PFAT and ISTF have worked out a program that we hope will increase the awareness of thrombosis internists and surgeons as the major complication and cause of mortality and morbidity in medical diseases and surgical interventions. To understand the predisposing and exposing risk factors, the underlying mechanisms and epidemiology is crucial to understand how to minimize this potential fatal complication. This will be highlighted in the first international PFAT / ISTF joint symposium on this topic in Poland. The arrangement of this symposium has been possible through a non-restricted grant by Pfizer.
Welcome to Warsaw, welcome to Poland!

Dear colleagues and guests!

On behalf of Polish Foundation Against Thrombosis it’s my great pleasure welcome all participants and members of faculty to Warsaw on First Warsaw Symposium on Thromboembolism, supported by unrestricted grant of Pfizer. Deep venous thrombosis and pulmonary embolism remain major health problems with potential very serious outcomes. Acute pulmonary embolism may be fatal and is still unrecognized and untreated in many patients. Although venous thromboembolism is potentially preventable, effective prophylaxis is still difficult to achieve.

I hope, First Warsaw Symposium on Thromboembolism will be important scientific opportunity for Polish clinicians to update themselves on the latest developments in management, treatment and prophylaxis of venous thromboembolism, resulting in improvement of everyday clinical practice.

Prepared by members of faculty, who are the leading world-wide recognized experts on venous thromboembolism, interesting two-day scientific programme includes plenary sessions as well as workshops, which provides delegates with the latest scientific achievements regarded venous thromboembolism.

I hope Polish Foundation Against Thrombosis will be in a position to organize in the next future successive meetings – second, third etc. - regarded rapidly developed proceedings in thromboembolism.

I trust you take home not only good impressions regarded scientific programme, plenary sessions and interesting discussions but also good vibrations connected with exciting days spent in Warsaw.

Witold Z. Tomkowski
President of Polish Foundation Against Thrombosis
Professor of Medicine, MD, PhD, FCCP
FRIDAY 6th June, 2008

Plenary session I Medical issues:

9.00 - 10.00  - Welcome coffee.

Chairmen: - M. Prins, - W. Tomkowski, - M. Wojtukiewicz

10.00 - 10.15 - Welcome. - W. Tomkowski (PFAT)

10.15 - 10.45 - Epidemiology of venous and arterial thrombosis. - K. Zawilska

10.45 - 11.15 - VTE prophylaxis in medical patients. - W. Tomkowski

11.15 - 11.45 - Management and treatment of VTE in 2008:
including critically ill patients. - B. Davidson

11.45 - 12.15 - Cancer, thrombosis and influence on life quality and expectancy.
- M. Prins

12.15 - 12.45 - Real life and guidelines in the lights of RIETE registry. - M. Monreal

12.45 - 12.55 - Closing remarks. - W. Tomkowski

13.00 - 14.15 - Lunch.

Plenary session II (A and B) Surgical issues:

II A Chairmen:
- O. E. Dahl, A. Górecki, W. Marczyński, D. Chmielewski

14.30 - 15.00 - Thrombotic events and its prevention in orthopedic surgery.
- O. E. Dahl

15.00 - 15.30 - Thromboprophylaxis in general and bariatric surgery. - J. Arcelus

15.30 - 16.00 - Unmet issues in thromboprophylaxis. - D. Bergqvist

16.00 - 16.10 - Closing Remarks. - O. E. Dahl

16.10 - 16.30 - Coffee break.

II B Chairmen: - B. Brenner, A. Jawień

16.30 - 17.00 - Prophylaxis of VTE in pregnancy and delivery - B. Brenner

17.00 - 17.30 - Long-term vascular sequela after surgery. Epidemiology, pathopsychology, prevention and treatment. - J. A. Caprini

17.30 - Closing remarks. - W. Tomkowski

20.00 - 23.00 - Dinner.
SATURDAY 7th June, 2008

10.30 - 12.15
- Meet the expert session (Polish/English session):
  - Workshop I. Post-Thrombotic Syndrome and other vascular complications.
    - J. A. Caprini, J. A. Arcelus, A. Jawień, P. Chęciński
  - Workshop II. Pregnancy, delivery and thrombin associated complications.
    - B. Brenner, R. Dębski, J. Burakowski
  - Workshop III. Challenges in orthopedic surgery.
    - O. E. Dahl, A. Górecki, D. Chmielewski, W. Marczyński
  - Workshop IV. Management and treatment of VTE in 2008. - B. L. Davidson,
    W. Tomkowski, P. Kuca

12.15 - 13.30
- Lunch.

