Decision analysis model of prolonged oral anticoagulant treatment in factor V Leiden carriers with first episode of deep vein thrombosis

François P Sarasin, Henri Bounameaux

Abstract

Objective: To assess the risks and benefits of oral anticoagulant treatment extended beyond 3 months after a first episode of deep vein thrombosis in patients who carry factor V Leiden mutation. Such patients have over twice the risk of recurrence after the recommended treatment period, but more information is required before widespread genetic screening can be recommended.

Design: A decision analysis Markov model (with data extracted from literature) representing the risks of developing symptomatic venous thromboembolism, the risks of major bleeding, and the efficacy of anticoagulant treatment.

Subjects: A hypothetical cohort of 1000 carriers of factor V Leiden recovering from a first episode of deep vein thrombosis in the lower limbs.

Main outcome measures: Risks and benefits of, firstly, stopping oral anticoagulation 3 months after first episode of thrombosis with reinitiation of treatment only after recurrent thrombosis and, secondly, extension of oral anticoagulation up to 1 to 5 years.

Results: Despite consistent biases in favour of extended oral anticoagulation, analysis revealed that among factor V carriers the number of major haemorrhages induced by oral anticoagulants would exceed that of clinical pulmonary emboli prevented over the entire range of duration of anticoagulation (1 to 5 years). On the other hand, the number of recurrent deep vein thrombi prevented would exceed that of iatrogenic major bleedings.

Conclusion: The lack of evidence of a net clinical benefit of prolonged oral anticoagulation, at least beyond 1 year, among patients recovering from acute deep vein thrombosis does not support the decision to promote widespread genetic screening programmes to detect the factor V mutation.

Introduction

A point mutation in which adenine is substituted for guanine at nucleotide 1691 in the gene coding for coagulation factor V results in the production of abnormal factor V (called factor V Leiden)¹ which is more resistant to inhibition by activated protein C² than the genuine factor V. This mutation is associated

with a threefold³ to sevenfold⁴ increase in the risk of deep vein thrombosis. Because its prevalence is quite high in Western populations (about 5% in Europe with a maximum of 15% in southern Sweden), there is a large debate among specialists as to whether genetic screening is indicated.⁵

Before screening for any abnormality is advocated in more or less selected groups of symptomatic or asymptomatic patients, however, data should demonstrate that carriers of the mutation would benefit from the diagnosis. For example, women who carry the factor V Leiden mutation and use oral contraceptives have a more than 30-fold increased risk of thrombosis compared with women who are not carriers of the mutation and do not use oral contraceptives⁶; screening for the mutation, however, would deny effective contraception to a large number of women while preventing only a small number of deaths due to pulmonary emboli.⁷ Similarly, the finding that factor V Leiden mutation is associated with a twofold risk of recurrent thrombosis,^{8,9} a finding that has recently been challenged,¹⁰ does not necessarily mean that patients who carry the mutation and present with acute deep vein thrombosis would benefit from more prolonged anticoagulation (some specialists advocate indefinite treatment) to prevent recurrent disease. This policy would imply the need for secondary screening programmes with factor V Leiden testing in all patients experiencing deep vein thrombosis. Ideally, the answer to that question should be derived from randomised trials comparing long term (but how long?) versus short term anticoagulation with adjusted dose oral anticoagulants in the secondary prevention of venous thromboembolism among patients heterozygous for factor V Leiden. Such trials with sufficiently large numbers of patients would be difficult to organise and their results would probably not be available for many months or even years. This prompted us to use a Markov decision analysis model explicitly considering the consequences of recurrent deep vein thrombosis and bleeding events and to quantify the risk-benefit trade offs for different durations of oral anticoagulant treatment in these patients at higher risk of recurrent thromboembolic events.

This kind of approach is particularly suited for assessing complex clinical issues by using the best

Medical Clinics and the Division of Angiology and Haemostasis, Department of Internal Medicine, Hospital Cantonal, University of Geneva Medical School, Geneva, Switzerland

François P Sarasin, senior registrar, department of internal medicine
Henri Bounameaux, head, division of angiology and haemostasis

Correspondence to: Dr F P Sarasin, Department of Internal Medicine, Hospital Cantonal, 24 rue Micheli du Crest, 1211 Geneva 14, Switzerland
sarasin-francois@diogenes.hcuge.ch

BMJ 1998;316:95-9

available evidence from the literature. Moreover, sensitivity analyses allow one to establish how robust the results are by modifying the value of the critical variables. Finally, its conclusion may help investigators to select more carefully the clinical issues that have to be covered in clinical trials.

