed for dental, surgical and other procedures and issues associated with the safe treatment when thromboprophylaxis is required following discharge from hospital.

The NPSA would be pleased to provide oral evidence on the 9 December and provide any additional information that would assist the Health Committee complete work on this topic

Table 1
PUBLISHED STUDIES INDICATING FAILURE TO TREAT OR
SUBOPTIMAL THROMBOPROPHYLAXIS

<i>Publication year</i>	<i>Country</i>	<i>Specialty</i>	<i>Summary</i>	<i>Reference</i>
2001	Scotland	All Surgical specialties	Postal questionnaire sent to all consultant surgeons in Scotland. Asked for opinion on best means of thromboprophylaxis. Responses evaluated against SIGN Guidelines 69% response rate. 35% of responses represented undertreatment and 16% overtreatment.	20
2002	England	General Surgery	Audit of thromboprophylaxis using Tinzaparin on a random day at the beginning and at the end of the junior house officer's six monthly rotation in general surgery. Tinzaparin was appropriately prescribed in 86% and 91% of elective admissions and in 58% and 85% of emergency admissions. The subcutaneous injection of tinzaparin was commenced on the day of admission in 67% and 75% of patients	21
1999	England	All hospital admissions	An open study of 8,648 admissions to hospital. The overall rate of clinically apparent hospital-acquired thromboembolic complications was 0.4% (n = 35). The rate of clinically apparent thromboembolic disease in the high risk group was 2.1% (n = 17). The incidence of thromboembolic problems appeared not to be reduce by prophylaxis apparently even when stratified by risk group.	22
2004	England	Obstetrics	Audit of thromboprophylaxis after caesarean section. Retrospective audit of 200 consecutive patients The majority of women (84.5%) had at least one risk factor for thromboembolism. Only 54% of cases received treatment.	23
2002	UK	Spinal injuries	All the 13 regional and national spinal injury referral centres within the British Isles were contacted to find out their protocols for thromboembolic prophylaxis in patients with acute spinal injuries. All units replied. A wide variation in methods used was found in different spinal units ranging from no chemical prophylaxis to oral anticoagulation with warfarin and contrasting views on the use of antithromboembolic stockings.	24
2002	Switzerland	Medical	Prospective study in 227 consecutive medical inpatients. 38% of 153 risk patients received some form of thromboprophylaxis. 22% of 153 risk patients received adequate thromboprophylaxis	25

Publication year	Country	Specialty	Summary	Reference
2004	USA	Medical	A retrospective chart review of 100 patients admitted to a hospital medicine service was conducted. 31% of patients with established VTE risk factors and no documented risk factors for bleeding were prescribed prophylaxis. An established regimen was prescribed in only 19% of those receiving prophylaxis.	26

REFERENCES:

- ¹ Department of Health (England). An organisation with a memory. 2000
- ² National Patient Safety Agency. Seven steps to patient safety.
- ³ Medical Defence Union 1996. Problems in General Practice—medication errors. The Medical Defence Union 1996.
- ⁴ Machin S J. Medico legal problems associated with oral anticoagulant services. In Oral anticoagulation management and stroke prevention: The primary care perspective. Editors D A Fitzmaurice and E T Murray. Newmarket: Hayward Medical Communications. 2002; p50–57.
- ⁵ Reardon M, Burns B, Brewer B, O'Sullivan J P. Deaths associated with warfarin in elderly patients. *Br J Clin Pract* 1995; 49:322–3.
- ⁶ Ferner. R E, Whittington, R M. Coroner's cases of death due to errors in prescribing or giving medicines or to adverse drug reactions: Birmingham 1986–91. *Journal of the Royal Society of Medicine*. 1994; 87: 145–148.
- ⁷ Eaton L. Coroner highlights prescribing error after patient dies from warfarin overdose. *Br Med J*. 2002; 325: 922.
- ⁸ Anon. Warfarin safety. *Br J Gen Pract*. 2002; 52: 102.
- ⁹ Department of Health. Patient Safety, medication error and handwriting. Chief medical Officer's Update 2003; 53: 10-12 www.doh.gov.uk/cmo/cmo—35.htm.
- ¹⁰ Cousins D H, Upton D R. Medication Errors: A national standard for supply of warfarin tablets? *Pharmacy in Practice* 1997; 7; 570.
- ¹¹ Cousins, D H, Upton D R. Medication Errors: Risk assess your dispensing. *Pharmacy in Practice* 1998; 8; 253–256.
- ¹² Department of Health (England). Improving medication safety. 2004.
- ¹³ Anon. Joint Commission IDs five high-alert meds. *ED Manage* 2000, 12:21-2.
- ¹⁴ Anon. High alert medications and patient safety. *Int J Qual Health Care* 2001, 13:339–40.
- ¹⁵ Runciman W B, Roughead E E, Semple S J, Adams R J. Adverse drug events and medication errors in Australia. In *J Qual Care* 2003, 15 Suppl. 1:i49–59.
- ¹⁶ Prophylaxis of Venous Thromboembolism SIGN Publication No 62. Scottish Intercollegiate Guidelines Network. 2002. <http://www.sign.ac.uk/guidelines/fulltext/62/index.html>.
- ¹⁷ Royal College of Obstetrics and Gynaecology. Thromboprophylaxis during pregnancy, labour and vaginal delivery. 2004.
- ¹⁸ Oates-Whitehead R M, D'Angelo A, Mol B. Anticoagulant and aspirin prophylaxis for preventing thromboembolism after major gynaecological surgery (Cochrane Review). *The Cochrane Library, Issue 4, 2004*.
- ¹⁹ Geerts W H, Pineo G F, Heit J A, Bergqvist D, Lassen M R, Colwell C W, Ray J G. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest*. 2004 Sep; 126(3 Suppl):338S–400S.
- ²⁰ Burns P J, Wilsom R G, Cunningham C. Venous thromboembolism prophylaxis used by consultant general surgeons in Scotland. *J R Coll Surg Edinb*. 2001 Dec; 46(6):329–33.
- ²¹ Fassiadis N, Stavrianiakis C, Moghraby O S, Gandhi P, Smedley F H. Venous thromboembolism. Prophylaxis on a Saturday morning in a district hospital. *Int Angiol*. 2002 Dec; 21(4):330–2.
- ²² Gidiri M, Sant M, Philips K, Lindow S W. Thromboprophylaxis for caesarean section—how can uptake and coverage be improved? *J Obstet Gynaecol*. 2004 Jun; 24(4):392–4.
- ²³ Deep K, Jigajinni M V, Fraser M H, McLean A N. Prophylaxis of thromboembolism in spinal injuries—survey of practice in spinal units in the British Isles. *Injury*. 2002 May; 33(4):353–5.
- ²⁴ Wright G, Elliott K, Wilkie C, Cuschieri R J, Bittiner B, Hughes K B. A prospective audit of hospital-acquired deep vein thrombosis and pulmonary embolism. *Int J Clin Pract*. 1999 Oct–Nov; 53(7): 497–504.
- ²⁵ Aujesky D, Guignard E, Pannatier A, Cornuz J. Pharmacological thromboembolic prophylaxis in a medical ward: room for improvement. *J Gen Intern Med*. 2002 Oct; 17(10): 788–91.
- ²⁶ Stark J E, Kilzer W J. Venous thromboembolic prophylaxis in hospitalized medical patients. *Ann Pharmacother*. 2004 Jan; 38(1): 36–40.
- ²⁷ Alikhan R, Cohen AT, Combe S, Samama M M, Desjardins L, Eldor A, Janbon C, Leizorovicz A, Olsson C G, Turpie A G; MEDENOX Study. Risk factors for venous thromboembolism in hospitalized patients with acute medical illness: analysis of the MEDENOX Study. *Arch Intern Med*. 2004 May 10; 164(9): 963–8.

- ²⁸ Cohen A T. Discoveries in thrombosis care for medical patients. *Semin Thromb Hemost.* 2002 Aug; 28 Suppl 3:13–7.
- ²⁹ Michota F A. Venous thromboembolism prophylaxis in medical patients. *Curr Opin Cardiol.* 2004 Nov; 19(6):570–4.
- ³⁰ Schunemann H J, Cook D, Grimshaw J, Liberati A, Heffner J, Tapson V, Guyatt G. Antithrombotic and thrombolytic therapy: from evidence to application: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest.* 2004 Sep; 126(3 Suppl):688S–696S.
- ³¹ Jeske A H, Suchko G D. Lack of a scientific basis for routine discontinuation of oral anticoagulation therapy before dental treatment. *J Am Dent Assoc.* 2003 Nov; 134(11):1492–7.
- ³² Cannon P D, Dharmar V T. Minor oral surgical procedures in patients on oral anticoagulants—a controlled study. *Aust Dent J.* 2003 Jun; 48(2):115–8.
- ³³ Dunn A S, Turpie A G. Perioperative management of patients receiving oral anticoagulants: a systematic review. *Arch Intern Med.* 2003 Apr 28; 163(8):901–8.
- ³⁴ Cohen A T, Khushf A. Extended thromboprophylaxis following lower limb arthroplasty: what do the clinical trials mean? *Haemostasis.* 2000;30 Suppl 2:88–94; discussion 82–3.
- ³⁵ Kearon C. Duration of venous thromboembolism prophylaxis after surgery. *Chest.* 2003 Dec; 124 (6 Suppl):386S–392S.
- ³⁶ Thodiyil P A, Walsh D C, Kakkar A K. Thromboprophylaxis in the cancer patient. *Acta Haematol.* 2001; 106(1-2):73–80.

Memorandum by the National Institute for Clinical Excellence (VT 16)

1. INTRODUCTION

1.1 The National Institute for Clinical Excellence (NICE) has been asked to develop three pieces of guidance relevant to the prevention of venous thromboembolism in hospitalised patients.

1.2 The purpose of this memorandum is to describe the role of the Institute, to detail the three pieces of guidance relevant to this inquiry, and to set out key features of the process that the Institute will follow when developing this guidance.

2. THE INSTITUTE AND ITS GUIDANCE

2.1 NICE was established as a special health authority in 1999. Our role is to provide advice to the NHS in England and Wales on the clinical and cost effectiveness of drugs and other treatments. Our advice is for people who rely on the NHS for their care and for health professionals. Further information about the work of the Institute can be found at www.nice.org.uk

2.2 A summary of the four main types of NICE guidance is set out below.

2.2.1 *Technology appraisals*: recommendations on the use of new and existing medicines and other treatments (devices, surgical and other procedures, diagnostic techniques and health promotion methods).

2.2.2 *Clinical guidelines*: recommendations on the appropriate treatment and care of patients with specific diseases and conditions, such as diabetes and schizophrenia.

2.2.3 *Cancer service guidance*: recommendations on the organisation and delivery of services for people with cancer.

2.2.4 *Interventional procedures*: guidance about whether interventional procedures used for diagnosis and treatment are safe enough and work well enough for routine use. An interventional procedure is one used for diagnosis or treatment that involves making a cut or hole in the body, entry into a body cavity or using electromagnetic radiation (including X-rays or lasers) and ultrasound.

2.3 We publish around 25 technology appraisals, 12 clinical guidelines and 60 pieces of interventional procedures guidance each year.

2.4 NICE guidance is a key component of the national standards to which the NHS is now expected to work. Technology appraisals and interventional procedures guidance are “core” standards, which require immediate implementation, and clinical guidelines are regarded as “developmental” standards, the implementation of which will take place over a longer period.

2.5 The Institute is based in offices in central London. It has a budget of nearly £20 million, which is largely provided by the Department of Health but also includes a contribution from the Welsh Assembly Government, to which the Institute is jointly accountable. The Institute directly employs around 100 people.

3. DEVELOPING GUIDANCE ON VENOUS THROMBOEMBOLISM

3.1 The Department of Health and Welsh Assembly Government are responsible for selecting the topics for the NICE technology appraisal and clinical guideline programmes. Full details of the process they follow can be found on the Department of Health website at www.dh.gov.uk. Once a topic has been referred, the development of the subsequent advice is entirely the responsibility of NICE.

3.2 To date, the Department of Health and Welsh Assembly Government have referred the following topics relevant to this Inquiry to the Institute:

3.2.1 A clinical guideline on the prevention of venous thromboembolism in patients undergoing orthopaedic surgery and other high-risk surgical procedures. The Institute is currently consulting on the scope for this guideline (attached for information as Appendix A), and the consultation period closes on 8 December 2004. The Institute expects to publish final guidance on this topic in May 2007.

3.2.2 Two technologies are in different stages of consideration by the Institute:

- (i) Ximelagatran (an inhibitor of thrombin) is for use in the acute treatment and longer term management of venous thrombosis and pulmonary embolism. Applications for marketing authorisation have been submitted in the UK but currently this technology is not licensed for use. This Institute is currently consulting on the scope for this appraisal and anticipates publishing guidance in the fourth quarter of 2006.
- (ii) The use of thrombophilia screening for the diagnosis of individuals at high risk of thrombosis. As a consequence of the responses received from stakeholders during consultation on the draft scope for this appraisal, the Institute has decided that further discussions are required with the Department of Health and Welsh Assembly Government to determine the nature of the final remit.

4. THE GUIDANCE DEVELOPMENT PROCESS

4.1 Since its inception, the Institute has taken the approach that those whom its decisions affect are entitled to express their views on how we go about our work and on the development of individual pieces of guidance. We define these groups as including, but not necessarily limited to:

- 4.1.1 patients, carers and the public, and those who speak for them;
- 4.1.2 healthcare professionals;
- 4.1.3 NHS management;
- 4.1.4 healthcare industries; and
- 4.1.5 the Government.

We recognise these constituencies as key stakeholders in our work alongside a much larger group including, for example, NHS agencies with related functions, research organisations and trade unions.

4.2 We make sure that our stakeholders (sometimes called consultees) have clear and reasonable opportunities to engage with us when we are developing guidance on a particular topic. The arrangements we have put in place have evolved as our experience of working with a diverse community of interested parties has grown. The main elements of these arrangements are summarised below.

- 4.2.1 Our processes and methods are developed in consultation with our stakeholders and with the independent experts who sit on our advisory committees. Drafts of our process and methods documents are exposed to public consultation and the comments received, together with the final versions of the documents, are approved by the Board in public session.
- 4.2.2 We consult with stakeholders on our interpretation (the “scope”) of the topics referred to NICE by the Department of Health and Welsh Assembly Government. These scopes form the basis of each guidance development project.
- 4.2.3 All draft guidance is subject to consultation with stakeholders and the wider public through the Institute’s website.
- 4.2.4 All documentation associated with the development of guidance, other than where we have agreed to restrictions for reasons of commercial or academic confidence, is released into the public domain.
- 4.2.5 Comments submitted to the Institute by stakeholders are made publicly available along with the Institute’s response.

4.3 We take the view that those who rely on our guidance should be able to understand how it has been developed. To this end each of our programmes displays a common set of characteristics, which are summarised below.

- 4.3.1 *Use of the best available evidence:* each programme secures a comprehensive evidence base, by contracting the work to an independent body or by undertaking the work in-house, and stakeholders are invited to check that all relevant evidence has been considered.