Plenary session III:

Chairmen: - A. G. G. Turpie, A. W. A. Lensing

13.30 - 14.00
- Summarising workshops. - [J. A. Caprini (7'), O. E. Dahl (7'),
  B. Brenner (7'), B. L. Davidson (7')]}

14.00 - 14.30
- Challenges in secondary prophylaxis - use of LMWH
  in long-term treatment and bridging therapy. - A. G. G. Turpie

14.30 - 15.00
- Chronic Thromboembolic Pulmonary Hypertension:
  management and treatment. - A. W. A. Lensing

15.00 - 15.20
- Closing remarks. - O. E. Dahl (ISTF) and W. Tomkowski (PFAT)
Faculty
Witold Z. Tomkowski

President of Polish Foundation Against Thrombosis, Chairman of Scientific Council and Head of Cardio-Pulmonary Intensive Care. Division at the National Tuberculosis and Lung Diseases Research Institute, Warsaw, Poland, Chairman of Anti-thrombotic Treatment Centre, Warsaw, Poland

Witold Z. Tomkowski is Professor of Medicine, specializing in cardiology, internal and vascular medicine. He is the Chairman of Scientific Council and Head of Cardio-Pulmonary Intensive Care Division at the National Tuberculosis and Lung Diseases Research Institute. He is also founder and President of Polish Foundation Against Thrombosis.

In 1980 Professor Tomkowski earned his MD at the Medical University in Warsaw. After graduating, he completed his research fellowship in cardiology, internal and vascular medicine. Professor Tomkowski has authored and co-authored more than 200 scientific articles, mainly in Polish and international scientific literature, concerning pericardial diseases and venous thromboembolism. He was a reviewer for the CHEST, CMAJ, AJC.

Professor Tomkowski has also maintained a vascular stream of clinical investigations, being involved as a member of steering committees in ARTEMIS trial dedicated to thromboprophylaxis in medical patients and AMADEUS clinical trial, which evaluated the long-acting anticoagulant idraparinux for prevention of stroke in patients with atrial fibrillation and is serving as a member of Study Management and Coordinating Committee in EINSTEIN II+III and BOTTICELLI trials, which evaluated rivaroxaban and apixaban in patients with venous thromboembolism. Professor Tomkowski is also, a pioneer in intrapericardial administration of different chemotherapeutic agents for management and treatment of malignant pericardial effusion and co-author of European Cardiology Society Guidelines on Management and Treatment of Pericardial Diseases.
Krystyna Zawilska received medical doctor's diploma in 1960 in K. Marcinkowski Medical Academy in Poznań. Since 1962, she has worked in the Hematology and Proliferative Hematopoietic Diseases Clinic of Poznań University of Medical Sciences. She obtained a PhD in 1967. Between 1972 and 1973, she had been in the Institute of Hematology in Paris, and between 1980 and 1981, in King's College in London.

She obtained a senior doctor's lecturer's title in 1977, an associate professor of medical sciences title in 1989 and became professor of medical sciences in 1996. She is a 2nd degree specialist in internal diseases, hematology and angiology.

Since 1995, she had been running the Hemostasis Laboratory of the Hematology Clinic; simultaneously, since 1997 she has acted as Head of the Hematology and Internal Diseases Department of the J. Struś Hospital in Poznań.
Her main scientific interests are blood coagulation disorders, particularly arterial thrombosis and venous thromboembolism. Since 2000, the Hemostasis Laboratory has been included in ECAT (European Concerted Action on Thrombosis) and has become one of the leading centers in the country, particularly in the field hemorrhagic diathesis diagnostics and thrombophilia.
Prof. Zawilska's scientific activity resulted in over 270 publications in Polish and foreign journals. She is also an author and co-author of 32 chapters of textbooks and monographs.
Prof. Zawilska is a member of the Thrombus and Hemostasis Committee at the Clinical Pathophysiology Association of PAN; member of the Board of Directors and President of the Hemostasis Group at the Polish Association of Hematologists and Transfusioists; a member of International Society on Thrombosis and Hemostasis, American Society of Hematology, European Hematology Association and International Union of Angiology. She actively participates in didactic activities for medical and medical analysis students as well as in doctors’ postgraduate training where she acts as a specialization director in the field of internal diseases and hematology.

Since 2002 she has been a regional hematology consultant in the Lubuskie province and between 2001 and 2005 she acted as regional hematology consultant also in the Wielkopolskie province.
Dr Bruce Davidson, board certified in Pulmonary and re-certified in Critical Care medicine, was educated at Haverford College and Temple University Medical School, received his training in internal medicine at the University of Texas Southwestern Medical Center in Dallas, in pulmonary medicine at the University of Pennsylvania, and in public health (epidemiology) at Johns Hopkins University. He most recently served as Clinical Professor of Medicine in the Pulmonary-Critical Care Medicine Division of the University of Washington School of Medicine before joining Weill Cornell Medical College of New York City at its branch campus in Doha, Qatar. There he is Senior Associate Dean for Clinical Affairs, Professor of Medicine, and Consultant in the Medical Intensive Care Unit at Hamad General Hospital.