Methods

Decision tree

We considered this general example of the problem. A patient carrying the factor V Leiden mutation is recovering from deep vein thrombosis in the lower limb and is at increased risk of recurrent thromboembolism compared with a patient without the mutation. If the patient is given prolonged oral anticoagulants (beyond the usually recommended 3 month period) the risk of bleeding is increased, while that of recurrent deep vein thrombosis is decreased. Either kind of event can produce death, pulmonary embolism, or permanent morbidity. Should prolonged oral anticoagulation be given?

We used the D Maker 7.1 (Pratt Medical Group, Boston, Massachusetts) decision analysis program to create a model representing and measuring the consequences of either stopping oral anticoagulation after 3 months with reinitiation of treatment only after a clinical recurrent deep vein thrombosis has occurred (triggered oral anticoagulation) or extending oral anticoagulation for up to 1, 2, 3, 4, or 5 years. We used a Markov simulation to model repetitive clinical events beyond the control of patient and physician.¹¹ In a Markov process patients move between various health states depending on the clinical events modelled in the decision tree and the probability of these events.

At the beginning of the Markov simulation patients are well and are in one of two states: taking oral anticoagulants or not taking oral anticoagulants. In either case, several groups of events are possible: recurrent deep vein thrombosis, pulmonary embolism, major bleeding events, or different combinations of those events. Patients on anticoagulant treatment incur risks related to anticoagulation but the risks of recurrent deep vein thrombosis with or without pulmonary embolism are diminished by the efficacy of the treatment. When treatment is discontinued patients again incur risks of recurrent thromboembolism, whereas the risks related to anticoagulation become zero. Patients not taking oral anticoagulants are at increased risk of recurrent deep vein thrombi and subsequent pulmonary emboli. The occurrence of those events will prompt treatment with oral anticoagulants. We calculated the average value (expected utility) of each strategy by tracking the number of recurrent deep vein thrombi and clinical pulmonary emboli prevented and the number of major bleeding events induced in the two strategies.

Assumptions

In formulating our model, we made several assumptions. Firstly, for patients taking oral anticoagulants we considered only the risks of major haemorrhagic events (intracranial, retroperitoneal, or those that resulted in admission to hospital, transfusion, or death). Secondly, we assumed that the occurrence of a major haemorrhagic event would lead to the

permanent discontinuation of treatment with anticoagulants, despite possible subsequent new thromboembolic events. Thirdly, in patients not receiving initial prolonged anticoagulation treatment, we assumed that any clinical recurrent thromboembolic event would lead to the initiation of indefinite anticoagulation treatment. Fourthly, we did not consider the inconvenience of taking anticoagulants in terms of determinations of international normalised ratio and the need to worry about bleeding, avoiding other drugs, and trauma. Fifthly, we ignored the potentially higher risk of bleeding in the period when treatment with anticoagulants is being initiated, thus we assumed the risk of bleeding to be relatively constant for the period being analysed. Finally, long term morbidity from recurrent deep vein thrombosis (the post-thrombotic syndrome) and from non-fatal pulmonary embolism (secondary pulmonary arterial hypertension) was not taken into consideration.

Parameters used in analysis

Risk of recurrent thromboembolism after proximal deep vein thrombosis—In patients who are not carriers of factor V Leiden most recurrent thromboembolism occurs during the first 2 years after the initial event, with a cumulative recurrence rate of about 8% at 1 year and 15% at 2 years.¹²⁻¹⁹ During the 3 subsequent years, recurrence seems less frequent with a rate of 1.7% a year. In factor V Leiden carriers the cumulative recurrence rate at 2 years is around 25%, whereas over the 3 following years it decreases around 15% (5% per year).⁷⁻⁹ Thus, patients who carry the factor V Leiden mutation have more than twice the risk of recurrent deep vein thrombosis when compared with non-carriers.