- 4.3.2 *Involvement of clinical and patient experts*: ensuring that our advisory bodies have access to clinical expertise and patient and carer perspectives as they interpret evidence is crucial both to the relevance of the recommendations and to their credibility.
- 4.3.3 *Independent advisory bodies*: the guidance that NICE publishes is prepared by independent standing committees (for technology appraisals and interventional procedures) and individual development groups (for clinical guidelines). All our advisory bodies include healthcare professionals working in the NHS and people who are familiar with the issues affecting patients and carers. The standing advisory committees also include people who are currently working in the healthcare industries.
- 4.3.4 *Genuine consultation*: all NICE guidance undergoes widespread consultation with stakeholders and the public. “Genuine” means that our advisory bodies will respond to reasoned argument that can stand up to independent scrutiny and, if necessary, change their original thinking.
- 4.3.5 *Regular review*: technology appraisal guidance and clinical guidelines are reviewed at regular intervals to ensure that they remain current. Review dates are set on the basis of the advisory body’s understanding of the anticipated pace of change in the evidence base.

5. SUPPLEMENTAL EVIDENCE

5.1 A copy of the draft scope for the clinical guideline on the prevention of venous thromboembolism in patients undergoing orthopaedic surgery and other high-risk surgical procedures is attached at Appendix A for information.

5.2 Members of the Health Select Committee are also invited to review the detail of our arrangements for engaging with stakeholders in the process document for the clinical guidelines programme, which is enclosed as Appendix B for information.

6. CONCLUSION

6.1 NICE has been asked by the Department of Health and Welsh Assembly Government to develop three pieces of guidance relevant to the prevention of venous thromboembolism in hospitalised patients.

6.2 Our guidance will be developed using the expertise of the NHS and the wider healthcare community including NHS staff, healthcare professionals, patients and carers, industry and the academic world.

6.3 Once published, our guidance will support healthcare professionals and patients and their carers when making decisions about treatment and healthcare. It will improve the care of hospitalised patients by setting national standards for the prevention of venous thromboembolism and promoting equal access to clinically effective and cost effective treatments for this condition across the NHS in England and Wales.

November 2004

APPENDIX A

Draft scope for clinical guideline on the prevention of venous thromboembolism in patients undergoing orthopaedic surgery and other high-risk surgical procedures

SCOPE

1. GUIDELINE TITLE

Venous thromboembolism: the prevention of venous thromboembolism in patients undergoing orthopaedic surgery and other high risk surgical procedures.

1.1 *Short title*

Venous thromboembolism.

2. BACKGROUND

(a) The National Institute for Clinical Excellence (“NICE” or “the Institute”) has commissioned the National Collaborating Centre for Acute Care to develop a clinical guideline on the prevention of venous thromboembolism for use in the NHS in England and Wales. This follows referral of the topic by the Department of Health and Welsh Assembly Government (see Appendix).² The guideline will provide recommendations for good practice that are based on the best available evidence of clinical and cost effectiveness.

² Not printed.

(b) The Institute's clinical guidelines will support the implementation of National Service Frameworks (NSFs) in those aspects of care where a Framework has been published. The statements in each NSF reflect the evidence that was used at the time the Framework was prepared. The clinical guidelines and technology appraisals published by the Institute after an NSF has been issued will have the effect of updating the Framework.

(c) NICE clinical guidelines support the role of healthcare professionals in providing care in partnership with patients, taking account of their individual needs and preferences, and ensuring that patients (and their carers and families, where appropriate) can make informed decisions about their care and treatment.

3. CLINICAL NEED FOR THE GUIDELINE

(a) Deep vein thrombosis occurs in about 30% of surgical patients and is commonly asymptomatic. However, the condition can lead to sudden death due to pulmonary embolism, or cause long-term morbidity due to venous ulceration and development of a post-thrombotic limb. Pulmonary embolism following lower limb deep vein thrombosis is the cause of death in 10% of patients who die in hospital.

(b) Most thrombi occur in the deep veins of the legs. Formation of thrombi is associated with inactivity and high-risk surgical procedures. The risk is particularly high in patients undergoing orthopaedic surgery and lengthy operations.

(c) Current preventative measures for patients undergoing high-risk surgical procedures include mechanical prophylaxis (such as graduated elastic compression stockings) and pharmaceutical prophylaxis (such as low molecular weight heparin). Clinical practice varies and it is estimated that four out of 10 orthopaedic patients do not receive any form of prophylaxis³.

(d) This guideline will examine the risk of venous thromboembolism and assess the evidence for preventative measures. It will provide recommendations on the most clinically and cost effective measures to reduce adverse events and morbidity and mortality.

(e) The Scottish Intercollegiate Guidelines Network issued guidance on the use of prophylaxis of venous thromboembolism in 2002⁴.

4. THE GUIDELINE

(a) The guideline development process is described in detail in two publications which are available from the NICE website (see "Further information"). *The Guideline Development Process—An overview for Stakeholders, the public and the NHS* describes how organisations can become involved in the development of a guideline. *The Guideline Development Methods—Information for National Collaborating Centres and Guideline Developers* provides advice on the technical aspects of guideline development.

(b) This document is the scope. It defines exactly what this guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health and Welsh Assembly Government (see Appendix).

(c) The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

- (a) The guidelines will cover adults (age 18 and older) undergoing:
- orthopaedic surgery (including total hip or knee replacement, surgery for hip fracture, knee arthroscopy);
 - major general surgery;
 - major gynaecological surgery;
 - urological surgery (including major or open urological procedures);
 - cardiothoracic surgery; and
 - major peripheral vascular surgery.

³ Department of Health (2003) Further action to tackle post-code lottery in care [press release]. <http://www.dh.gov.uk>

⁴ Scottish Intercollegiate Guidelines Network (2002) Prophylaxis of venous thromboembolism. *SIGN Publication* No 62. Edinburgh: Scottish Intercollegiate Guidelines Network.

4.1.2 Groups that will not be covered

Patients under the age of 18 will not be covered.

Adult patients who are at a high risk of developing venous thromboembolism but are not undergoing surgery will not be covered. For example, the following circumstances will be excluded from the guideline:

- acute myocardial infarction;
- acute stroke;
- cancer, including patients being treated with chemotherapy;
- pregnancy and the puerperium;
- use of oral contraceptives and hormone replacement therapy; and
- long-distance travel.

4.2 Healthcare setting

The guideline will offer guidance for use in secondary and tertiary care.

4.3 Clinical management

(a) The guideline will assess the risk factors associated with development of venous thromboembolism in the surgical procedures listed in 4.1.1.

(b) The guideline will review the clinical and cost effectiveness, and possible morbidity, of interventions to prevent venous thromboembolism in patients under going the high-risk surgical procedures outlined in section 4.1.1.

(c) Interventions that will be considered are:

- graduated elastic compression stockings;
- intermittent pneumatic compression devices;
- mechanical foot pumps;
- low-dose unfractionated heparin;
- low molecular weight heparin; and
- oral anticoagulants (warfarin).

(d) Patients' views on all areas within the scope will be incorporated into the guideline where available. The guideline will include advice on the prevention of venous thromboembolism for patients undergoing high risk surgery.

(e) Note that guideline recommendations on prescribing will normally fall within licensed indications; exceptionally, and only where clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use the Summary of Product Characteristics to inform their decisions for individual patients.

4.4 Status

4.4.1 Scope

This is the consultation draft of the scope. The consultation period is from 11 November to 8 December 2004.

There is a NICE technology appraisal in development entitled "Venous thromboembolism (VTE)—ximelagatran" (publication expected in May 2006).

4.4.2 Guideline

The development of the guideline recommendations will begin in March 2005.

5. FURTHER INFORMATION

Information on the guideline development process is provided in:

- The Guideline Development Process—An overview for Stakeholders, the public and the NHS.
- Guideline Development Methods—Information for National Collaborating Centres and Guideline Developers.

These booklets are available as PDF files from the NICE website www.nice.org.uk. Information on the progress of the guideline will also be available from the website.

APPENDIX 2

Referral from the Department of Health and Welsh Assembly Government

The Department of Health and Welsh Assembly Government asked the Institute to develop a guideline with the following title and remit:

Title: Venous thrombo-embolism: the prevention of venous thrombo-embolism in patients undergoing orthopaedic surgery and other high-risk surgical procedures.

Remit: To develop safety guidance for the NHS in England and Wales on prophylaxis against venous thrombo-embolism (VTE) for patients undergoing orthopaedic surgery and other surgical procedures for which there is a high risk of VTE. The guidance should set out the principles of clinical and cost effective practice and in particular should address:

- (i) the assessment of risk for particular procedures and for individual patients;
- (ii) the circumstances in which prophylaxis can be recommended as clinically and cost effective; and
- (iii) the appropriate selection of interventions including both pharmaceutical and mechanical methods of prophylaxis.

Witnesses: **Dr Roger Boyle**, National Director for Heart Disease, Department of Health, **Professor Sir Michael Rawlins**, Chairman, and **Professor David Barnett**, Chairman of the Appraisals Committee, National Institute of Clinical Excellence and **Professor David Cousins**, Head Safe Medication Practice, National Patient Safety Agency, were examined.

Q57 Chairman: Welcome to the second part of this morning's session. Could I thank our second group of witnesses; we are very grateful for your cooperation with our inquiry. I know some of you were here for most, if not all, the previous session so you have a broad idea of the areas we will be covering. Could I begin by asking you each to introduce yourselves to the Committee? Dr Boyle?

Dr Boyle: Roger Boyle. I am the National Director for Heart Disease, so strictly speaking this is not my policy area. My senior colleagues send their apologies because they are out of the country recuperating from the White Paper. I will do my best to fill in.

Sir Michael Rawlins: Michael Rawlins. I am Chairman of NICE but I am also a practising physician in Newcastle so I do see DVT.

Professor Barnett: David Barnett. I am a professor of clinical pharmacology in Leicester and a cardiovascular physician. For the last 28 years I have run a coronary care unit and have looked after patients with all sorts of thrombotic problems. For the last five years I have chaired the Appraisal Committee for NICE.

Professor Cousins: I am David Cousins, Head of Safe Medication Practice at the National Patient Safety Agency. My background is hospital pharmacy and academic pharmacy. The National Patient Safety Agency is currently undertaking some work concerning risk assessment on the use of anticoagulant therapy.

Q58 Chairman: Can I begin by putting a question to Dr Boyle, accepting the fact that you are substituting for a colleague. Could you comment a little bit on the concerns we heard expressed in the earlier session, in particular the extent to which venous thromboembolism is more of a problem than MRSA according to our previous group of witnesses. Does the Department view VTE as a

major public health problem and, if so, what steps are being taken to address some of the concerns we heard about earlier on?

Dr Boyle: I think the Department of Health does take this very seriously. It is certainly a contributor to the cardiovascular deaths which we monitor as part of the over-arching PSA target. Certainly the numbers that die from this condition are sufficient for us to take note of this and this is one reason why we have joined in the commissioning process to commission a guideline within the NICE framework—which you will be hearing about—to try to make it clearer and more explicit to the NHS at large as to what action should be taken. I am quite clear that there is insufficient uptake in the areas you have heard about already for patients going through elective procedures; their safety needs to be improved certainly.

Q59 Chairman: Do you concur with that last point that this is actually a more serious problem in terms of hospital deaths than MRSA?

Dr Boyle: It definitely is. I think it is a hidden issue really because MRSA declares itself but these conditions are often very difficult to diagnose. Even when we know that the patient is at high risk and liable to suffer from the condition it is still quite difficult to come to a clear diagnosis. For example, after a hip replacement it is almost normal for the leg to swell, but is that swelling due to a problem in the veins or is it just part of a natural process of an immobile patient after a major operation? Then also pulmonary embolism is often a difficult diagnosis to make. It may be silent; it may be in conjunction with other conditions—a patient may have a chest infection after an operation—and therefore it does not declare itself in a dramatic fashion except in the thankfully relatively rare cases when a patient just drops down dead. As we have

9 December 2004 Dr Roger Boyle, Professor Sir Michael Rawlins, Professor David Barnett
and Professor David Cousins

heard, coroners are not demanding such a thorough investigation of deaths and therefore post mortem evidence does not become apparent.

Q60 Chairman: You are pointing a finger at coroners here but others would say that post Alder Hey doctors themselves are pressing less for post mortems. Why do you say coroners in particular?

Dr Boyle: In the past if a patient died in hospital after a surgical procedure the rules bound you to report it to the coroner's office and then normally a directive would come that a post mortem would be required. I think you are right that doctors are less inclined to push for it and of course that can also be difficult because the relatives of a patient may not wish that to happen. All those factors have to be taken into account. However, I think the real problem at the crux of all of this is that these patients are in a variety of clinical scenarios that require a whole hospital approach to it and they are all segmentalised in terms of their own responsibilities and interests in that individual patient. I think probably to get to the bottom of all of this we are going to need to redesign the way hospitals actually work. For many surgical patients they need physicianary care as well as surgical care and at the moment we do not have the scope or the numbers of physicians able to handle that. In some orthopaedic departments they have formed alliances with all the services' teams so that they get supervision that way but it is normally to sort out the rehabilitation of patients afterwards rather than to be pro-active at the admission stage. I think that is a big step that we would like to see. However, I think what we are crying out for is an English guideline with a NICE kite mark which will then drive the NHS to take this more seriously and that should be the key next step. The process obviously takes time so we will not be with this guideline for another two and a bit years so there are some issues about what we do in the interim until the guideline comes into being.

Q61 Chairman: We heard in the previous session that the procedures in obstetrics are further advanced than in other areas of medicine. Does it strike you that lessons could be learned there? Obviously the confidential inquiry gives clear evidence as to the extent of the difficulties and if we had more direct concrete evidence through post mortems or whatever would that also drive forward changes in practice? Have we learned lessons?

Dr Boyle: Yes, we have. The thing that drives clinical change is data and we need audit in this area. I think that is an issue for the Health Care Commission who is responsible for driving that programme but we can certainly advise them that this is a key area that ought to be taken forward. They are very laborious to set up in a national sense but until you get it at a national level then individual trusts do not take it seriously either and may only revisit it on an audit cycle infrequently.

Q62 Chairman: So you see a role for the Commission? We asked on one or two occasions in the first session about the Commission's role here. You would certainly be pointing to their role in improving practice there.

Dr Boyle: Absolutely. This is an issue which is very much about hospital clinical governance. That is their modus operandi and that is what they should be inspecting organisations on. As we have heard, this is a high risk area with a major impact on mortality and morbidity and should therefore be high up their list of priorities.

Q63 Dr Naysmith: The question that really needs to be answered coming from what Dr Boyle has just said is: guidelines exist in Scotland and guidelines exist for the Royal College of Obstetricians, as we just heard in the previous session; the American College of Chest Physicians have guidelines; why do we not have guidelines in England?

Dr Boyle: The British Thoracic Society has guidelines on treatment which touch on prophylaxis but it is a recognised gap which is why the Department of Health joined in the commission process to ask NICE to fill this gap. I think it probably should have been higher up in the order of programme but it takes a lot of hard work to develop this and you have to prioritise. Clearly, from my point of view, the excellent work they have done in heart failure guidelines and other guidelines around heart disease have been a higher priority because actually the finite number of deaths from those conditions and the morbidity from those conditions has been infinitely greater than that for VTE. We are now in a position where I think we need to move on and include this in the process.