Dr Davidson has directed development of a low molecular weight heparin and participated as an investigator, steering committee member, outcome adjudication committee chair, and data safety monitoring board chair for many anticoagulants in development. His particular interests are in anticoagulant pharmacology, clinical study design, analysis of diagnostic tests, and critical care medicine. He is a past President of the USA National Tuberculosis Controllers Association, past Governor of the American College of Chest Physicians for the state of Washington, and is an Associate Editor of the journal, CHEST.
Faculty

Martin H. Prins
Manuel Monreal

Department of Medicine, Hospital Universitari Germans Trias i Pujol de Badalona, Spain

Manuel Monreal is head of the Unit of Vascular Medicine at the Internal Medicine Service, Hospital Universitari Germans Trias i Pujol de Badalona, Spain. He was made Professor of Medicine at the Universitat Autònoma, Barcelona, in 1978 and was awarded a PhD in 1991. He is a member of the editorial board of Medicina Clinica and is an occasional peer reviewer for J Thromb Haemost, Thromb Haemost, Am J Med and Chest.

Professor Monreal’s research is focused mainly on venous thromboembolism and peripheral artery disease. He is the Coordinator of Registro Informatizado de Pacientes con Enfermedad Tromboembólica (RIETE) and the Registro Informatizado sobre Factores de Riesgo y Enfermedad Arterial (FRENA). He has published many articles, including 11 articles in Chest, 10 in Thromb Haemost, 9 in J Thromb Haemost, 2 in Am J Med and one in Circulation.
Ola E. Dahl

MDSci received his medical education and academic degrees at the University of Oslo in Norway. He became a specialist, initially in general surgery and later in orthopaedic surgery. He has been involved in laboratory and clinical research for many years. His discovery of the lung vasculature as thrombin-generating organs during bone surgery was a break through in the understanding of the occurrence of posttraumatic systemic thromboembolic complications and vascular mortality as the major cause of deaths after major orthopaedic surgery. He pioneered studies on out-of-hospital hypercoagulation and thromboembolism, which later have been confirmed in North America and Europe.

Dahl has been a frequent invited speaker, chaired and been on the boards of expert conferences at international conventions, and co-operated with colleagues worldwide. He is one of the international opinion leaders within the field of thrombosis and haemostasis related to trauma and surgery. He has published numerous papers and abstracts on a variety of surgical and toxicological issues. In particular, with emphasis on posttraumatic pathophysiology, bone cement cytotoxicity, bleeding, initiation and duration of hypercoagulability, its clinical consequences and several long-term epidemiological studies on vascular outcomes following major surgical procedures. Professor Dahl has extensive experience with clinical development programs of new anticoagulant compounds. He is a referee for several journals and a member of different societies. He is an Executive Director of International Surgical Thrombosis Forum (ISTF), a global Society bridging front knowledge within thrombosis and haemostasis with skilled surgical experience. In addition, he is attending the Thrombosis Research Institute in London, UK as Honorary Professor.
Juan I. Arcelus

University of Granada Medical School, Granada, Spain

Juan Arcelus graduated from the University of Granada School of Medicine, Spain, and also obtained an PhD specializing in thrombosis in 1998. Dr Arcelus is Professor of Surgery at the University of Granada School of Medicine, and practices at the Hospital Universitario Virgen de las Nievas, also in Granada.

He is Visiting Professor to several hospitals and universities in Spain and abroad. His main research interests include the diagnosis, prevention, treatment and follow-up of venous thromboembolism in medical, general and orthopaedic surgery patients. A member of numerous scientific societies, he has written several book chapters, presented over 300 abstracts and lectures at international meetings, published many papers in peer-reviewed journals, including original contributions on risk stratification and prevention of venous thromboembolism in general, orthopaedic, and laparoscopic surgery, and use of different modalities of compression for the management of post-thrombotic syndrome. He is actively involved in the Spanish Computerised Registry on Venous Thromboembolism, and a member of the International Surgical Thrombosis Forum (ISTF). Dr Arcelus is the coordinator for the Spanish Association of Surgeons working group on thrombosis.
David Bergqvist was born in 1941. He studied medicine in Uppsala, Sweden and his PhD thesis examined hemostatic plug formation and stability in the rabbit mesenteric microcirculation. Professor Bergqvist completed his surgical training at the county hospital in Skövde, Sweden and became Associate Professor of surgery at the University of Lund, Sweden in 1979. Since 1993, he has been Professor of Vascular Surgery at the University of Uppsala, Sweden and Head of Vascular Surgery at the University Hospital, Uppsala, Sweden.