Risk of symptomatic pulmonary embolism given recurrent deep vein thrombosis—Symptomatic pulmonary emboli have been reported in 10% to 20% of patients with untreated proximal deep vein thrombosis.²⁰⁻²¹ Among those events, 2% to 8% may be fatal.²²⁻²³

Efficacy of anticoagulant treatment—The efficacy of chronic oral anticoagulant treatment in preventing recurrent deep vein thrombi and subsequent pulmonary emboli ranges between 70% and 90%.²⁴

Risk of major haemorrhagic complications—The incidence of bleeding in patients given oral anticoagulants because of deep vein thrombosis has been the subject of several reports.²⁵⁻²⁶ Of note, it has been shown that among patients with deep vein thrombosis the risk of bleeding is higher compared with patients with other medical conditions (for instance, prosthetic heart valves, chronic atrial fibrillation).²⁵ Anticoagulation of moderate intensity is used because the risk of haemorrhage is clearly dependent on the intensity of anticoagulant treatment and a targeted international normalised ratio of 2-3 is now firmly established for venous thromboembolism. In a systematic review of prospective studies the rate of fatal or major haemorrhage was 4.8% (95% confidence interval 3.6% to 7.2%) per year.²⁶

Results

By using the data defined in the table we measured the consequences of different durations of oral anticoagulation treatment after a first episode of deep vein

Summary of data extracted from literature and used in analysis. Figures are cumulative risk of recurrent deep vein thrombosis after first episode (percentages)

Variable	Baseline analysis	Range used in sensitivity analyses
Non-carriers of factor V ¹²⁻¹⁹ :		
Year 1	7.2	6.5-9.4
Year 2	14.3	12.4-16.2
Year 5	19.5	15.9-23.0
Carriers of factor V ⁷⁻⁹ :		
Year 1	13	
Year 2	26	
Year 3	35	
Year 5	39	29
Risk of clinical pulmonary embolisms in deep vein thrombosis ²⁰⁻²³	20	10-20
Treatment efficacy ⁴	90	70-90
Yearly risk of major bleeding ²⁵⁻²⁶	3.6	3.6-7.2

thrombosis for a hypothetical cohorts of 1000 carriers and non-carriers of factor V Leiden. The figure depicts the clinical benefit of pursuing anticoagulation treatment beyond the usually recommended 3 month period versus anticoagulation triggered by clinically overt recurrent deep vein thrombi. To avoid overlooking a benefit favouring prolonged prophylactic anticoagulation, we deliberately biased this analysis. Thus, we used the extreme ranges of clinical data (see table) that would consistently favour the clinical benefits provided by anticoagulants: high rate of clinical pulmonary emboli (20%), maximum efficacy of anticoagulants (90%), and low risk of bleeding (3.6% per year). Despite this favourable set of clinical data representing the best case scenario favouring prolonged anticoagulation, our analysis suggests that among factor V carriers the number of major haemorrhages induced by anticoagulants exceeds the number of clinical pulmonary emboli prevented over the entire range of duration of anticoagulation. Practically, the results of this intentionally biased analysis obviate the need for multiple sensitivity analyses, whose results would in any setting (that is, increased bleeding risk, lower efficacy of anticoagulation) reinforce our results. In other words, if the use of the most optimistic clinical data favouring prolonged anticoagulation does not result in a clear therapeutic benefit (more pulmonary emboli prevented compared with the number of major bleedings induced), any other scenario (with less optimistic data) will invariably lead to the conclusion that the risks of prolonged anticoagulation overwhelm its benefits. Finally, we measured the "threshold" rate of major haemorrhages below which the number of clinical pulmonary emboli prevented would exceed the number of bleedings induced, thus favouring prolonged oral anticoagulation. This analysis revealed that it is only when the risk of bleeding is below 2.5% per year (0.2% per month) that prolonged anticoagulation becomes the preferred strategy.

On the other hand, the number of recurrent deep vein thrombi prevented by prolonged prophylactic treatment widely exceeds the number of iatrogenic haemorrhages induced. In sensitivity analyses this benefit is maintained even with less favourable assumptions. As expected, with the same set of favourable assumptions among patients who are not carriers of

factor V the risks of prolonged antithrombotic treatment overwhelm its benefit.