Q64 Dr Naysmith: I am going to come on to ask Sir Michael a question in a minute; I have discussed prioritisation with him on at least a couple of occasions in the past. Do you have any views on this? Why are we only coming to it now?

Sir Michael Rawlins: I am very glad we are doing it with one proviso because I know from practical experience how much of a problem it is, just as a physician in Newcastle. We are moving on now with this guideline on prophylaxis for surgical patients, but I think it is important to state up front that this is surgical patients and does not cover medical patients. I would very much hope we would get a referral soon for medical patients because the issues are somewhat different and I think we need to address them. It would be wrong to try to shoehorn medical patients in with surgical patients because it would make it so massive—as you have already heard, the whole thing is a pretty complicated issue anyway—that it would be some time in the next millennium before we had completed it all. We need a separate guideline on prophylaxis in non-surgical patients.

9 December 2004 Dr Roger Boyle, Professor Sir Michael Rawlins, Professor David Barnett
and Professor David Cousins

Q65 Dr Naysmith: That was going to be my next question, that you are very restricted in the high risk surgical patients and that is what you are being asked to look at. As we heard in the previous session there are medical patients and a whole host of other patients: cancer patients, trauma patients, those in intensive care and those with spinal cord injuries.

Sir Michael Rawlins: Unquestionably we accept that. Quite clearly there are two forms of risk here. You are dealing with the risk of the procedure but there is also the risk of the patient and we need to patch those together. We are looking at the detailed scope—of which I think we have already sent you a draft version, which will get changed as a result of consultation—which does make it clear that we want to look at both elements of risk and take a broader view than the rather limited original referral that came from the Department of Health.

Q66 Dr Naysmith: Why do you think it was so limited?

Sir Michael Rawlins: In a sense we almost encouraged the Department to give us a fairly limited one-liner and then we undertake a detailed scoping exercise ourselves with all the interested parties. To be honest with you, we would rather have it that way than get it in detail from the Department. It seems to us to be better, easier and more satisfactory at the end to have a really large discussion about it with all the players at NICE discussing the scope and then revising it in the light of that.

Q67 Dr Naysmith: This raises something that you and I have talked about before, how do things get pushed up the agenda for NICE? Is it a question of this being something really significant which we have overlooked for some reason or has it been pushed up the agenda because people are lobbying for it?

Sir Michael Rawlins: I think there is a combination of factors. In part it is what seems to be a public health imperative; in part whether there is a need there. I would agree with Roger Boyle that it is a pity this was not sent to us two years ago and we could have come to you in slightly better shape.

Q68 Mrs Calton: I understand what you are saying about surgical and medical needing to be treated differently and we heard evidence earlier that indicated that different conditions need to be treated differently so far as the risk benefit analysis is concerned. We also heard that a perfectly good set of guidelines already exists so why is it going to take such an awful lot of time to go over the ground again, meanwhile patients are dying and ending up with conditions which really they should not get?

Sir Michael Rawlins: I do appreciate that and, of course, in the meantime there are other guidelines available which I hope my colleagues would adopt, but there are a number of limitations to the ones that have been developed. First of all, there is a rather large number of them, in fact; the American College of Chest Physicians is just one. Secondly, none of them take into account cost effectiveness. This starts

becoming quite an issue. You heard from previous witnesses about how some people recommend five weeks thromboprophylaxis after surgery. If we start thinking about the logistics of organising people coming round to your house perhaps, giving you injections for five weeks, where does the balance between benefit and cost lie there? We do not know and that would have to be looked at very, very carefully. The third problem is that actually the American College guidelines do not say anything about the duration itself. They just say “give it” and then presumably you go out of hospital and you do not get it any more. We just do not know; it does not go into that at all. There is nothing in those guidelines about another very important group of patients who might be having low risk procedures but are themselves high risk because they are on, for example, oral contraceptives or hormone replacement therapy. That is a very important and significant issue, particularly nowadays. Finally, the American College guidelines are good as far as they go on surgical prophylaxis; they are actually rather weak on medical prophylaxis and there are all sorts of circumstances like stroke, for example, where you would not wish to go down the route that they recommend. We need our own guidelines to accommodate our own particular circumstances, to accommodate the patterns of medical practice, surgical practice in the UK. Remember, in the United States most people who have a hip replacement are out after 48 hours whereas in the UK they stay much longer; they are a ruthless lot and send you home limping. So there are whole host of reasons why we cannot just adopt them wholesale.

Q69 Mrs Calton: I heard all your reasons. It still sounds to me, from the evidence we had earlier, that this is a relatively cheap set of preventative measures that could be taken which would bring huge benefits to a substantial number of patients. We are not just talking about the odd one, but a substantial number.

Sir Michael Rawlins: Yes, and there is no reason why trusts should not adopt, so far as they go, the American College guidelines if they wish, but I am not going to be prepared to endorse them and the Institute is not prepared to endorse somebody else’s guidelines. It is up to individual trusts if they want to take them up to do so.

Q70 Mrs Calton: You would say then that while NICE goes its way around all the different things that need to be looked at meanwhile the evidence coming from the States in 2001 is that the United States Agency for Health Care Research and Quality ranked 79 patient safety interventions based on the strength of the evidence and the highest ranked out of all 79 safety practices was the appropriate use of prophylaxis to prevent VTE in patients at risk.

Sir Michael Rawlins: I would not disagree with that.
Mrs Calton: And while we are waiting for two, four, five years for the medical cases—possible longer—patients are dying and suffering unnecessary disease.

9 December 2004 Dr Roger Boyle, Professor Sir Michael Rawlins, Professor David Barnett
and Professor David Cousins

Q71 Dr Naysmith: Presumably there is nothing stopping our physicians adopting the American Chest Physicians.

Sir Michael Rawlins: No, if they want to.

Q72 Dr Naysmith: I want to ask Dr Barnett why is it such a restrictive number of risks that NICE has been asked to look at and do you think it should be widened?

Professor Barnett: I think the application of prophylaxis for venous thromboembolism across the whole hospital environment is very patchy and it is particularly true within the medical framework because there are groups of patients who are already being given large numbers of drugs which are going to influence clotting. In the experience I have had over the last 30 years looking after patients who had had myocardial infarction the incidents of venous thrombosis and pulmonary embolism have become very, very small. In fact we now almost never see VTE in patients within the in-hospital phase of myocardial infarction because there are guidelines to manage them and frequently the drugs they are taking already prophylax against these other problems.

Q73 Dr Naysmith: Presumably that is because you are dealing specifically with the circulatory system.

Professor Barnett: That is precisely right. It is equally true to say that the other extreme—for example patients who are rehabilitating from a stroke, elderly patients who are admitted with chronic chest diseases—there is no absolute certainty about the appropriate management of those patients. Therefore it is a catch as catch can basically whether they should be given subcutaneous heparin, whether they should be given aspirin, how they should be managed. The most important change has been early mobilisation and that is also true for surgical practice; the more rapid early mobilisation is a kind of cheap way of getting round treating patients.

Q74 Dr Naysmith: It is cheaper than pumps.

Professor Barnett: Cheaper than pumps and cheaper than drugs of course. That has been a major change. I would also agree that we are looking at the tip of the iceberg because we see the symptomatic patients so there may be a lot who are at significant risk. I would argue very strongly that the biggest area where we have the least evidence and also the least consistency in guidance is in the medical group, particularly those outside the strict groups like myocardial infarction, post stroke and so on.

Q75 Dr Naysmith: Sir Michael is suggesting that he would like the Government to tell him to look at that as well; that is not quite what he said. Are you in favour of that?

Professor Barnett: I am very much in favour of that. I have to say, it is not an easy job. I am not suggesting that the surgical prophylaxis is easy but

I would say it is easier because of the way in which research has been directed specifically to that group of patients and appropriately so.

Q76 Dr Taylor: I think we are all very conscious of the amount of work NICE has to do so I am rather with Patsy here: I would love to see you being able to speed up the one for surgical procedures building on the American College guidelines (which are absolutely excellent so far as I can see) and building on the Scottish guidelines. We have recently been to Australia and looked at their therapeutic guideline series. I do not know what is in there, but it would seem to me that there is plenty on the surgical field already and you could save your efforts for the medical one if you could get the surgical one out very much more quickly using a lot of the background that there is.

Sir Michael Rawlins: Our guidelines programme requires about two years. About half that time is spent on consulting and talking to all the stakeholders; we cannot get out of that year. The second thing is that we do need to take the evidence further; it is not just a matter of listing the systematic review from the American College of Chest Physicians because we do need to have a look at cost effectiveness and we do have to look at some of these other questions too. I think we have to do it properly and get a job done that everyone will have confidence in, but in the meantime—as I was saying—there are guidelines out there that trusts and organisations can adopt and which will do a lot of good.

Q77 Dr Taylor: Do you have advice about how we should be recommending that these existing guidelines get implemented?

Sir Michael Rawlins: I think there is a question of broadly clinical governance and I think there are several issues there. Firstly, of course, chief executives of trusts have a legal responsibility for clinical governance in their institutions like they have corporate governance. The Health Care Commission has a responsibility for clinical governance and it could be specifically asked to look at practices for prophylaxis and DVT and ask trusts what arrangements they have in place, ask trusts what figures they are getting in terms of in-patient mortality and so on. Those would be reasonable things to do. I think those sorts of comments and questions could actually go quite a long way to focus minds on the problem.

Q78 Dr Taylor: Going to Professor Cousins, what recommendations have you made from your organisation to NICE?

Professor Cousins: We have just engaged with them at this time. Just to come in from a slightly different view, we do not necessarily believe that guidelines are the way forward. They are helpful but just knowing is not necessarily doing. We are finding through all our work that we are encountering patient harm because of the failure of the NHS to implement effectively, so often times there are plenty

9 December 2004 Dr Roger Boyle, Professor Sir Michael Rawlins, Professor David Barnett
and Professor David Cousins

of guidelines out there but because of the volume of traffic, the business that everyone is facing, they have difficulties implementing. Actually trusts and the NHS desperately need methodology given to them to implement effectively. For instance, there is a particularly interesting topic in the publication from the American College of Chest Physicians relating to from evidence to application. In that they actually found that having computer reminders—because in those particular cases they had some electronic prescribing—they found that they could impact on the prescribing of anticoagulants appropriately and when they took the computer reminders off the physicians went back to the original poor rates of compliance so that it was not to do with not knowing, it was to do with building into the system trips and safeguards that actually make it easier for you to do what is required. I think in the case of the NHS much more use could be made of the multi-disciplinary team to identify that patients are not getting the prophylaxis that they need. Nurses and pharmacists can make a useful contribution for raising the issues with the medical team why the patients are not receiving their prophylaxis. I think as well as determining what exactly the fine tuning of the guidelines should be, a great deal of attention should be paid to how we actually implement them. The NPSA works closely with the National Programme for IT because we feel that in the designs of the electronic prescribing and the electronic patient record we should be building in these prompts and these safeguards at this time and people will more willingly and more conscientiously follow the appropriate procedures rather than having to remember. I say again, knowing is not doing. We need to build systems into the NHS that make the doing much more reliable and in the patient's best interests.

Q79 Dr Taylor: So if everybody were on electronic prescribing there could be a reminder on that.

Professor Cousins: That could make a useful contribution. We are a few years away from that but there are other methods such as pre-operative assessment and clinics where making decisions about trust-wide implementation involves the four multi-disciplinary team delivering that which I think could be far more reliable than we have at the moment.

Q80 Dr Taylor: Did you imply that this was a job for a ward pharmacist?

Professor Cousins: They could make a useful contribution as could the ward nurses and specialist nurses. I feel we are not giving full value to the team and relying too much on junior doctors. As we are finding, when patients are on oral anticoagulant, unfortunately it is in the delivery step—when you are dosing oral anticoagulants or discharging patients out of hospital—when senior doctors are not present and that is where the delivery falls short of what was initially intended.

Q81 Dr Taylor: That is a very easy recommendation. The ward pharmacist exists; nurses exist.

Professor Barnett: I completely concur with that. The issue about implementation and particularly making sure that the steps are mandated appropriately, I would concur the ward pharmacists are very helpful. I am also concerned it de-skills the doctors from learning those processes as well, but there is a combination effect here. My concern would be much more the translation between hospital care and the requirement for prophylaxis continuing on into primary care because that step is fraught with difficulties. There are a lot of issues about communication with PTCs and with general practitioners and ensuring that there is on-going care and management. Within the hospital environment we are fairly well controlled. There is always someone looking over our shoulder, maybe not effectively but there is always something going on. There is the ward sister, the ward pharmacist, the junior clerk, et cetera but when the patient moves across that barrier there are many steps. We are talking about a group of patients about whom it is now suggested that they continue with prophylaxis for five weeks and getting that in step would also very difficult.

Q82 Chairman: What I am struggling with from the suggestions you are making, picking up the points from the previous session where there are clear differences between clinicians in their view of how you view this whole area, how can you introduce a system of the kind you are talking about and also accept that clinicians will have—rightly—different approaches in different cases?

Professor Cousins: I do not think we should overplay the differences. If you look at the human factors theory there are intentional decisions and unintentional decisions and my impression is that it is as much failure to deliver on what has already been agreed at senior level in committees but actually does not happen on a day to day basis as much as it is pharmacological concerns or clinical concerns. This is not purely one of doing what is best for one's patients; oftentimes it is to do with delivery on the ground. Those decisions which were agreed in 12 months' time when you do the audit—if indeed you ever do the audit—you find that somehow you have not delivered on what you thought you were going to.

Professor Barnett: I would concur with that. Thirty years ago I remember looking after a patient with a pulmonary embolism following a hip replacement and the orthopaedic surgeon—he has long retired so it is irrelevant—saying to me that there is always a bit of clot floating around when he does a hip replacement. I am not suggesting that is an appropriate thing for anybody to say, but things have changed since then and everybody is aware of it. I think variations around a theme are small compared to the acceptance of a requirement for doing prophylaxis properly.

9 December 2004 Dr Roger Boyle, Professor Sir Michael Rawlins, Professor David Barnett
and Professor David Cousins

Q83 Dr Taylor: Again to Professor Cousins, your written evidence dwells quite a lot on the problems with warfarin. We have all seen the horrendous problems with the different tablet sizes.

Professor Cousins: Can I just mention that our concern about that is that some of the thromboprophylaxis regimes that could be recommended could increase the usage of warfarin and, as my colleague was saying, this transfer into the community causes us great concern so we have real concerns about an increase in the use of warfarin; the new indications that atrial fibrillation (which is another form of thromboprophylaxis that we have not discussed here today) caused huge increases in the number of patients on warfarin which made the anticoagulant services find it very difficult to cope with and the idea of additional warfarin patient load on those services would be of major concern. If the thromboprophylaxis five week regime comes into play and there is not an ability for district nurses to come in and give injections to patients and you cannot convince the patients to self-inject themselves, our worry is that will again increase the use of oral anticoagulation with all these problems that you referred to. We would put a note of caution on that, that oral anticoagulants are poorly managed, they are a subject that we are doing a lot of work on at the NPSA and we would not want to see an increase in that load unless safe systems of work could be developed over the next few years.