Professor Bergqvist has authored around more than 700 original articles, several reviews and book chapters and three text books. His main areas in research deal with prophylaxis of post-operative venous thromboembolism, epidemiological and pathogenetic aspects on aortic aneurismal disease and formation of pseudointimal lesions with arterial reconstructive surgery and balloon trauma. He is an honorary member of the Royal Australiasian College of Surgeons Division of Vascular Surgery, Hellenic Angiological Society, American Venous Forum and the Vascular Surgical Society of Great Britain and Ireland.
Benjamin Brenner

Faculty of Medicine, Technion, Israel Institute of Technology, Haifa, Israel

Benjamin Brenner qualified as a medical doctor from the Israel Institute of Technology in 1981. Following residency in internal medicine and hematology at the Rambam Medical Center in 1981-6, and a postdoctoral research fellowship in fibrinolysis at the University of Rochester, New York, USA, 1987-8, he returned to Haifa as a senior hematologist and was appointed as Director of the Thrombosis and Hemostasis Unit and Deputy Director of the Hematology Institute at Rambam Medical Center in 1994.

Currently, he is a Professor of Medicine (Hematology) and Caster chair in Leukemia Research at the Bruce Rapport Faculty of Medicine, Technion Israel Institute of Technology. His research interests over the years have included: fibrinolysis and thrombolysis, inherited bleeding disorders and studies of new antithrombotics and hemostatic agents.

Dr Brenner’s studies in the field of inherited and acquired thrombophilia concentrated on procoagulant in leukemia and solid tumors and on the effect of combined thrombophilic defects on the expression of thrombosis. His main interest focuses on issues related to thrombosis in women, in particular the association of thrombophilia with pregnancy loss and late gestational vascular complications. He has published on prevention of pregnancy loss in women with thrombophilia by LMWH and has recently conducted the LIVE-ENOX trial, a multi-center study using two dose regimens of enoxaparin in this indication.
Joseph A. Caprini, M.D., is Professor of Surgery at the Feinberg School of Medicine, Northwestern University, in Chicago, Illinois, and Professor of Biomedical Engineering and Applied Sciences at the Robert R. McCormick School of Engineering and Applied Science at Northwestern University, Evanston, Illinois. He also holds the Louis W. Biegler Chair of Surgery at Evanston Northwestern Healthcare in Evanston, Illinois.

Dr. Caprini earned his B.S. in biology at Villanova University in Villanova, Pennsylvania, his M.S. at Northwestern University, and his M.D. at Hahnemann Medical College (now known as Drexel University College of Medicine) in Philadelphia, Pennsylvania. He completed his internship in medicine at Evanston Hospital and his residency in general surgery at Northwestern University Medical School. He fulfilled a fellowship in surgical hematology at Northwestern University Medical School (now known as the Feinberg School of Medicine).

Dr. Caprini has authored or co-authored more than 335 articles and abstracts and has presented more than 1320 lectures and 90 exhibits on the study and treatment of venous thromboembolism, venous insufficiency, and related topics. His articles are published in Journal of Thrombosis and Thrombolysis, Archives of Internal Medicine, Journal of Arthroplasty, and Journal of Vascular Surgery.
to name a few. He serves on the editorial board or as a reviewer for Journal of Vascular Surgery, European Journal of Vascular and Endovascular Surgery, Phlebology, and Journal of Blood Coagulation and Fibrinolysis, among others. He is a member of many societies, including the International Society on Thrombosis and Haemostasis, the American Venous Forum, where he currently serves as President-elect, the Society for Vascular Surgery where he has just been elected as a distinguished fellow, and is a Founding Member and the first Honorary Fellow of the European Venous Forum. He is a Fellow of the American College of Surgeons and the American College of Phlebology, a member of the Royal Society of Medicine of London and the American Society of Hematology, and a founding member and Trustee of the International Surgical Thrombosis Forum. Dr. Caprini has received numerous honors and awards, among which are the Schweppe Foundation Career Development Award and the Coon Fellowship, and he occupies the Louis W. Biegler Chair of Surgery at Evanston Northwestern Healthcare.
Alexander G.G. Turpie is Professor of Medicine at McMaster University and an internist at Hamilton Health Sciences, Hamilton, Ontario. He completed his medical education, at the University of Glasgow, Scotland and, after completing a residency at the Royal Infirmary, and a residency and clinical research fellowship at Stobhill General Hospital in Glasgow, he became a lecturer at the University of East Africa Medical School in Nairobi, Kenya. After returning to the University of Glasgow for additional training in haemostasis and thrombosis, Alexander Turpie was appointed MRC Fellow at McMaster University in Hamilton, Canada. Dr Turpie’s research interests include new antithrombotic drugs for the management of venous and arterial thrombosis and anticoagulant therapy in patients with prosthetic heart valves. He has served on numerous professional and university-related committees, and is a frequent lecturer at professional meetings worldwide. Dr Turpie has also authored over 700 published articles, abstracts and books. He has served as a reviewer for many journals, including the Annals of Internal Medicine, Circulation, The Lancet and the New England Journal of Medicine. He also serves on the editorial boards of Vascular Medicine Review and Heart Drug.
Anthonie W. A. Lensing

Department of Vascular Medicine
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1988 MD
1996 Vascular neurologist
1986-1988 Post-doc, university of Padua, Italy
1990-1992 Post-doc, university of Hamilton, Canada