Discussion

For all patients (factor V Leiden carriers and non-carriers) recovering from an acute deep vein thrombosis in the lower limbs, the decision whether to prolong the usually recommended 3 month course of anticoagulation treatment rests on a trade off between the efficacy of anticoagulants in preventing thromboembolism and the risks of precipitating a haemorrhagic event. The thromboembolic events of concern are recurrent deep vein thrombi, but clinical pulmonary embolism deserves special consideration because it can be fatal. The risk associated with oral anticoagulants is bleeding. Major bleeding may also be life threatening and result in permanent morbidity. As some experts advocate prolonged or even indefinite oral anticoagulant treatment to prevent recurrent deep vein thrombi and possible subsequent pulmonary emboli among factor V carriers our model measures the potential risks and benefits of this option.

If we assume that one pulmonary embolism prevented equals one major iatrogenic bleeding episode, the results suggested by our model are clear. With the best available evidence the analysis of risks and benefits of prolonged prophylactic anticoagulants among factor V carriers suggests that despite use of clinical data deliberately and consistently favouring anticoagulant treatment, prolonged prophylactic oral anticoagulants result, at least beyond 1 year, in more risks (major haemorrhages) than benefits (pulmonary emboli prevented).

Additional number of clinical thromboembolic events (pulmonary embolism and deep vein thrombosis) prevented and major haemorrhages induced by different durations of oral anticoagulation (1 to 5 years) after the usually recommended 3-month treatment compared with antithrombotic treatment triggered only by the occurrence of clinical events for a hypothetical cohort of 1000 factor V Leiden carriers and non-carriers, respectively

Put simply, should we encourage widespread genetic screening to detect factor V carriers until we can prove that prolonged antithrombotic treatment does not work, or should we avoid screening until we can prove that the treatment does work? One end of the spectrum is advocated by those who argue that it is important to marshal all available resources to reduce the risk of adverse events until controlled trials prove (if they ever prove) that such efforts are ineffective or cause net harm. At the other extreme, more cautious groups emphasise the need to avoid the risks of early genetic detection unless a net benefit of screening can be definitively shown in clinical trials. We tend to support the latter perspective. Moreover, as resources available for healthcare expenditures become more limited the decision to promote a strategy of unproved benefit would be a very expensive policy for society.

Limitations of the study

The present analysis has three main limitations. Firstly, it is based on data from literature, which are limited or controversial, as is often the case in complex issues. Thus, our results are valid only within the framework of the model and the limits of the clinical data. Specifically, the real incidence of bleeding, a key parameter in our analysis, is difficult to assess because patients at increased risk of haemorrhage are systematically excluded from experimental trials. In clinical practice, or in observational studies, it is likely that patients present higher rates of bleeding.²⁷ Our model suggests, however, that genetic screening and subsequent prolonged oral anticoagulant treatment may be harmful for patients despite simultaneous use of a set of clinical data consistently favouring the clinical benefit provided by prolonged oral anticoagulation (low bleeding risk extracted from experimental studies, high rate of clinical pulmonary emboli, maximum efficacy of oral anticoagulants). Consequently, our conclusions are robust, and physicians might feel comfortable about their therapeutic option. Secondly, our results assume that one pulmonary embolism prevented equals one major bleeding episode induced, which is certainly not true, also perhaps from a medicolegal point of view. It is our impression, however, that the decision whether to give prophylaxis to a patient is mostly influenced by the frequency at which the two potentially fatal clinical events may occur. Ideally, we recognise that long term morbidities from intracranial bleeding (for instance, hemiplegia), recurrent deep vein thrombosis (the post-thrombotic syndrome), and pulmonary embolism (pulmonary hypertension) should be stratified by degree of disability, with a utility value specified for each category. The incidence of chronic disability after these events is uncertain, however, and has not been characterised well enough to make such adjustments reliable. Moreover, mortality from major haemorrhage due to anticoagulant treatment is of the same order of magnitude as mortality from pulmonary embolism.^{21 22 26} Thirdly, the necessary assumptions we made may not apply to all patients, and options like reduced intensity of anticoagulation (international normalisation ratio 1.5-2) were not considered.