Q84 Dr Taylor: I think we have all got that message but really the question was, if you are using the low molecular weight heparins or some of the newer things with unpronounceable names the monitoring is going to be much less.

Professor Cousins: I fully endorse that provided the patients can actually receive their therapy and that is the problem. How do you get elderly patients to inject themselves or do you ask the district nurse to come in? Have they got the capacity for doing that? Then is the second choice oral anticoagulation which we would really be concerned about? I totally endorse the idea of low molecular weight heparin being much less risky as long as you can administer the dosage in the community setting.

Dr Taylor: The important point which I think has been well made is that we would not be advocating widespread use of warfarin because of the extra risks.

Q85 Dr Naysmith: We have already heard that many medical and non-surgical patients suffer from venous thrombosis and pulmonary embolism but in fact 70 or 80% of all fatal pulmonary embolism occur in non-surgical patients.

Professor Barnett: That is right.

Q86 Dr Naysmith: Again it brings us back to urging the Department of Health to look at these things as well as the rather small area that NICE is going to focus on.

Dr Boyle: I think we have received that message very clearly.

Professor Barnett: The use of statistics is very helpful and 70 to 80% of, if you like, venous thromboembolism may be in non-surgical cases but the issue is whether or not there is enough evidence to suggest that across the board those are effectively prophylaxed in a certain way or they occur in groups of individuals who are at the end of their lives and this is a natural progression of the disease. I am not suggesting that is an appropriate way to look at it, but we do not know and the epidemiology is such that which of those patients is most appropriate to deal with? We have groups of patients where we know there is a high risk in medical circumstances and I have mentioned a couple of those. The others are not quite so evidence based and are more difficult to look at but not unimportant.

Q87 Dr Taylor: If we come up with recommendations or you come up with recommendations, making sure that they are implemented is something we have already talked about, but do you have any suggestions or ideas? You must have had experiences of NICE recommending things, doing guidelines and then finding they are not being implemented.

Sir Michael Rawlins: Yes, and the best data we have is that there is about a 50% uptake for full implementation. That is not good enough and that is why, as you know, we are making arrangements within NICE to take a much more significant responsibility for implementation although when we were originally set up it was not part of our brief. However, I think there are a number of important factors. The first is, as I said already, that it is incumbent now on chief executives to take overall responsibility for clinical governance. Secondly there is very little doubt that generally speaking people are more prepared to take up guidelines in which they have confidence and the confidence not only comes from the way it is done but also who is doing it. The guidelines on surgical prophylaxis are getting done by the Royal College of Surgeons so the fact that it is surgeons, as it were, behind it really helps implementation which I think is one of the reasons why the obstetricians have done so well because the Royal College of Obstetricians have been behind it. That is an important factor. I think there is also the issue that it is increasingly likely that the courts will look at NICE guidance as an alternative to the Bowlam principle in medical negligence. In other words, adherence to NICE guidance is a reason why negligence would fail. As a consequence to that my advice to doctors has always been that if you decide to depart from NICE guidance you must write it in the medical records at the time you make the decision and not five years later when the writ comes in because it is not very convincing. I think in the fullness of time we will see people writing in patients' notes why they are not given prophylaxis rather than why they are. I think the final thing is that it is quite clear from the Health Commission that they are taking a much more vigorous approach to the implementation of NICE guidance than the old Commission for Health Improvement did. The recent documents that have

9 December 2004 Dr Roger Boyle, Professor Sir Michael Rawlins, Professor David Barnett and Professor David Cousins

come round indicate that the Health Care Commission is taking very seriously as part of its clinical governance the uptake of NICE guidance.

Dr Boyle: To add to that, I think despite its difficulties the National Programme for IT has some real gems within it. One of these is called *Medic to Medic* which is a decision support system that takes you through a guideline, if you like, so that a non-specialist can behave as if a specialist were present. It also triggers audit points so that you can actually go back retrospectively and see if the guideline was adhered to or no. That then makes the whole audit process so much easier. As I mentioned before, it is data that drives these things. We had a similar problem with the use of secondary prevention drugs after heart attacks when we were using very low levels about five years ago and our National Audit Programme has now driven that up so that we are now the best in the world. There is a 96% adherence rate to the use of aspirin after heart attack for example. We need that data to inform the clinicians about their own performance and that is the thing that gets the implementation process ahead of steam and gets it going.

Q88 Dr Naysmith: We had in our written evidence that it is proposed that specialist teams be established in each hospital to promote, educate and oversee risk assessment and the appropriate use of prophylaxis in this condition. What is the Department's view of this proposal?

Dr Boyle: From clinical experience and also from the last five years in implementing the National Service Framework for coronary heart disease, having specialist skills available to run and fund hospital programmes would be a very useful way forward. Sometimes it gets a little confusing because you have specialist nurses who are much better at doing structured care than doctors by and large and they would know very well where to focus their efforts in terms of identifying the risks and just getting a ward mentality right so that the risk assessment that we were talking about earlier becomes much more part of routine practice. So it is awareness raising. You may not necessarily have to have the teams in place in perpetuity but to get the ball rolling I think it is a model that has been shown to work. We have done exactly the same for making sure thrombolysis for acute heart attack is introduced substantially. There are two or three nurses who man the gateway to the hospital and who support the A and E staff, educate them about how to do it and then suddenly you find the whole skill level has risen substantially right across the Service. There is a whole host of examples where resuscitation training officers fulfil a similar role. They train staff and they develop a network of agents around the wards to make sure that the standards of the trust are defined for that process.

Professor Cousins: I think that is a very good idea. I would just raise the issue that we are so concerned about the dosing and the discharge of patients on all anticoagulants from hospitals that it may well be that the same sort of skill set—not only prophylaxis but actually when you are treating patients—having

specialist schemes to look at that whole thrombosis issue might be extremely helpful on more than one account.

Q89 Dr Taylor: Would a partial answer to this be to make sure that in each hospital that is undertaking—and I am only picking out joint replacements because they are so high risk—had one orthopaedic surgeon or one haematologist with a special interest in thrombotic prophylaxis?

Sir Michael Rawlins: I am not sure how easy it would be to implement that. It would be sensible if orthopaedic surgeons as a group in a hospital engaged in a discussion with appropriate colleagues as to what their routine practice should be and put in training and arrangements to make sure that was happening.

Q90 Dr Taylor: So again it comes down to audit.

Professor Cousins: Actually the American Chest Physician paper says that audit is not very effective; it is actually ways of delivering what needs to be done in the first place and I would have thought that the Drugs and Therapeutics Committee with that multi-disciplinary approach, working in collaboration with whatever discipline we are talking about—orthopaedic surgeons or general surgeons or whatever—and having some very detailed methodology as to how they intend to implement the excellent guidelines that are out there, it is that implementation piece that is the key here. Whose responsibility is it on the ground? It needs a senior person but on a day to day basis, minute to minute. Who is it that is going to be doing that?

Professor Barnett: I think a senior champion is a good idea. I do not think you need a specialist in that particular area, but you do need a senior champion and I think the idea of a protocol driven but appropriately constructed team to run and make sure that these processes are put in place.

Q91 Dr Taylor: Who would that senior champion best be? Would it be yet another job for a haematologist?

Professor Barnett: No, I think it could well be within the surgical community, the clinical surgical directorate, a senior member of that team could say they were responsible for ensuring that this process is undertaken, review the audit trail and so on.

Sir Michael Rawlins: Many orthopaedic units have very close relationships with the care of the elderly physicians so one of those, for example, could take on the role.

Q92 Chairman: We understand that each hospital is required to have a transfusion committee. Is that correct?

Professor Cousins: Yes.

Q93 Chairman: Would accept the idea of a thromboprophylaxis committee to ensure its implementation?

Dr Boyle: I think it would be a very sensible suggestion.

9 December 2004 Dr Roger Boyle, Professor Sir Michael Rawlins, Professor David Barnett
and Professor David Cousins

Q94 Chairman: Could I just end the session by asking Dr Boyle a question about the whole issue of informing and counselling patients on risks of VTE. I think you may have heard Linda de Cossart's comments about the problems that she has experienced. There seems to be some confusion over the role of junior doctors in this respect. Can you clarify what the current procedures are? Do you think there are other steps that might be taken to more appropriately inform patients of the risks in this area?

Dr Boyle: I think that consent is a very difficult area to get right, to get the balance right in terms of explaining risks and also the benefits. I think that it is an area that needs to be improved very substantially. I think it needs to be improved in the context of the policy of choice for patients so that they fully understand what they are letting themselves in for. I think it requires closer attention. It is certainly in the interests of the Department of Health to improve those processes. I think it is often left to a junior person straight from medical school to do the business and that is not necessarily the best way of doing it. I think there should be more consultant

involvement in the process because it may be a routine event for the surgeon but it is certainly not a routine event for the patient.

Professor Barnett: There are obviously two sides to this. One extreme is consent, say, in a surgical practice to undertake the surgery, the risks and benefits of it all. If we are talking about treatment for, say, evidence based proven prophylactic therapy such as a venous thromboembolism the question would be: is the consent to say to the patient, if you do not want to accept this therapy then it is okay not to do so, even though we suggest it will save your life. We often have this situation with thrombolysis in patients with myocardial infarction and quite often junior members of staff on my team have given that possibility to patients who are so confused by the possibilities of risk and benefits that they have refused therapy and therefore to their detriment. It is a very complex issue.

Chairman: If there are no further questions can I thank our witnesses for a very useful session. We are most grateful for your cooperation in this inquiry. I hope what we eventually produce may be of some help. Thank you very much.

Written evidence

APPENDIX 1

Memorandum by Dr Ricky Autar (VT 2)

1. SCALE OF THE PROBLEM

Venous Thromboembolism (VTE) poses a serious threat to patients; recovery. It is widely viewed as a complication of hospitalisation (Anderson & Wheeler, 1995). It is a silent killer (Autar, 1996) and accounts for 10% of death in the general hospital population (Sandler & Martin, 1989). As clinical manifestation of Deep Vein Thrombosis (DVT) is notoriously unreliable and asymptomatic, its frequency is underestimated (Verstraete, 1997). Data extrapolation from studies suggests that the annual rate of DVT is approximately 160 per 100,000 of the general population (Anderson et al, 1991; Nordstrom et al, 1992). 2.5 million people annually develop Pulmonary Embolism (PE) and Post Thrombotic Syndrome (PTS); Clagett et al 1992). The scale of the problem is highlighted in Table 1.

Table 1

INCIDENCE OF DVT BY SPECIALITIES

Risk Level by Patient Group

<i>Speciality</i>	<i>DVT % (weighted Mean)</i>
General Surgery	25
Orthopaedic surgery	45–51
Urology	9–32
Gynaecological surgery	14–22
Neurosurgery including Strokes	22–56
Multiple trauma	50
General medicine	17

Data: International Consensus Statement 1997–2002

2. PREVENTION OF VENOUS THROMBOEMBOLISM

DVT is preventable and routine prophylaxis saves between 4,000–8,000 lives annually (Hull et al, 1990). Essentially there are two approaches to VTE prophylaxes: primary and secondary.

Primary prophylaxis is the proactive prevention of DVT. This is achieved by assessment and stratification of risk followed by the initiation of the most effective prophylaxis. Conversely, secondary prophylaxis is reactive to the treatment of DVT, in order to prevent fatality from PE and disability from PTS (Clagett et al, 1992).

Primary prophylaxis is superior to secondary prophylaxis, both in terms of cost and quality of care perspective (Anderson and Spencer, 2003). However, despite compelling evidence that prophylaxes are effective in the prevention of DVT, they are underutilised (Caprini et al, 1991; Anderson & Wheeler, 1995; Autar 2002).

3. JUSTIFICATION FOR DVT RISK ASSESSMENT

In the light of the evidence overwhelmingly supportive of the efficacy of prophylaxes (Wells et al 1994; Kakkar et al, 1997, National and International Consensus groups on VTE (Table 2) are vigorously recommending DVT risk assessment and stratification followed by the appropriate prophylaxis for the calculated individual risk category.

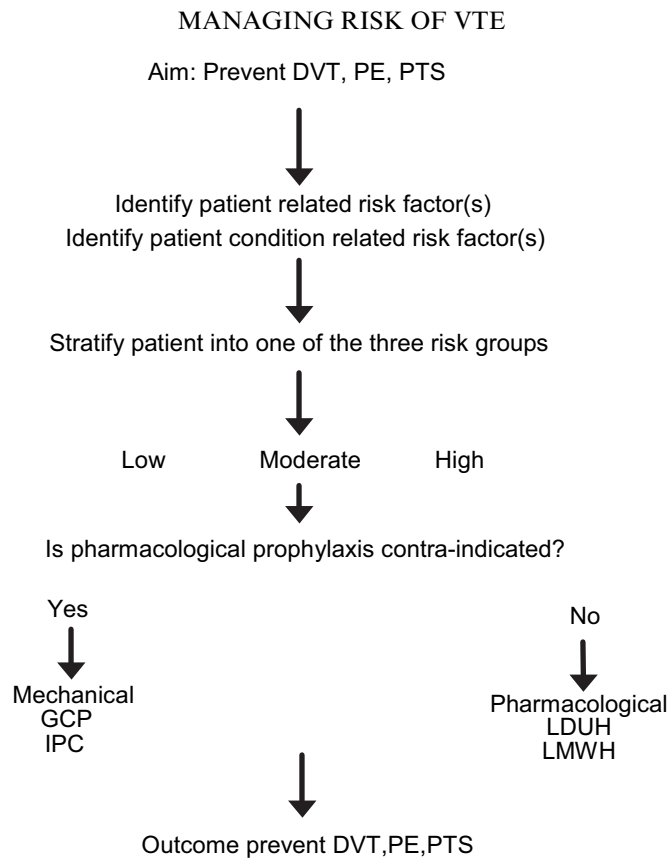
Table 2

VTE CONSENSUS GROUPS

National Institutes of Health (NIH 1986)
 European Consensus Statement (1991)
 Scottish Intercollegiate Guidelines Network (SIGN 1995/2002)
 American College of Chest Physicians (ACCP 1996)
 THRIFT (1992/1998)
 International consensus Statement (1997/2002)

4. MANAGING THE RISK OF VTE

A cascading framework for a systematic and comprehensive strategy for managing the risk of VTE is outlined in flow chart below:



4.1 DVT risk stratification

Clinical risk stratification places patients into a definitive risk category which then facilitates the implementation of the appropriate interventions (THRiFT;1992;1998).DVT risk stratification involves consideration of the patients related risk factor(s) with their condition related risk factor(s), which additively calculate the overall category of risk (Anderson and Wheeler, 1995; Autar, 1998). One risk factor may be present in the low risk category and between 2–4 factors for the moderate risk group. In the high risk patients, over 5 risk factors may be present (Caprini et al, 1991; International Consensus Statement, 1997). The association between DVT and the number of risk factors present is illustrated in Table 3 (Anderson & Wheeler, 1995).