1986-2008 Department of Vascular Medicine, Academic Medical center, Amsterdam, the Netherlands
1999-2004 consultant for Organon, the Netherlands and Sanofi-Synthelabo for conducting clinical studies with fondaparinux and idraparinux
2004-2008 consultant for Bayer Healthcare and Johnson & Johnson for conducting clinical studies with oral Xa inhibitors

Publications >130 international peer-reviewed articles
Venous thromboembolism (VTE), comprising deep-vein thrombosis (DVT) and pulmonary embolism (PE) is often asymptomatic, misdiagnosed, and unrecognized at death, and there is a lack of routine post-mortem examinations. These factors are thought to result in marked underestimates of VTE incidence. In the United States VTE occurs at an annual incidence of about 71 - 117/100,000 adults, which results in 900,000 events annually. Rates increase sharply after age 45 year, and are slightly higher in men than in women in older age.

It is often a chronic condition, with recurrence rates estimated at 5% to 7% annually after a first episode. Post-thrombotic syndrome affects 20% to 50% of patients after a first DVT. Pulmonary hypertension occurs in 4% - 5% of patients following PE.

PE accounts for 5 - 10% of death in hospital patients. The ENDORSE study, a cross-sectional survey in nearly 70,000 patients admitted to hospital in 32 countries has shown that two-thirds of surgical patients and more than two-fifth of medical patients were deemed eligible for antithrombotic prophylaxis.

By combining the best available evidence from clinical, epidemiological and autopsy studies in a model the VITAE (VTE Impact Assessment Group in Europe) investigators have estimated, that annual number of VTE events across 25 EU countries is about 1.5 million. This figure includes 543,000 deaths, 435,000 cases of PE and 684,000 cases of documented symptomatic DVT. This exceeds the combined total deaths due to AIDS, breast cancer, prostate cancer, and transport accidents. The cost of treating VTE and related morbidity is substantial. Data from the UK suggest that the combined direct and indirect annual costs of VTE are placed at approximately £ 640 million (€ 950 million). Estimates of the number of annual VTE events in Poland, based on extrapolation from six the EU model countries, are 68,000 DVT events, 67,000 PE events, and 45,400 of VTE-related deaths.

The separate nature of arterial and venous disorders has been challenged, as several recent studies have shown that subjects with VTE are at higher risk of subsequent arterial cardiovascular events than matched controls. In the USA the annual rate of myocardial infarction or ischemic stroke is lower than that of VTE events, as well as the corresponding mortality. In Poland myocardial infarction and ischemic stroke affect annually about 100,000 and 60,000 persons, respectively.
Venous thromboembolism (VTE) is a common complication among medical patients and can be fatal due to pulmonary embolism (PE). Risk factors for VTE in medical patients are connected with medical conditions such as stroke, congestive heart failure III + IV NYHA class, respiratory disease, infections, inflammatory diseases (rheumatic disease, inflammatory bowel disease), myocardial infarction, reduced mobility, malignancy, chemotherapy in cancer patients, prior VTE, recent surgery or trauma, advancing age, obesity (BMI > 30), central venous catheterization, estrogen therapy, varicose veins and inherited or acquired coagulation disorders. High rate of deep venous thrombosis (DVT) is observed especially in stroke patients and medical intensive care population patients.

It should be especially underscore that fatal PE is the leading cause of sudden death in hospitalized acute medical patients population. In three large randomized trials addressed to general medical patients population, the rate of proximal DVT was 5% in placebo group.

It is worth to underscore that asymptomatic proximal DVT is associated with higher mortality rate compared to those with isolated calf DVT. In spite of knowledge and existing guidelines only 39.5% globally assessed medical patients (in Poland 50%) being at VTE risk, received recommended prophylaxis. Acutely ill medical patients should be screened for risk of VTE.

In-hospital strategies assessing VTE risk should be implemented, together with measures that ensure that at-risk patients receive appropriate VTE prophylaxis. Both ambulation and exercises involving foot extension improve venous flow and should be encouraged as the simplest prophylactic method. For acutely ill medical patients fulfilling indications for VTE, pharmacologic prophylaxis with LDUH 5000 IU 3x per day, LMWH (enoxaparin 40 mg 1x per day or dalteparin 5000 U 1x per day) or fondaparinux 2.5 mg 1x per day are recommended. Patients treated in intensive care units (ICU) should received LDUH or LMWH unless contraindications limit their use. In patients at risk of VTE whom risk of bleedings outweigh the benefits of anti-thrombotic agents delivery, intermittent pneumatic (IPC) device or graduate compression stockings (GCS) should be used. In medical patients being at high risk for development of VTE complications in the post-discharge period, continuation of LMWH use at home, should be considered. Compression ultrasound underestimate the incidence of proximal and distal DVT in acutely ill medical patients without thrombosis symptoms and seems to be not useful clinically for screening individual medical patient at VTE risk.
Bruce Davidson

Management and treatment of VTE in 2008: including critically ill patients
Martin H. Prins

Cancer, thrombosis and influence on life quality and expectancy
There are several sources of medical information: randomised clinical trials, administrative databases or registries, among others.