Key messages

- Patients who carry the factor V Leiden mutation have a more than twice the risk of recurrence after a first episode of deep vein thrombosis
- Before screening for the abnormality is advocated in all patients recovering from acute deep vein thrombosis, it should be determined whether carriers of the mutation would benefit from the diagnosis
- The risks (major haemorrhage) of extended oral anticoagulation beyond the usually recommended 3 month period would exceed its benefits, in terms of clinical pulmonary emboli prevented
- The decision to promote widespread screening programmes to detect factor V mutation should be questioned in the absence of clinical benefit provided by extended use of oral anticoagulants

Conclusions

In conclusion, even if the most favourable set of assumptions is used, our model suggests that the benefits of prolonged oral anticoagulant treatment in factor V Leiden carriers after a first episode of deep vein thrombosis are usually overwhelmed by its risks. Specifically, for all different durations of prophylactic treatment (1 to 5 years) tested, our model demonstrates that the risks of major haemorrhage exceed the number of clinical pulmonary emboli that could be prevented. Prolonged anticoagulation treatment would be beneficial only if one assumes that one episode of recurrent deep vein thrombosis prevented equals one major bleeding event. Consequently, this lack of clinical evidence showing a net benefit of prolonged anticoagulation should question the decision to promote genetic screening programmes to detect the factor V mutation in all patients recovering from acute idiopathic deep vein thrombosis. This questioning is even more necessary as three studies suggested recently that the risk of pulmonary embolism in carriers of the factor V Leiden mutation might be less than the risk of deep vein thrombosis,²⁸⁻³⁰ a fact which should further decrease the utility of prolonging anticoagulant treatment and, consequently, the benefit of screening. On the other hand, two recent reports point to the fact that factor V Leiden might be a significant risk factor for recurrent deep vein thrombosis only after the age of 50 years,^{10 31} which would restrict our conclusions to this category of patients, at least in men. Lastly, our conclusion is confined to screening for the factor V Leiden mutation in an unselected population of patients with a first episode of deep vein thrombosis and does not imply that extensive thrombophilia screening (including factor V Leiden, protein C, protein S, antithrombin, prothrombin 3' polymorphism, lupus anticoagulant, anticardiolipin antibodies, plasminogen) should not be performed in a young patient presenting with a thromboembolic event or in the presence of recurrent episodes of idiopathic deep vein thrombosis or if there is a strong familial history of thrombophilia.

Contributors: HB initiated the formulation of the primary hypothesis of the study, discussed core ideas, and participated in data collection and in writing the manuscript. FPS participated in the formulation of the primary hypothesis of the study, discussed core ideas, and designed and built the decision analysis model. He also collected the data from the literature, analysed and interpreted the results, and wrote the manuscript.

Funding: No external funding.

Conflict of interest: None.