Table 3
ASSOCIATION BETWEEN DVT AND RISK FACTORS

<i>No of risk factors</i>	<i>DVT %</i>
0	11
1	24
2	31
3	50
> = 4	100

Source: Anderson & Wheeler, 1995

5. VENOUS THROMBOPROPHYLAXIS CONTRAINDICATIONS

Following risk assessment and stratification which identify the individual into one of the three categories of risk, prior to implementation of the most appropriate prophylaxes, in the prime interest of patients’ safety, any thromboprophylaxis contraindications are seriously considered. Tables 4 and 5 exhibit the mechanical and pharmacological contraindications.

Table 4**MECHANICAL PROPHYLAXIS CONTRAINDICATIONS**

Venous ulceration
 Gangrenous limb
 A recent graft
 Arteriosclerosis
 Peripheral Vascular Disease
 Doppler pressure index < 0.8
 Cellulites
 Limb deformity
 Oversized thigh circumference

Table 5**PHARMACOLOGICAL PROPHYLAXIS CONTRINDICATIONS**

Haemophilia
 History of haemorrhagic stroke
 Severer liver disease
 Active GI bleed
 Severe hypertension
 Oesophageal varices
 Recent eye surgery
 Non operatively managed hepatic
 and splenic injuries
 Undergoing a thyroidectomy

CONCLUSION AND RECOMMENDATIONS

In the presence of overwhelming evidence supporting the efficacy of venous thromboprophylaxis, it amounts to omission of duty of care and clinical negligence not to provide prophylaxis to the moderate and high risk patients. Venous thromboprophylaxis consensus groups (Table 2) have vigorously recommended that every hospital should develop a formal strategy that addresses the prevention of VTE. For each patient, the degree of risk should be estimated and evidence based guidelines applied. In brief, all hospital patients should be assessed for clinical risk factors and overall risk of thromboembolism, so that the relevant variables can be controlled or eliminated (Autar, 2002).

REFERENCES

- ACCP (1996) Associated College of Chest Physicians Consensus Committee on Pulmonary Embolism. Opinions regarding the diagnosis and management of venous thromboembolic disease. *Chest* 109: 233–237.
- Anderson FA & Wheeler (1995) Venous Thromboembolism. Risk Factors and Prophylaxis. *Clinics in Chest Medicine*. Volume 16, No 2:235–251.
- Anderson FA & Spencer FA (2003) Risk Factors for Venous Thromboembolism. *Circulation*. 107: 1–9–1–1–16.
- Autar R (1996) *Deep Vein Thrombosis: the silent killer*. Quay Books. Mark Allen Publishing. Wiltshire.
- Autar R (1998) Calculating patients' risk of deep vein thrombosis. *British Journal of Nursing*. Vol 7, No 1: 7–12.
- Autar R (2002) *Advancing Clinical practice in the management of Deep vein Thrombosis (DVT). Development, Application and Evaluation of the Autar DVT scale*. PhD thesis. De Montfort University in collaboration with Leicestershire Health NHS Trust.
- Caprini JA, Arcelus, JI Hasty JH et al (1991) Clinical Assessment of Venous Thromboembolic Risk in Surgical Patients. *Seminars in Thrombosis and Hemostasis*. (Supplement 3), Vol 17: 304–312.
- Clagett GP, Anderson FA, Levine MN, Salzman E, Wheeler HB (1992) Prevention of Venous Thromboembolism. *Chest*. Vol 102, No 4: 391S–407S.
- European Consensus Statement (1991) *Prevention of venous thromboembolism*. Med-Orion Publishing, London.
- Hull R, Raskob GE, Gent M et al (1990) Effectiveness of Intermittent Pneumatic Leg Compression for preventing Deep Vein Thrombosis after Total Hip Replacement. *JAMA*. Vol. 263, No 17: 2313–2317.
- International Consensus Statement (1997) *Prevention of Venous Thromboembolism Guidelines according to scientific evidence*. Med-Orion Publishing Company.
- International Consensus Statement (2002) *Prevention of Venous Thromboembolism. Guidelines according to scientific evidence*. Med-Orion Publishing Company.

Kakkar VV, Boeckl, Boneu B et al (1997) Efficacy and safety of low molecular weight heparin and standard unfractionated heparin for prophylaxis of post operative venous thromboembolism. *World Journal of Surgery*. 21: 2–9.

National Institutes of Health (1986) Consensus development conference on the prevention of venous thrombosis and pulmonary embolism. *J Am Med Ass*. 25b: 744–749.

Nordstrom M, Linblad B, Berqvist D, Kjellstrom (1992) A prospective study of the incidence of deep vein thrombosis within a defined urban population. *Journal of Internal Medicine*. 232: 155–160.

Sandler DA, Martin JF (1989) Autopsy proven pulmonary embolism in hospital patients: Are we detecting enough deep vein thrombosis? *Journal of Royal Society of Medicine*. 82: 203–205.

SIGN (1995) Scottish Intercollegiate Guidelines Network. Prophylaxis of venous thromboembolism. A national clinical guideline recommended for use in Scotland.

SIGN (2002) Scottish Intercollegiate Guidelines Network. Prophylaxis of Venous thromboembolism. SIGN Publication. No 62. Edinburgh: Scottish Intercollegiate Guidelines Network.

THRIFT (1992) Risk and Prophylaxis for venous thromboembolism in hospital patients. *British Medical Journal* Vol 305:567–574.

THRIFT (1998) Risk of and Prophylaxis for Venous Thromboembolism in Hospital Patients. *Phlebology*. 13: 87–97.

Verstraete M (1997) Prophylaxis of venous thromboembolism. *British Medical Journal*. Vol 314: 123–125.

Wells P, Lensing AW, Hirsh J (1994) Efficacy of Graduated Compression Stockings: a meta analysis. *Arch Intern Med*. Vol. 154: 62–72.

APPENDIX 2

Memorandum by Mr John Scurr (VT 3)

John Scurr is a Consultant Vascular Surgeon involved in research into deep vein thrombosis and pulmonary embolism, its diagnosis and prevention, since 1974. My appointments have included Senior Lecturer at University of London, Consultant Surgeon, University College Middlesex Hospital, Member of the Scientific Executive Committee World Health Organisation and a participant in four consensus conferences. I was a member of the Thrombosis Research Group, THRIFT 1 and Chairman of THRIFT 2. My research has involved looking at mechanical methods of deep vein thrombosis prophylaxis, elastic compression stockings, intermittent pneumatic compression and the use of low molecular weight Heparin. I was the first person to draw attention to the continued risk of deep vein thrombosis following hospital discharge (BMJ 1989) and I have continued to campaign for risk assessment and the application of appropriate methods of DVT prophylaxis.

INTRODUCTION

In 1972 one third of patients undergoing major general surgical procedures developed a deep vein thrombosis. By 1984, using adequate methods of DVT prophylaxis, the risk of developing a deep vein thrombosis was reduced to < 7%. With surveillance and early treatment, even those patients who developed a DVT, had a very low risk of developing a pulmonary embolism. Despite good scientific evidence < 50% of surgeons routinely assessed their patients and applied adequate prophylaxis in 1984.

In 2004 most hospitals will now have a risk assessment programme and DVT prophylaxis is more common place but by no means routine. In Scotland guide lines exist (SIGN) but similar guidelines do not exist in England and Wales.

Three hundred million pounds per annum is spent on dressings for venous ulcers, over 50% of which arise as a direct consequence of deep vein thrombosis, probably preventable given adequate prophylaxis.

CURRENT PROBLEMS

In the absence of guidelines risk assessment remains variable and prophylactic regimes also vary from hospital to hospital. Whilst most patients now entering hospital do have a risk assessment, little thought is given to the continuing risk of developing deep vein thrombosis following discharge.

There have been many studies showing the efficacy of low molecular weight Heparin and its safety. We still lack large studies to demonstrate the efficacy of mechanical methods of prophylaxis including stockings and intermittent pneumatic compression. Studies showing a reduction in the incidence of DVT are clear. Studies demonstrating a reduction in pulmonary embolism have yet to be completed.

EFFICACY OF ELASTIC COMPRESSION STOCKINGS

We have been aware for some time that a number of anti-embolism stockings have been introduced and are currently in use within the NHS but have no proven efficacy. These stockings will simply attempt to copy a clinically proven brand. Commercial considerations have led to their introduction in some hospitals with disastrous consequences. A recent attempt to introduce a new compression stocking, unproven, into the Middlesex Hospital, resulted in the development of pressure sores and their rapid withdrawal.

RECOMMENDATIONS

It is important to establish proper guidelines that are universally accepted. These guidelines should be applicable to all medical and surgical specialties. The guidelines should accommodate differences in clinical practice. Only clinically tested products should be used and the results of their application carefully monitored.

Further large studies looking at the efficacy of mechanical methods of prophylaxis in preventing pulmonary embolism should also be undertaken. Studies on the cost benefit of DVT prophylaxis are also required.

23 November 2004

APPENDIX 3

Memorandum by Huntleigh Healthcare (VT 5)

Huntleigh Technology PLC is a leading medical, engineering, manufacturing and service group providing patient solutions within the healthcare market.

Huntleigh Healthcare's association with Deep Vein Thrombosis (DVT) prevention originates from the 1970's when we worked closely with a London teaching hospital to develop the foundation for our prophylaxis systems.

INCIDENCE/PREVALENCE OF DVT AND PULMONARY EMBOLISM (PE)

DVT (clinically recognised) and/or PE occurs in 2:1,000 persons each year in the general population¹. In the hospitalised population DVT and PE are much more common due to a combination of acute injury/surgery and immobilisation.

The Scottish Intercollegiate Guidelines Network (SIGN) issued National Clinical Guidelines on prophylaxis of venous thromboembolism in 1995 (due to be updated June 2000). They reported the results of screening studies of hospitalised patients that showed DVT incidence in moderate risk patients of 10-40% and of 40-80% in high-risk patients. The risk of fatal PE in the high-risk group was between 1 and 10%.

DVT and PE incidence in hip and knee replacements is estimated at around 4%, major trauma has a fatal PE rate of about 1% and a venographic DVT prevalence of 58%. Urological surgery has DVT rates of 40-80% for calf vein and 10-20% for thigh vein and 1-5% for fatal PE. Pulmonary embolism is the commonest cause of maternal death during pregnancy and the puerperium².

DVT prevalence from post-mortem studies of a cross-section of patients range from 54-62%, in part due to differences in the dissection techniques used³. The incidence of symptomatic and asymptomatic PE was found to be 6.5% and 11.5% respectively in a group of post-operative patients⁴. A retrospective analysis of autopsy reports found PE as a cause of death in 10% in general hospital patients, 83% of these patients had DVT in the legs at autopsy⁵.

The THRiFT report highlights the need to consider long-term cost effectiveness, and cites the direct cost to primary care and society such as death, recurrent DVT, chronic insufficiency and post-phlebotic syndrome as important factors⁶.

Several studies have investigated the relationship between the acute DVT, long-term venous haemodynamic disturbances and the incidence of post-thrombotic syndrome. The incidence of post-thrombotic syndrome has been reported to be 35-69% at 3 years after DVT and 49-100% at 5-10 years⁷.

Venous ulcers develop in at least 300 per 100,000 population and the proportion due to DVT is approximately 25%. The annual cost of treating venous ulcers has been estimated to be 400 million pounds for the UK⁷.

Appropriate prophylaxis is believed to be able to halve the incidence of DVT (Ref No 5 in the Stephen McAndrew article); 0.9% of hospitalised patients die of a PE (approximately 10 times as many as die of Hospital Acquired Infections).

Highly effective prophylactic measures exist. Selection is dependent on a patient's risk level, contraindications related to an individual's clinical condition and physician choice; in high and very high risk patients prophylactic methods are generally combined to provide additional protection.

Methods of prophylaxis are early mobilisation, graduated compression stockings, pharmaceutical agents such as low molecular weight, Heparin and Intermittent Pneumatic Compression.

The consequences of DVT and PE are such that they can be regarded as public health issues. National policy making needs to address two fundamental issues; firstly the lack of agreed and universally applied protocols of care, even though national, European and international consensus statements exist, and secondly, a joined up approach to funding where the provision of prophylaxis crosses the responsibility of more than one hospital department (for example operating theatres and wards) and from hospital into the community, where extended prophylaxis is required.

Business Director

REFERENCE LIST

1. The Scottish Intercollegiate Guidelines Network (SIGN)(1995). National Clinical Guidelines on prophylaxis of venous thromboembolism. University of Dundee.
2. Turnbull, A Tindall, V, Beard, R et al (1989). Confidential enquiry into maternal deaths in England and Wales 1982–84, London HMSO pp: 28–36.
3. Griffin, J (1996). Deep Vein Thrombosis and Pulmonary Embolism. Office of Health Economics, London.
4. Rodzynek JJ et al (1985). Incidence of asymptomatic pulmonary embolism after surgery. *Thrombosis and Haemostasis*, 54:39.
5. Sandler DA and Martin JF (1989). Autopsy proven pulmonary embolism in hospital patients: Are we detecting enough deep vein thrombosis? *Journal of the Royal Society of Medicine*, 82:203–205.
6. THriFT II (1998). Risk of and prophylaxis for venous thromboembolism in Hospital Patients. *Phlebology* 13: 87–97.
7. International Consensus Statement. Prevention of Venous Thromboembolism, London: Med-Orion Publishing, 1997.

APPENDIX 4

Memorandum by Tyco Healthcare (UK) (VT 7)

1. EXECUTIVE SUMMARY

1.1 Tyco Healthcare is pleased to be able to have an opportunity to submit evidence to this inquiry by the Healthcare Select Committee into the prevention of thromboembolism in the hospitalised patient. Media attention over recent years has focused on the risk associated with travel related thrombosis and this matter has also been raised in the House of Lords. However the actual risk of Deep Vein thrombosis developing in the hospitalised patient is considerably greater. This memorandum will focus on the clinical evidence showing the risk of patients developing venous thromboembolism and more specifically of the development of thrombosis located in the deep veins of the lower limbs commonly known as Deep Vein Thrombosis (abbreviated to DVT). The evidence supporting strategies to prevent DVT in hospitalised patients with a focus on mechanical measures will also be presented drawing on evidence from clinical trials and recommendations from consensus groups and government bodies such as the National Institute for Health NIH (USA).

2. ABOUT TYCO HEALTHCARE

2.1 Tyco Healthcare is a leading manufacturer, distributor and servicer of medical devices worldwide. The company's portfolio includes disposable medical supplies, monitoring equipment, medical instruments and bulk analgesic pharmaceuticals and chemicals.

2.2 The author of this memorandum is the Vascular UK Product Manager, Nicholas Tiller, who is responsible for the marketing activities within the UK associated with the prevention of Deep Vein Thrombosis. This is namely in the form of Anti-Embolic Stockings and Intermittent Pneumatic Compression Devices.

2.3 Position Statement: Tyco Healthcare aims to provide world-class expertise both in technology and clinical support to enable clinicians and healthcare professionals to provide evidence based DVT prophylaxis to all risk categories of patients. Clinical evidence emphasises that to maximise potential DVT reduction all appropriate measures should be incorporated into an integrated package of DVT prophylaxis, including anticoagulation and mechanical measures both IPC and Antiembolic Stockings. Our approach

includes consultation with leading independent clinical professionals. We offer a program of clinical symposia where the evidence platform is reviewed; these symposia are open to all both within the NHS and private hospital groups.