Clinical trials have been considered the top level studies in medicine, because there is a blind randomisation of the different arms in study, and their results serve to compare different diagnostic strategies, or different therapeutic or prophylactic measures. However, clinical trials also have some limitations: they are usually performed in limited geographic areas, involve selected patients (that means, patients with strict inclusion and exclusion criteria), compare fixed therapies, but then their results would be applicable to patients in other geographic areas, patients with exclusion criteria, etc.

Administrative databases serve to gather information on consecutive patients in a particular community. However, the quality of the information has been questioned since in most cases this is an administrative secretary who fills the data, because there is no information on the results of the diagnostic tests (only if they have been performed), and because usually there is no information at all about the therapeutic options (the drug, the dose, the duration…).

A Registry may complement many of these drawbacks. A good registry, with a large amount of information on the clinical characteristics of the patients, the diagnostic tests (and their results), the therapeutic options (including the drug, the dosage, the date of start and end, even with the reason to discontinue) and clinical outcome, with all this information filled by the very attending physician, may be an invaluable source of information for clinicians. And very useful to answer some specific questions, as I will show you later on.

This is the reason why several registries have been set-up in recent years. RIETE (Registro Internacional de Enfermedad TromboEmbolica) is an international, multicenter, prospective registry on consecutive patients with acute, symptomatic, objectively proven VTE (either DVT or PE). It is independent because, at variance with many other registries, it belongs to us, the doctors. Our aim is to provide information in real time about what we are doing in real life. We started in March 2001 and since then the recruitment rate has maintained a steady increase. Three years ago we translated the web site to English aimed to expand the RIETE registry to other countries.
The idea was that if we were able to share a database with the information generated by all patients of a group of colleagues from different sites in Spain, we would probably accede to some information that would be useful to learn how to treat these specific patients better.

In RIETE every member can request a download of the data from all patients to produce a manuscript. Of course, there are some conditions. The requesting members have to have their homework done. I mean: to have recruited at least 1 patient in the last 3 months, 20 patients in the last 12 months, and at least 65% have to be validated. If they don’t comply these conditions but have recruited patients in the last 6 months they will appear at the end of the article, included in the list of participating members.

There are some limitations, inherent to all registries. The most important, RIETE was not designed to answer questions regarding the relative efficacy and safety of different modalities of prophylaxis or therapy. On the contrary, any data are hypothesis-generating and provide feedback from real-world clinical situations.
Screening studies on asymptomatic DVT in selected patients, meta-analyses based on these studies, citation of old studies that drives up the VTE rate and extrapolation of those data to the general surgical population, are not believed to reflect current clinical reality. In addition, lack of information on side effects of surgical interest has been requested for years.

Recent epidemiological studies on elective major hip joint operated patients have shown an overall excess of mortality of about 0.2% relative to the death rate in the normal population. The death rate is highest the day of surgery, decreasing until it crosses the death rate in the normal population after about one month and then continues to decrease until it stabilizes after approximately 3 months. Thrombotic vascular events dominate this statistics. Markedly higher mortality is seen in old and comorbide non-selected orthopaedic patients that suffer from hip fracture. They have a substantial higher mortality than the normal population and it persists life-long.

Thrombin driven arterial and venous complications like microembolism syndrome (“fat” embolism), MI, stroke, DIC, ARDS, SIRS and VTE are seen from the time of the orthopaedic trauma and for a long time down stream (vide supra). This persistent hypercoagulable state is driven by thrombin activity that involves both the acute haemostatic process needed to minimize critical bleeding and a long-lasting inflammatory healing process that parallels a reduction in lower limb blood flow followed by a second phase of event recurrence.

By controlling the underlying prothrombotic thrombin driven process with chemical compounds, general vascular deaths seem to be reduced to the same extend as fatal PE i.e. approximately 50%.

A paradigm shift has started, driven by new scientific knowledge and the surgeons demand for clinically relevant studies and guidelines. Focus has shifted from venous thrombosis that was a frequent and serious clinical complication several decades ago, via screening studies on asymptomatic DVT to studies that take into account all thrombin driven vascular complications, the main cause of peri- and postoperative mortality and morbidity. A challenge to scientists and the industry
to catch up and respond on this demand and design studies that mirror the wide span of real-life vascular complications related to trauma and surgery in order to apply the best available therapy for each individual patient.

References:
Venous thromboembolism (VTE) is a common complication in patients undergoing surgery. Without prophylaxis, up to 30% of general surgical patients develop deep-vein thrombosis (DVT) and up to 0.9% die from a fatal pulmonary embolism (PE). The risk of postoperative VTE depends on a combination of a patient’s predisposing risk factors, such as cancer, advanced age, obesity, varicose veins, and history of previous VTE, plus other exposing or triggering factors such as the type and duration of surgery, immobility, infections, etc.¹

DVT can be triggered by several complex mechanisms. The three precipitants for venous thrombosis, i.e. venous stasis, damage to the vessel wall, and increased coagulability, were first proposed by Virchow over 150 years ago. Venous stasis results from reduced mobility due to the surgery itself. Damage to the vessel wall can result directly from trauma due to surgery. The subsequent injury to the endothelium triggers the release of procoagulant factors (tissue factor and factor VIIa) and exposes the subendothelial matrix, which, in turn, activates platelets and coagulation, leading to thrombin formation.

A variety of strategies for preventing VTE are available, including mechanical methods (e.g. graduated compression stockings) and pharmacological methods (e.g. unfractionated heparin [UFH], low-molecular-weight heparin [LMWH]). The ideal prophylactic method should be effective, safe, easy-to-use, and cost-effective. Although no method fulfils all of these criteria, LMWs have become the option of choice for general surgical patients in most European countries.

Current guidelines generally recommend thromboprophylaxis for surgical patients with a moderate-to-high risk of VTE.¹² However, recent epidemiologic studies indicate that a substantial proportion of surgical patients at risk of VTE do not receive any prophylaxis. Moreover, those who do receive prophylaxis often receive suboptimal prophylaxis, according to current guidelines and based on the patient’s risk level.³⁴

Obese patients (BMI>30 Kg/m²) undergoing bariatric surgery for weight reduction are at risk to develop postoperative VTE. Indeed, according to the International Bariatric Surgery Registry (www.asbs.org) the main cause of postoperative death among 38000 patients worldwide
si fatal PE. Recommended prophylactic regimens for these patients include pharmacological methods, such as subcutaneous or intravenous heparin, at fixed or adjusted doses. Most European patients receive LMWHs: enoxaparin (40-80 mg daily), nadroparin (5700-9000 U daily) or dalteparin (5000 U daily). Mechanical methods are not recommended as the sole method in patients with morbid obesity (BMI>40 Kg/m2) and several risk factors. However, they are adjuncts to pharmacological methods and the only available option in patients at very high bleeding risk in whom anticoagulants are contraindicated. More perspective studies are needed to assess the optimal dosing and duration of prophylaxis in bariatric surgery.

References:
Thromboprophylaxis can be considered established in many surgical situations and the evidence is there that postoperative venous thromboembolism (VTE), also fatal pulmonary embolism, can be prevented. There are several guidelines, both national and international, which can be used to provide the busy clinician with relevant recommendations. In spite of the massive amount of research which has been published, especially since the 1950’s, there are still areas of uncertainties. The presentation will focus on pathophysiological characteristics of VTE to design the optimal prophylactic attack with emphasis on new prophylactic principles, choice of optimal end point and the relation between asymptomatic calf vein thrombosis and pulmonary embolism, the relation between venous and arterial thromboembolism in an elderly population, the optimal design of studies on VTE where sometimes scientific and industrial interests may be contraproducive, how to monitor complications and the role of DSMB (most studies are not sized to analyze complications and here there may be a role of systematic post-marketing surveillance), identification of surgical patients where the information on prophylaxis is insufficient due to lack of studies, when to start prophylaxis and when to stop it, that is identifying risk operations for late VTE in need of extended prophylaxis and defining the duration of the risk period. A further unmet need is how to implement the knowledge on prophylactic effect and to analyze cost effectiveness of prophylaxis.
Pregnancy is an acquired hypercoagulable state due to increase in coagulation factors, decrease in natural anticoagulants and impaired fibrinolysis. The procoagulant activity increases as pregnancy progresses with the highest levels of prothrombin fragment 1+2, fibrinopeptide A, and D-dimer just before delivery. Overall the risk for VTE increases 10-folds during pregnancy and 30-folds during the post-partum period. Thrombophilia can be found in the majority of women with gestational venous thrombosis. Acquired risk factors of VTE include among others, age over 35 years, BMI>30 cesarean section, gestational vascular complications (i.e. preeclampsia, placental abruption) and multiple pregnancy. Risk stratification is crucial for timely fashioned prophylaxis. Heparins are the mainstay of anticoagulation during pregnancy, and LMWH are the drug of choice due to their high-efficacy and safety profile. In women with thrombosis at index pregnancy full dose anticoagulation is recommended and monitoring of anti-Xa levels is advised due to physiological changes during gestation. A role for LMWH in prevention of pregnancy complications particularly in women with recurrent miscarriages and severe gestational vascular complications has been suggested by several studies and is currently under on-going investigation.
Venous thromboembolism (VTE) is a significant medical problem that manifests in a variety of short-and long-term clinical presentations. It has been estimated that nearly 900,000 cases occur annually in the US alone. The most dramatic problem is serious or fatal pulmonary emboli (PE), which is relatively uncommon but of great clinical significance. Clinically significant deep vein thrombosis (DVT) presents a variety of issues for patients, including taking anticoagulants and sometimes altering life-styles. The long-term clinical course of DVT may be complicated by the post-thrombotic syndrome (PTS) in as many as 25% of patients and in 7% it is so severe that it causes permanent disability. This syndrome consists of leg swelling, discomfort, skin changes, and in some patients open ulceration. It has been estimated that 2,000,000 work days are lost annually because of PTS, and 15 million Americans are thought to be affected, including 4% of the US population who currently have or will develop a venous leg ulcer during their lifetime. Recurrent DVT may be seen in up to 30% of patients who have adequate treatment, and a recurrence will increase the patient's chance of developing PTS by six-fold.