2.4 Please note that Tyco Healthcare would be pleased if requested to supply oral evidence during the session planned for the 9 December, if attendance is required please make contact using the information at the end of this memorandum.

3. SUBMISSION TO THE COMMITTEE

3.1 The severity of the problem: Incidents of DVT in the hospitalised patient

3.1.1 As outlined in the introduction, considerable media attention has focused on the incidence of travel thrombosis and in particular a number of high profile deaths from Pulmonary Embolism (PE) associated with long haul plane travel. It is of note however that the incidence of DVT in hospitalised patients is much greater. This can be confirmed by reviewing the following studies; The Lonflit 4 study showed that asymptomatic DVT in the long-haul flight passenger is in the region 4–6% Belcaro et al⁽¹⁾. In-contrast the International Consensus⁽²⁾ study entitled “Prevention of venous thromboembolism guidelines according to clinical evidence” (2002) concluded that the incidence in hospitalised cases could be as high as 55% if no preventative measures were taken. In the afore mentioned study it was concluded that DVT incidence calculated by summarising published clinical studies, without preventative measures, was as follows:

3.1.2 Stroke patients 51 to 61%; Elective Hip Replacement 48 to 54%; Neurosurgery 17 to 24%. Patients groups undergoing minimal invasive surgical procedures were still shown to be significantly at risk for example patients undergoing transurethral resection of the prostate 5 to 15%⁽²⁾.

3.2 Costs associated with the treatment of Deep Vein thrombosis and associated secondary diseases

3.2.1 The office for Healthcare Economics⁽³⁾ estimated in 1993, that the annual costs in the UK of treating patients that developed post-surgical DVT and PE was in the region of 204.7 to 222.8 million pounds. The International Consensus Statement⁽²⁾ also stated that approximately 25% of patients that have in the past suffered from deep vein thrombosis will later in life develop the debilitating condition of venous leg ulceration. They also estimated that the annual costs of the treating venous leg ulcers in the UK was in the region of 400 million pounds.

3.3 The asymptomatic nature of DVT development in the hospitalised patient

3.3.1 Studies have shown that prophylactic measures are still not practiced with the full proportion of patients that are at risk of DVT development.^(4,5,6,7) A possible reason why DVT preventative measures are under-utilised is the asymptomatic nature of DVT this could cause medical professionals to consider that it is not a problem effecting patients under their care. A hospitalised patient who has developed a DVT will often have no outward signs that show that they have developed the condition. For this reason DVT has sometimes been referred to as the “silent killer” as the first indication may be a symptomatic or fatal pulmonary embolism PE. The clinically silent nature of DVT has been confirmed in several clinical studies. Sandler and Martin⁽⁸⁾ reviewed the autopsy records of patients who had died from PE. They showed that less than 19% of patients showed clinical symptoms of a DVT prior to their death. Patients with non-fatal but symptomatic pulmonary embolism have also been shown to have an underlying asymptomatic DVT. This was shown in a study published in 1999 by Girard⁽⁹⁾ in which the authors used venography to confirm that 68% of patients with a symptomatic PE had an undiagnosed underlying asymptomatic DVT.

3.3.2 Due to the asymptomatic nature of DVT development, preventative strategies have focused on risk assessment in order to assign appropriate interventions to maximise the opportunities to reduce the incidence of DVT according to the patients individual level of risk.

3.4 Risk Assessment strategies for the prevention of DVT

3.4.1 It has been recognised for many years that hospitalised patients are at significant risk of developing this condition, especially if inadequate preventative measures are taken, for example in 1968 Morrell⁽¹⁰⁾ commented “Pulmonary embolism remains the most common preventable death in hospital”.

3.4.2 Measures to reduce the risk of DVT development in the hospitalised patient have focused on the design and implementation of patient focused DVT risk assessment tools. These are designed to assess individual patients of risk of DVT development and implement appropriate levels of preventative measures. Many authors have published risk assessment

tools with recent examples including Autar⁽¹¹⁾ and Caprini⁽¹²⁾. These tools assess factors such as: patient mobility; age; complexity of surgery; and predisposing underlying medical conditions such as cancer and haematological or blood clotting disorders.

- 3.4.3 The theory behind risk stratification for DVT preventions takes into account the underlying pre-disposing factors that can trigger DVT. These factors and their reduction also underpin the prevention strategies that the risk assessment models propose. The following section will therefore briefly review some of these factors as defined by the 19th Century researcher Virchow⁽¹³⁾.

3.5 Trigger Factors for DVT development: Virchow's identified three main trigger factors or mechanism that caused DVT to develop: Venous Stasis; Endothelial Damage and Alterations in the blood clotting mechanism.

- 3.5.1 Venous Stasis: When patients are immobile during surgery or in the immediate post-operative period there is a reduction in the efficiency of blood return from the lower limbs. Primarily this is caused by a reduced muscular activity, specifically the contraction of the calf muscle that in healthy mobile adults has a natural "blood pumping" action that assists with blood return to the heart. This reduction in blood flow or venous return to the heart results in blood becoming stagnant in the lower limb. It should be noted that the three factors strongly interact with each other, venous stasis as a result of reduced blood flow results in the accumulation of trigger factors that would otherwise be dispersed by normal blood flow.
- 3.5.2 Endothelial damage to the vein wall: A result of the immobility discussed above the veins of lower limb dilates this can be especially pronounced in valves that are found within the deep veins and superficial veins of the lower limb. The function of these valves is to prevent backflow of blood towards the distal extremity (feet). Dilatation of these valves as a result of venous stasis if not prevented eventually may lead to tearing of the delicate cell layer (endothelium) lining the veins. This effect and the increased risk of Deep Vein thrombosis that it can cause has been shown in studies by Coleridge⁽¹⁴⁾ and Comerata⁽¹⁵⁾. The damage to vein wall can release factors that activate the clotting cascade as discussed in more detail in the following section.
- 3.5.3 Alterations in the blood clotting mechanism: The third factor identified by Virchow was inherited or acquired factors that increase the tendency for blood to clot. Certain individual patients may have inherited blood-clotting disorders that pre-dispose them to an increased risk of DVT formation. However after surgery there are generalised factors that affect many patients increasing the likelihood of DVT formation. As mentioned above one of these is endothelial damage particularly within the valve pocket that results in the triggering of the clotting cascade due to the exposure of sub-endothelial collagen, which is strongly thrombogenic.
- 3.5.4 Virchow⁽¹³⁾ emphasised in his seminal study in the 19th century that the interaction between the different factors that cause DVT is critical to the formation of deep vein thrombosis and that each factor multiplies the risks caused by the other factors. It is important to address all factors to reduce the risk of DVT development to a minimum.

3.6 Evidence Supporting the Prevention of Deep Vein Thrombosis with a focus on mechanical interventions.

- 3.6.1 Prophylaxis to prevent DVT aims to reduce the effect of the above-mentioned three factors and thereby reducing the likelihood of a patient developing a DVT. The clinical evidence that mechanical measures can reduce the clinical evidence of DVT will be discussed in more detail in section 3.8.
- 3.6.2 Venous Stasis: The use of Antiembolism Stockings has been shown to be significantly reduce the development of venous stasis. Studies have shown increased blood flow velocity when antiembolism stockings are worn as well as faster clearance of blood from the areas such as the valve cusps where venous stasis has the most pronounced effect Lewis⁽¹⁶⁾ Benko⁽¹⁷⁾.
- 3.6.3 In Higher risk Patients intermittent pneumatic compression systems such as the SCD system supplied by Tyco Healthcare have been shown to be effective. The SCD system is designed to increase blood flow velocity in the lower limb. The sequential action of the system is designed to collapse the veins in a distal to proximal manner ie starting at the ankle and progressing upwards. The system is also graduated applying greatest pressure at the ankle. The combination of this technology has been designed to cause a progressive collapse of the

veins from the ankle upwards to ensure that not only is blood velocity is increased, but also to ensure that the pockets of stagnant blood in the vein valve pockets are reduced as far as possible. Evidence that SCD Systems are effective Scurr⁽¹⁸⁾ Janson⁽¹⁹⁾ Kamm⁽²⁰⁾.

- 3.6.4 Endothelial damage: Venous dilation that can cause endothelial damage has also been shown in a number of studies to be prevented by Antiembolism Stockings, Colerdige.⁽¹⁴⁾ It has also been shown that the combination of the use of intermittent pneumatic compression together with Antiembolism Stockings has been shown to be more effective than either measure used alone, Scurr.⁽¹⁸⁾
- 3.6.5 Alterations in the blood clotting mechanism: Anticoagulants are often used to reduce the risk of thrombus formation and to compensate for the reduction in the body's natural fibrinolytic activity. Interestingly recent evidence has shown that intermittent pneumatic compression can also reduce this risk by increasing localised fibrinolysis within the lower limb. Hartman⁽²¹⁾ et al 1982 commented, "In patients who are to have an operation on the hip, therefore, it would theoretically be more beneficial to use thigh-length sleeves, as in the present study, than to use knee-length sleeves. The longer sleeves compress a greater muscle mass and they do not interfere with the surgical incisions for operations on the hip. Fitting the cyclic sequential-compression sleeves to the patient on the evening before the operation would also have the beneficial effect of 'gearing up' the patient's fibrinolytic capacity and thereby reducing the magnitude of the fibrinolytic shutdown." A more recent study by Hoppenstadt⁽²²⁾ has also shown similar results.

3.7 Combined methods of prophylaxis It is emphasised in the above references that combined methods of prophylaxis are required to effectively address the risk of DVT development. A number of studies have shown the effectiveness of such regimes of patient care.

- 3.7.1 It is logical that by preventing DVT the incidence of pulmonary embolism will also be reduced. A recent study by Ramos⁽²³⁾ showed that the addition of IPC to a regime of subcutaneous heparin further reduced the incidence of PE by 62%. Over 2,500 patients were included in this trial and it showed clearly the effectiveness of the SCD Sequel Compression System to reduce the incidence of Pulmonary Embolism. A study by Hooker⁽²⁴⁾ in orthopaedic patients showed that when anticoagulants are not chosen for prophylaxis the SCD Sequel System has been shown to be as effective as anticoagulants used alone.

3.8 Clinical evidence showing the effectiveness of Antiembolism Stockings in a clinical setting.

- 3.8.1 As well as individual clinical studies describing the effectiveness of antiembolic stockings in the prevention of Deep Vein thrombosis there have been a number of meta-analysis that have overviewed the effectiveness of this intervention in the prevention of Deep Vein Thrombosis.
- 3.8.2 A meta-analysis by Wells Lensing et al⁽²⁵⁾ 1994, which included many of the above papers, this showed an overall reduction in DVT incidence of 72.5%. This meta-analysis by Wells Lensing and Hirsch was reviewed by Rumano Dickson of the centre for health economics at York University in 1996 and the following conclusions were drawn. *"This review provides an excellent opportunity to translate statistical analysis into implications for clinical practice. . . this means treating nine patients with graduated compression stockings will prevent the development of one DVT"*
- 3.8.3 A review of the effectiveness of Antiembolism stockings in the prevention of Deep Vein Thrombosis published by the Cochrane Library 2003 authored by Amaragiri.⁽²⁶⁾ This review by the Cochrane Library is one of the most recent overviews or meta-analysis relating to the prevention of DVT using Antiembolism stockings. The authors of this report again included the "core" TED studies that had previously been quoted in the 1984 review by Wells et al. This again emphasises the validity of these studies and the unique quality of this research supporting the efficacy of TED. Antiembolism stockings.

3.9 Recommendation of National and International consensus panels on the prevention of Deep Vein Thrombosis in relation to the use of Antiembolic Stockings.

- 3.9.1 Many National and International panels have published evidence-based guidelines concerning the reduction in the incidence of Deep Vein Thrombosis. These guidelines make recommendations according to levels of clinical evidence; the more substantial the evidence base the stronger the clinical recommendation or practice implication stated within the guideline, the following are recent examples:
- 3.9.2 International Consensus Statement⁽²⁷⁾ (Guidelines According to Clinical Evidence 2002);
- 3.9.3 Prevention of Thromboembolism⁽²⁸⁾ (Sixth Consensus Conference on Antithrombotic Therapy American College of Chest Physicians CHEST2001);
- 3.9.4 Prophylaxis of Venous Thromboembolism A National Clinical Guideline Scottish Intercollegiate Guidelines Network (SIGN Guideline 2002)
- 3.9.5 The authors of the SIGN guideline made the following overall conclusion about the use of Antiembolic Stockings "GECS are effective in prophylaxis of Asymptomatic DVT and

symptomatic PE in surgical patients page 5 SIGN Guidelines” the authors also made the following comment about the length or style of antiembolic stocking that should be used “Above Knee GECS are preferred to below knee stockings for the prophylaxis of DVT”

- 3.9.6 Note in the above study the authors of the SIGN guidelines refer to Antiembolic stockings using the generic term abbreviation “GECS” this is more commonly used to describe therapeutic compression hosiery. In general terms the included studies within the sign guidelines are similar to the selection identified by Wells et al and by the International Consensus Statement and also the Cochrane review.
- 3.9.7 In the above clinical reviews no distinction is made between the manufactures of included studies however many of the included studies used the TED brand from Tyco Healthcare. Attention has however been drawn to this point in a clinical study published in 1995 by Wille-Jorgenson⁽²⁹⁾ “*Two methods of compression prophylaxis have gained wide acceptance-intermittent pneumatic compression (IPC) and graduated compression stockings (TED). ‘TED’ is a Kendall Company trademark, but the term has become generally used for all kinds of compression stockings. This is unfortunate, as it is only the original TED stocking which has been thoroughly investigated in prospective clinical trials.*” It should be noted that Kendall is a trading division of Tyco Healthcare.
- 3.9.8 The above summary is not totally exhaustive list of evidence that Tyco healthcare (UK) is aware of supporting the use of antiembolic stockings and intermittent pneumatic compression for the prevention of DVT in the hospitalised patient. If further clinical information is required the company would be pleased to submit this at a later date.
- 3.10 Conclusions and recommendations:
- 3.10.1 In order to prevent DVT adequately within the context of the hospitalised patient it is important that a combination of interventions are used in order to maximally reduce the incidence of Deep Vein Thrombosis. This should include the use of pharmacological measures and mechanical measures both antiembolic stockings and intermittent pneumatic compression.
- 3.10.2 The use of clinically based risk assessment tools to stratify patients according to their risk levels should become more widespread. Prevention options based on such tools should be firmly evidenced based to ensure that interventions will have the maximum clinical impact.
- 3.10.3 The increased deployment of DVT Nurse Specialists to encourage the dissemination and implementation of Risk assessment based strategies could lead to significantly improved patient care.
- 3.10.4 Cost pressures within the healthcare system could lead to the selection of the lowest cost available mechanical interventions and not necessarily those that are strongly supported by clinical evidence.

REFERENCES

- ¹ Belcaro Lonflit 4.
- ² Int cons statement.
- ³ Office of Healthcare economics
- ⁴ Morris GK. Prevention of venous thromboembolism: A survey of methods used by orthopaedic and general surgeons. *Lancet* 1980; ii: 572–574.
- ⁵ Brenkel IJ et al. Total Hip replacement and antithrombotic prophylaxis. *Br J Hosp Med* 1989; 42:282–284.
- ⁶ Bergqvist D. Prophylaxis against postoperative venous thromboembolism a survey of surveys. *Thromb Haemorrh Disorders* 1990.
- ⁷ Laverick MD et al. Orthopaedic surgeons and thromboprophylaxis. *Br Med J* 1991; 303:549–550.
- ⁸ Sandler DA and Martin et al; Autopsy proven pulmonary embolism in hospital patients: are we detecting enough deep vein thrombosis? *J Ryl Soc. Med* April 1989 Vol 82.
- ⁹ Girard Phillip et al High prevalence of detectable venous thrombosis in patients with acute pulmonary embolism; *Chest* Oct 1999 vol. 116 No 4 pge 903–908.
- ¹⁰ Morrell MT The post-mortem incidence of pulmonary embolism in a hospital population. *Br J Surg.* May 1968 Vol 55 No 5 Pge 347–52.
- ¹¹ Autar R. Calculating patients’ risk of deep vein thrombosis; *Br J Nursing* 1998 Vol. 7 No 1 pge 7–12.
- ¹² Caprini Joseph A et al Effective Risk Stratification of surgical and nonsurgical patients for venous thrombembolic disease. *Semin Hematol* 38 (Suppl 5): 12–19. Copyright 2001 by W.B.. Saunders Company.
- ¹³ Virchow R. Die Cellularpathologie in ihrer begrunung auf physiologische und pathologische gewebelehre. A. Hirschwald, berlin, 1858. cited in Bergqvist D et al 1988 The economics of general surgery thromboembolic prophylaxis.

-
- ¹⁴ Coleridge-Smith PD. Venous Stasis and Vein Lumen Changes During Surgery *Br J Surg* 1990 Vol. 77, 1055–1059.
- ¹⁵ Comerata AJ: Operative venodilation; A previously unsuspected factor in the cause of postoperative deep vein thrombosis: *Surgery* Aug 1989 Vol 106 No 2.
- ¹⁶ Lewis CE Elastic Compression in the Prevention of Venous Stasis: A Critical Reevaluation *The American Journal of Surgery* 1976 Vol. 132, 739–743.
- ¹⁷ Benko T. The physiological effect of graded compression stockings on blood flow in the lower Limb; An assesment with colour duplex doppler ultrasound. *Phebiology* 1999 Vol 14; 17–20.
- ¹⁸ Scurr JH. Regimen for improved effectiveness of intermittent pneumatic compression in deep venous thrombosis prophylaxis *Surgery* Vol. 102, No. 5, 816-820, November 1987
- ¹⁹ Janson HF. The role of venous Blood flow in the prevention of Deep vein Thrombosis 38th Annual meeting, orthopaedic research Society, Feb 17th 1992.
- ²⁰ Kamm J. Bioengineering Studies of Periodic External Compression as Prophylaxis Against Deep Vein Thrombosis Part I: Numerical Studies, Part II: Experimental Studies on a Simulated Leg *Journal of Biomechanical Engineering* Vol. 104, 87–95, May 1982.
- ²¹ Hartman .T. Cyclic Sequential compression of the Lower limb in prevention of Deep Venous Thrombosis *The Journal of Bone and Joint Surgery* Vol. 64-A, No. 7, 1059–1062, September 1982.
- ²² Hoppensteadt DA. The Role of tissue factor pathway inhibitor in the mediation of the antithrombotic actions of heparin and low-molecular-weight heparin. *Blood coagulation and Fibrinolysis* 1995 Pt 1 Vol 6; S57–S64.
- ²³ Ramos R. the efficacy of Pneumatic Compression stockings in the prevention of pulmonary embolism after cardiac surgery *Chest* Jan 1996 Vol 109 Pge 82–85.
- ²⁴ Hooker J. A. Efficacy of prophylaxis against thromboembolism with intermittent pneumatic compression after primary and revision total hip arthroplasty. May 1999 *Jnl Bone & joint Surg* Vol. 81–A No 5 Pge 690–696.
- ²⁵ Wells P.S. et al Application of a Diagnostic Clinical Model for the Management of Hospitalised patients with Suspected Deep-Vein Thrombosis *Thromb Haemost* 1999 Pt 81;486–492.
- ²⁶ Cochrane Library: Amaragiri SV, & Lees TA. Elastic Compression Stockings for Prevention of Deep Vein Thrombosis 2003.
- ²⁷ Nicolaidis Editor AN “Prevention of Venous Thromboebolism” International Consensus Statement Guidelines according to clinical evidence, *Int Angio* 2001 Vol20 No 1–37.
- ²⁸ Jack Hirsch. The Sixth (2000) ACCP Guidelines for Antithrombotic Therapy for Prevention and Treatment of Thrombosis *CHEST* 2001; 119:1S–2S).
- ²⁹ Prophylaxis of Venous Thromboembolism, A National Clinical Guideline. Scottish Intercollegiate guidelines network (SIGN). 2003 www.sign.ac.uk
- ³⁰ Wille-Jorgenson P: Prophylaxis of postoperative thromboembolism with a combination of heparin and graduated compression stockings *Sept 1996 Int. Angio* Vol 15 suppl 1 to No 3 pge 15–20.
-

APPENDIX 5

Memorandum by Sanofi-aventis group (VT 8)

1. INTRODUCTION AND CONTEXT

1.1 The sanofi-aventis group is the world’s 3rd largest pharmaceutical company, ranking number 1 in Europe. Backed by a world-class R&D organisation, sanofi-aventis is developing leading positions in seven major therapeutic areas: cardiovascular disease, thrombosis, oncology, diabetes, central nervous system, internal medicine, vaccines.

1.2 Sanofi-aventis manufacture and market the drug, enoxaparin (Clexane). Enoxaparin is a type of heparin known as “low molecular weight heparin”, which has anti-thrombotic activity because of its capacity to inhibit clotting activity in the body.

1.3 Enoxaparin is licensed throughout the world for both the prevention “thromboprophylaxis” and treatment of thrombosis.

1.4 Enoxaparin is the most widely prescribed anticoagulant of its type and has been used in more than 130 million people in 96 countries, including more than 470,000 patients in the United Kingdom in 2000.

2. VENOUS THROMBOEMBOLISM—THE DISEASE

2.1 Venous thromboembolism (VTE) is a common medical condition caused by the formation of blood clots that partially or completely block a vein.

2.2 The most common form is deep vein thrombosis (DVT), which occurs when blood clots form in the deep veins of the body, usually of the legs. DVT partially or completely blocks veins and disrupts the normal flow of blood back to the heart.

2.3 Parts of the clot may break off and lodge in the arteries that supply the lungs forming a “pulmonary embolus” (PE). A PE is a medical emergency that can cause irreversible damage to the lungs and which, when it occurs, frequently results in death.

2.4 DVT and PE occur frequently in people with certain risk factors (particularly those who are hospitalised). Identification of these risks allows us to put in place preventative mechanisms to stop them occurring. At present too little attention is paid to prevent DVT and PE from occurring in those at risk.

3. VENOUS THROMBOEMBOLISM—A PUBLIC HEALTH PROBLEM

3.1 Robust clinical data confirm that VTE is a major public health problem. New cases of DVT occur at a rate of about 1 per 1,000 of the population¹ and new cases of non-fatal PE presenting to hospital occur at about 0.5 cases per 1,000². In the UK this equates to approx. 59,000 new cases of DVT and 29,500 new cases of non-fatal PE per year.

3.2 45% of patients presenting with PE die within 30 days³.

3.3 In addition to those patients presenting to hospital with PE it has been estimated that PE may account for rates of sudden death at up to 0.40 per 1000 population⁴ equating to over 24,000 deaths per year in the UK.

3.4 As outlined in the Confidential Enquiry into Maternal Deaths 2000-2002 thromboembolism is the single biggest killer of pregnant women.

3.5 Each year more people will suffer VTE-related mortality than composite mortality associated with breast cancer, AIDS and traffic accidents.

3.6 In addition to sudden death, there are other significant long-term complications associated with DVT and PE, which cause substantial illness and suffering.

3.7 Patients who survive a PE may go on to develop chronic pulmonary hypertension, a serious and frequently fatal complication caused by obstruction of the pulmonary blood vessels by blood clots. This complication is more common than had been thought, with almost 4% of PE patients developing the condition within two years with only 30% surviving for five years⁵.

3.8 Approximately 50% of persons who develop a DVT will go on to develop a PE and the initial diagnosis of DVT is often missed⁶.

3.9 Patients who suffer an episode of DVT are at risk of developing long-term complications in the form of post-thrombotic syndrome, a painful, unpleasant and potentially disabling condition often resulting in the development of leg ulcers, which are persistent and difficult to heal. A recent study has shown that over 20% of patients who suffer venous thromboembolism will develop post-thrombotic syndrome within 10 years⁷.

3.10 Recent estimates of the total direct cost burden of VTE management on UK secondary care services are in the region of £340 million per annum. Indirect costs may increase the cost burden to in excess of £500 million.

4. VENOUS THROMBOEMBOLISM—PATIENTS AT RISK

4.1 VTE can occur suddenly and without warning in any individual, but certain risk factors have been clearly identified which place patients at high risk of developing the condition.

4.2 Public awareness of VTE has been increased by media coverage of “traveller’s thrombosis”, but the role of travel in the development of VTE is both equivocal and, if present, small.

4.3 The risk of developing DVT after hip replacement surgery has been estimated to be as high as 50% of patients when thromboprophylaxis is not used. The use of appropriate thromboprophylaxis (such as low molecular weight heparin) can reduce this risk to between 10 and 15% of patients.

4.4 The risk of developing DVT in certain patients immobilised with a medical illness is similarly high, with approx. 40–50% of patients admitted with stroke or myocardial infarction developing detectable venous thrombosis. A recent trial has shown that even “moderate risk” medical patients admitted to hospital have a 15% chance of developing detectable venous thrombosis after 14 days⁸. The use of appropriate thromboprophylaxis (such as low molecular weight heparin) can reduce this risk to 5% of patients.

4.5 The recent Government response to the Select Committee report on “Air travel and health” reported a detailed and accepted list of risk factors for VTE.

-
- Immobilisation for a day or more.
 - Increased clotting tendency.
 - Pregnancy.
 - Recent major surgery/injury, especially to lower limbs (eg hip replacement) or abdomen.
 - Inherited or acquired impairment of blood clotting mechanism.
 - Oestrogen hormone therapy, including oral contraceptives.
 - Former or current cancer.
 - Types of cardiovascular disease or insufficiency (heart failure and respiratory disease).
 - Depletion of body fluids causing increased blood viscosity.
 - Personal or family history of DVT.
 - Increasing age above 40 years.

5. PREVENTING VENOUS THROMBOEMBOLISM—GUIDELINES ARE AVAILABLE

5.1 In many instances venous thromboembolism is a preventable disorder. There are clinical guidelines that offer recommendations for therapies that can prevent VTE occurrence.

5.2 A number of learned, professional bodies have undertaken to assimilate and analyse results from the clinical trials and produce guideline recommendations for the prevention of VTE.

5.3 The guidelines provide specific recommendations as to which groups of hospital patients should receive prophylaxis, how it should be provided and the type of drug or other agent that should be used. Each recommendation is based on an assessment of the level of risk for that patient group and is provided with a grading based on the strength of the clinical evidence that supports it.

6. PREVENTING VENOUS THROMBOEMBOLISM—RECOMMENDED ACTIONS

6.1 Frequently, a lack of awareness of the condition within the medical profession, means that those patients who are at risk of VTE because of clearly defined risk factors fail to receive appropriate treatment. This is particularly the case in those patients at the highest risk of developing VTE: patients in hospital.

6.2 Despite the high risk of VTE in patients undergoing major surgery some 40% or more of patients undergoing major surgery still do not receive an effective form of thromboprophylaxis⁹. Standards of care and risk assessment for VTE prevention need to be set and followed in all forms of major surgery.

6.3 Standards of care also need to be improved in immobilised patients on medical wards. Only 40% of medical at risk patients eligible for preventive treatment (approx 25% of all those in hospital for an acute medical condition) receive an effective thromboprophylactic agent⁹. Standards of care and risk assessment for VTE prevention need to be set and followed in all patients hospitalised for an acute medical illness.

6.4 Effective measures are needed to increase awareness of the risk of VTE and to require action to assess the risk of thrombosis in all hospitalised patients. Hospitals should measure and be assessed on how effectively they prevent VTE occurring in patients under their care.

6.5 The development of a “National Thrombosis Standard” that would require the assessment of all hospital patients for their thrombosis risk would significantly improve patient care; reducing the morbidity, mortality and cost of this disease.

REFERENCES

- ¹ Oger E. Incidence of venous thromboembolism: a community-based study in Western France. EPI-GETBP Study Group. Groupe d'Etude de la Thrombose de Bretagne Occidentale. *Thromb Haemost* 2000; 83(5):657–660.
- ² Nordstrom M, Lindblad B, Bergqvist D, Kjellstrom T. A prospective study of the incidence of deep-vein thrombosis within a defined urban population. *J Intern Med* 1992; 232(2):155–160.
- ³ Heit J. *Seminars in Thrombosis and Haemostasis*. Vol 28, Supplement 2. 2002.
- ⁴ Lindblad B, Sternby NH and Bergqvist D: Incidence of venous thromboembolism verified by necropsy over 30 years. *BMJ*, 1991; 302: 709–711.
- ⁵ Pengo V, Lensing AW, Prins MH et al. for the Thromboembolic Pulmonary Hypertension Study Group. Incidence of Chronic Thromboembolic Pulmonary Hypertension after Pulmonary Embolism. *N Engl J Med* 2004;350:2257–2264.
- ⁶ White RH. The epidemiology of venous thromboembolism. *Circulation* 2003;107(23) S:14–18.
- ⁷ Heit J. Venous thromboembolism epidemiology: implications for prevention and management. *Semin Thromb Hemost* 2002;28(2):3–13.
- ⁸ Samama MM et al. *N Eng J Med* 1999;341:793–800.
- ⁹ O'Shuaghnessy D. VERITY Venous Thromboembolism Registry Second Annual Report 2004. ISBN 1-903968-08-9.

APPENDIX 6

Memorandum by Mr Alexander Cohen (VT9)

INTRODUCTION

Venous thromboembolism (VTE) consists of two related conditions: deep vein thrombosis (DVT) and pulmonary embolism (PE). In general, venous thrombosis is defined as a pathologic event in which a blood clot partially or totally occludes a vein. DVT usually occurs in the deep veins of the calf muscles and, less commonly, in the proximal (more central) deep veins of the leg and upper extremities.

VTE is a potentially lethal disease with death most often occurring as a result of PE. Death can occur when the venous thrombi break off and form emboli, which pass to and obstruct the arteries of the lungs. Diagnosis of PE often occurs too late in the disease course to provide effective treatment. Most clinical studies report the incidence of DVT to be approximately twice that of PE¹. VTE is a major public health problem and is both prevalent and costly². Over half of all VTE is associated with recent hospitalisation with medical and surgical conditions having similar attributable risk (about one quarter each)².