The best treatment for this syndrome is appropriate thrombosis prophylaxis according to evidenced-based guidelines. It is important to adequately treat the first episode of DVT which may consist of 6-12 months of therapy in those with idiopathic DVT. Some evidence suggests that treatment should continue as long as evidence of residual clot damage is present on the duplex scan. When these duplex scan changes resolve the anticoagulation can be stopped. D-dimer levels should be checked one month after stopping therapy and if they are abnormal, the anticoagulation should be resumed for a period of time and the process repeated. Patients with cancer should receive LMWH for the first 6 months of treatment rather than oral anticoagulation since the recurrence rate and overall bleeding rate are lower using LMWH. Oral anticoagulation can then be used for as long as appropriate. Patients with iliofemoral DVT should be considered for mechanical and pharmacologic thrombolysis followed by venous stenting where appropriate. The use of appropriate pressure graduated compression stockings should also be used in these patients and have reduced the incidence of PTS by 50% in controlled clinical trials. The mainstay of the treatment of PTS is compression stockings of at least 30-40mmHg. Many times calf length hose may be used to increase the efficiency of the calf muscle pump.
They are more convenient and compliance is better than thigh-length stockings. Short-stretch bandages, Velcro band appliances, and intermittent pneumatic leg or foot compression also need to be employed in some cases. Appropriate correction of associated superficial venous insufficiency with surgery, thermal or laser ablation techniques, or sclerotherapy should also be done.

Appropriate risk assessment of all patients is the cornerstone for providing thrombosis prophylaxis tailored to the unique risk factors of the individual patient. Unfortunately it is impossible to extrapolate clinical trial results to all patients, especially those who fit “exclusion” criteria in clinical trials. Tailoring the type, strength, onset, and duration of prophylaxis for the individual patient will produce the best results. Many patients will need out-of-hospital prophylaxis due to ongoing risk and this is best guided by calculating their overall level of risk. In the final analysis many of the complications of VTE may be avoided by utilization of prophylaxis in everyone “at risk.” Unfortunately, statistics from many countries have documented the poor use of prophylaxis which, at best, is used in 50-60% of patients. Hospital-wide programs, clinical alert systems, and pay-for-performance issues have all been suggested to improve adherence to established clinical guidelines.
Abstracts

Alexander GG Turpie

Challenges in secondary prophylaxis - use of LMWH in long-term treatment and bridging therapy
Chronic Thromboembolic Pulmonary Hypertension: management and treatment

BACKGROUND: Chronic thromboembolic pulmonary hypertension (CTPH) is associated with considerable morbidity and mortality. Its incidence after pulmonary embolism and associated risk factors are not well documented.

METHODS: We conducted a prospective, long-term, follow-up study to assess the incidence of symptomatic CTPH in consecutive patients with an acute episode of pulmonary embolism but without prior venous thromboembolism. Patients with unexplained persistent dyspnea during follow-up underwent transthoracic echocardiography and, if supportive findings were present, ventilation-perfusion lung scanning and pulmonary angiography. CTPH was considered to be present if systolic and mean pulmonary-artery pressures exceeded 40 mm Hg and 25 mm Hg, respectively; pulmonary-capillary wedge pressure was normal; and there was angiographic evidence of disease.

RESULTS: The cumulative incidence of symptomatic CTPH was 1.0 percent (95 percent confidence interval, 0.0 to 2.4) at six months, 3.1 percent (95 percent confidence interval, 0.7 to 5.5) at one year, and 3.8 percent (95 percent confidence interval, 1.1 to 6.5) at two years. No cases occurred after two years among the patients with more than two years of follow-up data. The following increased the risk of CTPH: a previous pulmonary embolism (odds ratio, 19.0), younger age (odds ratio, 1.79 per decade), a larger perfusion defect (odds ratio, 2.22 per decile decrement in perfusion), and idiopathic pulmonary embolism at presentation (odds ratio, 5.70).

CONCLUSIONS: CTPH is a relatively common, serious complication of pulmonary embolism. Diagnostic and therapeutic strategies for the early identification and prevention of CTPH are needed.