Management of VTE comprises both prophylaxis and treatment of DVT and PE, plus management of the long-term sequelae of VTE, including post-thrombotic syndrome (PTS). Until recently, the majority of care was given in a secondary (hospital) setting, but long term secondary prevention is also managed by primary care physicians.

ESTIMATING THE BURDEN AND COSTS

Two approaches can be taken and these are described below.

The available data from population based epidemiology studies can be used to calculate the burden and costing this problem. However, this incidence-based approach may not assess much of the burden from hospital costs in high risk groups who require preventive therapy, as it is based on reported events. VTE is notoriously inaccurately reported with rates as low as 30% being found in many studies. It also does not assess asymptomatic events which can have both short term and long term sequelae and costs

It is also possible to do similar calculations using a “bottom up” approach. The “bottom up” approach examines hospital and community data, as well as assessing at risk populations and then annualises the current and future resource use for estimating the burden and cost. However the “bottom up” approach cannot estimate the burden of sudden death or undiagnosed mortality from this condition (in the absence of data from prospective cohorts or country specific autopsy data).

We have recently undertaken a review of the burden and cost of venous thromboembolism using these two approaches to check the validity of each other, with the known limitation that they will measure different things. The results are presented below.

 INCIDENCE-BASED APPROACH

The most robust European data come from the only two population based epidemiology studies from Nordstrom³ and Oger⁴ which have shown new (incident) DVT rates as 117 per 100,000 and 87 per 100,000 respectively (pooled estimate is 99 per 100,000 population). New (incident) PE rate was only reported in Oger⁴ and was 46 per 100,000. Lindblad and coworkers have shown in a population based autopsy study that autopsy diagnosed fatal PE occurs in around 40 per 100,000 population⁵. The original estimate of 40 fatal PEs per 100,000 (93 in 230,838 population) in the Linblad paper was based on an autopsy rate of 76.9%. Assuming 100% autopsy rate, fatal PEs rate was re-calculated as 52 per 100,000 population. Heit et al⁶) reported that 10.7% of the new PE cases would die within 14 days of hospitalisation, therefore these patients would already be counted as new non-fatal PEs. In order to avoid double counting, 10.7% of 52 per 100,000 were excluded, which gave the final estimate of sudden fatal PEs as 47 per 100,000 population.

Therefore new cases of VTE has an estimated incidence of 145 per 100,000 diagnosed premortem and 47 per 100,000 diagnosed at post mortem in the developed world and hence is an important cause of morbidity and mortality^{3,4,5}. One study reports that 11% of patients do not survive to one hour post PE event⁷. Initial treatment of DVT and PE is costly and patients who have DVT often develop serious long-term complications,⁸ which inevitably add to the cost burden on the Health Services^{9,10}.

“BOTTOM UP” APPROACH:

The hospital data model estimates approximately 49,000 expected annual cases of hospital acquired DVT and over 11,000 cases of Pulmonary Embolism. The community model estimates over 55,000 expected annual cases of community acquired DVT and over 20,000 cases of Pulmonary Embolism.

The cost of illness (COI) model comprises two components, a community VTE algorithm and a hospital induced VTE algorithm. The hospital models annual costs for VTE management in the UK are estimated to be around £280 million. The community model costs are estimated at £360 million.

The total cost burden (direct and indirect costs) to the UK of management of VTE is estimated at approximately £640 million. Approximately 60% of this total is attributable to community rather than hospital based incidence. Inpatient treatment costs account for almost 50% of the total cost burden and approximately 20% of costs are attributable to the chronic care costs of PTS.

SUMMARY OF THE RESULTS

INCIDENCE-BASED APPROACH

	<i>DVT</i>	<i>PE</i>	<i>Total VTE</i>	<i>Cost (£million)</i>
UK Population	59,000	27,000 diagnosed 28,000 sudden death	114,000	340

BOTTOM UP APPROACH

	<i>DVT</i>	<i>PE</i>	<i>Total VTE</i>	<i>Cost (£million)</i>
Community	55,000	20,000	75,000	360
Hospital	49,000	11,000	60,000	280
Total UK Population	104,000	31,000	135,000	640

SUMMARY

Whichever approach is taken it is clear that VTE is a major burden and cost to the UK and the NHS. The variation in figures reflects that the different approaches measure different things.

VTE is a condition that is associated with medical and surgical settings and occurs in the community and hospitals. Most people are aware of travel related VTE, but the other associations, in particular hospitalisation are more common and require attention.

The utilisation of appropriate and effective prevention (thromboprophylaxis) results in a reduction in the burden of 60–80% that would lead to major cost savings and, more importantly, a reduction in morbidity and mortality¹¹⁻¹⁴.

REFERENCES

- ¹ White RH. The epidemiology of venous thromboembolism. *Circulation* 2003; 107(23 Suppl 1):I4-I8.
- ² Heit JA. Venous thromboembolism epidemiology: implications for prevention and management. *Semin Thromb Hemost* 2002; 28 Suppl 2:3-13.
- ³ Nordstrom M, Lindblad B, Bergqvist D, Kjellstrom T. A prospective study of the incidence of deep-vein thrombosis within a defined urban population. *J Intern Med* 1992; 232(2):155-160.
- ⁴ Oger E. Incidence of venous thromboembolism: a community-based study in Western France. EPI-GETBP Study Group. Groupe d'Etude de la Thrombose de Bretagne Occidentale. *Thromb Haemost* 2000; 83(5):657-660.
- ⁵ Lindblad B, Sternby NH and Bergqvist D: Incidence of venous thromboembolism verified by necropsy over 30 years. *BMJ*, 1991; 302: 709-711.
- ⁶ Heit JA, Silverstein MD, Mohr DN, Petterson TM, Lohse CM, O'Fallon WM et al. The epidemiology of venous thromboembolism in the community. *Thromb Haemost* 2001; 86(1):452-463.
- ⁷ Kearon C. Natural history of venous thromboembolism. *Circulation* 2003; 107(23 Suppl 1):I22-I30.
- ⁸ Heit JA. Risk factors for venous thromboembolism. *Clin Chest Med* 2003; 24(1):1-12.
- ⁹ Bergqvist D, Jendteg S, Johansen L, Persson U, Odegaard K. Cost of Long-Term Complications of Deep Venous Thrombosis of the Lower Extremities: An Analysis of a Defined Patient Population in Sweden. *Annals of Internal Medicine* 1997; 126(6):454-457.
- ¹⁰ Cohen A, Botteman M, Stephens J, Ewing M, Collier P, Pashos C et al. Cost effectiveness of two anticoagulants for the prophylaxis of DVT and subsequent long-term complications (PTS and recurrent VTE) in total hip replacement surgery in the United Kingdom. Poster Presentation. XVIIIth Congress of the International Society on Thrombosis and Haemostasis, Paris, France. *Thromb Haemost* 2001; suppl—CD-ROM.
- ¹¹ Geerts W et al Prevention of venous thromboembolism. Seventh ACCP Recommendations. *Chest* 2004; 126:338S-400S
- ¹² Samama MM, Cohen AT, Darmon J-Y, et al. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. *N Engl J Med* 1999; 341: 793-800.
- ¹³ Cohen, AT, Davidson BL, Gallus AS, Lassen MR, Tomkowski W, Turpie AGG, Cariou, Egberts JFM, Lensing AWA. Fondaparinux for the Prevention of VTE in Acutely Ill Medical Patients. *Blood* 2003;102: Abstract number 42.
- ¹⁴ Cohen AT, Edmondson RA, Phillips MJ, Ward VP, Kakkar VV. The changing pattern of venous thromboembolic disease. *Haemostasis* 1996; 26: 65-71

APPENDIX 7

Memorandum by Dr S Kakkos, and Mr G Geroulakos (VT10)

INTRODUCTION

In the 21st century, venous thromboembolism still accounts for 10% of deaths in hospital patients (autopsy-proven pulmonary embolism).

Professor Hull has stated that pulmonary embolism is the most common preventable cause of postoperative death.

Goldhaber recently quoted that “a surprisingly high number of hospitalised patients develop venous thrombosis because of failed (rather than omitted) prophylaxis”,¹ and that most deaths from pulmonary embolism (PE) among patients hospitalised for other conditions occurred in the setting of failed prophylaxis rather than omitted prophylaxis”.²

There is no doubt that hospitalised patients are a particularly high risk group,³ because of risk factor aggregation, like age, malignancy, major surgery, immobility, trauma etc.

Deep vein thrombosis (DVT) often causes an internal scarring in the veins destroying the valves, which prevent back flow. The destruction of the venous valves is often followed by swelling, pain and occasionally leg ulceration a condition known with the name post-phlebotic syndrome.

Venous ulcers develop in at least 300 per 100,000 population and the proportion due to DVT is approximately 25%.^{4,5}

It has been estimated that the management of venous ulcers in the UK costs £100-300 million every year, nursing time accounting for most of this cost.^{6,7}

Evidence supporting prophylaxis for venous thromboembolism in hospitalised patients

There is now evidence that combined methods increase efficacy and reduce death and morbidity rates without increasing bleeding risk. This evidence is shown below:

- In paraplegic patients, the combination of heparin, elastic stockings and pneumatic compression reduced the incidence of DVT from 35% to 5% ($p=0.04$).⁸
- In patients with stroke combined heparin and pneumatic compression reduced the incidence of DVT by 40 times, from 9.2% to 0.2%.⁹
- In general surgery patients, combined pneumatic compression and pharmacological prophylaxis reduced the incidence of DVT from 26.7% to 1.5%.¹⁰
- Combined modalities (heparin plus IPC) reduced the incidence of symptomatic PE after cardiac surgery (from 4% to 1.7%) or oesophagectomy (from 3.2% to 0.7%), compared to heparin alone.^{11,12}
- More recently, the combination of LMWH and IPC, practically eradicated DVT after total hip and knee replacement.¹³

Consensus statements for the prevention of postoperative thromboembolism

To address the problem of venous thromboembolism, three consensus statements have been published.¹⁴⁻¹⁶ These documents have addressed specific issues on thromboembolism and provided guidelines of the appropriate method(s) that should be used according to the risk for each patient individually.

There is a general agreement that a combination of prophylactic modalities is much more effective than each of modalities used on their own and should be used in high risk patients.

Audits on prevention of thromboembolism from national and international reports

An audit on the implementation of DVT prophylaxis in general surgical patients in a teaching Hospital in London. Overall, prophylaxis was correctly prescribed in 36 (72%) patients and adequately implemented in 30 (60%) patients. 15 patients had no prescribed or implemented prophylaxis. In only 5 of them this was justified.¹⁷

In a recent audit in a teaching Hospital in Barcelona appropriate adherence to all guideline recommendations was observed in 42% of patients. Appropriate prophylaxis was higher in critical care and surgical wards than medical wards.¹⁸

In an audit in 130 inpatient admissions over a 4-week period in South Australia the decisions regarding DVT prophylaxis were inappropriate in 32% of cases.¹⁹

Conclusions

Thromboprophylaxis is generally used in hospital patients but adherence to guidelines is variable. Continuing medical education, dissemination of guidelines and regular clinical audit are necessary to improve prophylaxis.

PS. The above views are personal and do not necessarily reflect the views of the institutions to which the authors are affiliated

REFERENCES

- ¹ Goldhaber SZ. Prophylaxis of Venous Thrombosis. *Curr Treat Options Cardiovasc Med* 2001;3:225-235.
- ² Goldhaber SZ, Dunn K, MacDougall RC. New onset of venous thromboembolism among hospitalized patients at Brigham and Women's Hospital is caused more often by prophylaxis failure than by withholding treatment. *Chest* 2000;118:1680-4.
- ³ Kakkar VV, Howe CT, Nicolaidis AN, Renney JT, Clarke MB. Deep vein thrombosis of the leg. Is there a "high risk" group? *Am J Surg* 1970;120:527-30.
- ⁴ Callam M. Prevalence of chronic leg ulceration and severe chronic venous disease in Western countries. *Phlebology* 1992;7 Suppl 1:6-12s
- ⁵ Hume M. Presidential address; A venous renaissance? *J Vasc Surg* 1992;15:947-51
- ⁶ Laing W, *Chronic Venous Diseases of the leg*. Office of Health Economics. London 1992
- ⁷ Bosanquet N. Costs of venous ulcers: from maintenance therapy to investment programmes. *Phlebology* 1992;1(suppl 1):44-46.
- ⁸ Merli GJ, Herbison GJ, Ditunno JF, Weitz HH, HENZES JH, Park CH, Jaweed MM. Deep vein thrombosis: prophylaxis in acute spinal cord injured patients. *Arch Phys Med Rehabil* 1988;69:661-4.
- ⁹ Kamran SI, Downey D, Ruff RL. Pneumatic sequential compression reduces the risk of deep vein

- thrombosis in stroke patients. *Neurology* 1998;50:1683-8.
- ¹⁰ Borow M, Goldson HJ. Prevention of postoperative deep venous thrombosis and pulmonary emboli with combined modalities. *Am Surg* 1983;49:599-605.
 - ¹¹ Ramos R, Salem BI, De Pawlikowski MP, Coordes C, Eisenberg S, Leidenfrost R. The efficacy of pneumatic compression stockings in the prevention of pulmonary embolism after cardiac surgery. *Chest* 1996;109:82—85.
 - ¹² Tsutsumi K, Udagawa H, Kajiyama Y, Kinoshita Y, Ueno M, Nakamura T, Tsurumaru M, Akiyama H. Pulmonary thromboembolism after surgery for esophageal cancer: its features and prophylaxis. *Surg Today* 2000;30:416-20.
 - ¹³ Silbersack Y, Taute BM, Hein W, Podhaisky H. Prevention of deep-vein thrombosis after total hip and knee replacement. Low-molecular-weight heparin in combination with intermittent pneumatic compression. *J Bone Joint Surg Br* 2004;86:809-12.
 - ¹⁴ Nicolaidis AN, Breddin HK, Fareed J, Goldhaber S, Haas S, Hull R, Kalodiki E, Myers K, Samama M, Sasahara A. Prevention of venous thromboembolism. International Consensus Statement. Guidelines compiled in accordance with the scientific evidence. *Int Angiol* 2001;20:1-37.
 - ¹⁵ Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwell CW, Ray JG. Prevention of Venous Thromboembolism: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004;126(3 Suppl):338S-400S.
 - ¹⁶ Scottish Intercollegiate Guidelines Network. Prophylaxis of Venous Thromboembolism. Publication No. 62. October 2002. <http://www.sign.ac.uk/guidelines/fulltext/62/index.html>. Accessed 25/11/2004.
 - ¹⁷ Agu O, Handa A, Hamilton G, Baker DM. Deep vein thrombosis prophylaxis: Audit of practice in general surgical patients in a teaching hospital. *Phlebology* 2000;15:71-74.
 - ¹⁸ Vallano A, Arnau JM, Miralda GP, Perez-Bartoli J. Use of venous thromboprophylaxis and adherence to guidelines recommendations: a cross sectional study. *Thromb J* 2004;2(1):3
 - ¹⁹ Lerhinan ER, Alderman CP. Venous thromboprophylaxis in a South Australian teaching hospital. *Ann Pharmacother* 2003;37:1398-1402.
-

ISBN 0-215-02252-1



9 780215 022523