- Bertina RM, Koeleman BPC, Koster T, Rosendaal FR, Dirven RJ, de Ronde H, et al. Mutation in blood coagulation factor V associated with resistance to activated protein C. *Nature* 1994;369:64-7.
- Dahlback B. Inherited thrombophilia: resistance to activated protein C as a pathogenic factor of venous thromboembolism. *Blood* 1995;85:607-14.
- Ridker PM, Hennekens CH, Lindpainter K, Stampfer MJ, Eisenberg PR, Miletich JP. Mutation in the gene coding for coagulation factor V and the risk of myocardial infarction, stroke and venous thromboembolism in apparently healthy men. *N Engl J Med* 1995;332:912-7.
- Koster T, Rosendaal FR, de Ronde H, Briet E, Vandenbroucke JP, Bertina RM. Venous thrombosis due to poor anticoagulant response to activated protein C: Leiden thrombophilia study. *Lancet* 1993;342:1503-6.
- Koepeke JA. Testing for hereditary hypercoagulability. Activated protein C resistance (editorial). *Am J Clin Pathol* 1996;106:161-2.
- Vandenbroucke JP, Koster T, Briet E, Reitsma PH, Bertina RM, Rosendaal FR. Increased risk of venous thrombosis in oral-contraceptive users who are carriers of factor V Leiden mutation. *Lancet* 1994;344:1453-7.
- Vandenbroucke JP, van der Meer FJM, Helmerhorst FM, Rosendaal FR. Factor V Leiden: should we screen oral contraceptive users and pregnant women? *BMJ* 1996;313:1127-30.
- Ridker PM, Miletich JP, Stampfer MJ, Goldhaber SZ, Lindpainter K, Hennekens CH. Factor V Leiden and risks of recurrent idiopathic venous thromboembolism. *Circulation* 1995;92:2800-2.
- Simioni P, Prandoni P, Lensing AWA, Scudeller A, Sardella C, Prins MH, et al. The risk of recurrent venous thromboembolism in patients with an Arg⁵⁰⁶ → Gln mutation in the gene factor V (factor V Leiden). *N Engl J Med* 1997;336:399-403.
- Eichinger S, Pabinger I, Stümpflen A, Hirschl M, Bialonczyk C, Schneider B, et al. The risk of recurrent venous thromboembolism in patients with and without factor V Leiden. *Thromb Haemost* 1997;4:624-8.
- Sonnenberg FA, Beck JR. Markov models in medical decision making: a practical guide. *Med Decis Making* 1993;13:322-8.
- Research Committee of the British Thoracic Society. Optimum duration of anticoagulation for deep-vein thrombosis and pulmonary embolism. *Lancet* 1992;340:873-6.
- Schulman S, Rhedin AS, Lindmarker P, Carlsson A, Lators G, Nicol P, et al. A comparison of six weeks with six months or oral anticoagulation after a first episode of venous thromboembolism: duration of anticoagulation trial study group. *N Engl J Med* 1995;332:1661-5.
- Levine MN, Hirsh J, Gent M, Turpie AGG, Weitz J, Ginsberg J, et al. Optimal duration of oral anticoagulant therapy: a randomized trial comparing four weeks with three months of warfarin in patients with proximal deep vein thrombosis. *Thromb Haemost* 1995;74:606-11.
- Schulman S, Lockner D, Juhlin-Dannfelt A. The duration of oral anticoagulation after deep vein thrombosis. *Acta Med Scand* 1985;217:547-52.
- Holmgren KAJ, Andersson G, Fagrell B, Johnsson H, Ljunberg B, Nilsson E, et al. One- month versus six-month therapy with oral anticoagulants after symptomatic deep vein thrombosis. *Acta Med Scand* 1985;218:279-84.
- Beyth RJ, Cohen AM, Landefeld CS. Long-term outcomes of deep-vein thrombosis. *Arch Intern Med* 1995;218:279-84.
- Prandoni P, Lensing AWA, Büller HR, Carta M, Cogo A, Vigo M, et al. Comparison of subcutaneous low-molecular-weight heparin with intravenous standard heparin in proximal deep-vein thrombosis. *Lancet* 1992;339:441-5.
- Koopman MWM, Prandoni P, Piovello F, Ockelford PA, Brandjes DP, van der Meer J, et al. Treatment of venous thrombosis with intravenous unfractionated heparin administered in the hospital as compared with subcutaneous low-molecular-weight heparin administered at home. *N Engl J Med* 1996;334:682-7.
- Monreal M, Ruiz J, Olazabal A, Arias A, Roca J. Deep venous thrombosis and the risk of pulmonary embolism: a systematic study. *Chest* 1992;102:677-81.
- Ginsberg JS. Management of venous thromboembolism. *N Engl J Med* 1996;335:1816-28.
- Carson JL, Kelley MA, Duff A, Palevitch M. The clinical course of pulmonary embolism. *N Engl J Med* 1992;326:1240-5.
- Paraskos JA, Adelstein SJ, Smith RE, Rickman FD, Grossman W, Dexter L, et al. Late prognosis of acute pulmonary embolism. *N Engl J Med* 1973;289:55-8.
- Claggett GP, Anderson FA, Heit J, Levine MN, Wheeler HB. Prevention of venous thromboembolism: Fourth American College of Chest Physicians consensus conference on antithrombotic therapy. *Chest* 1995;108(suppl):312-34S.
- Levine M, Raskob GE, Landefeld CS, Hirsh J. Hemorrhagic complication of anticoagulant treatment: Fourth American College of Chest Physicians consensus conference on antithrombotic therapy. *Chest* 1995;108(suppl):276-90S.
- Bounameaux H, de Moerloose P, Sarasin FP. Optimal duration of oral anticoagulant therapy following deep vein thrombosis of lower limbs. *Blood Coagul Fibrinolysis* 1996;7:507-14.
- Landefeld CS, Beyth RJ. Anticoagulant-related bleeding: clinical epidemiology, prediction, and prevention. *Am J Med* 1993;95:1710-1.
- Desmarais S, De Moerloose P, Reber G, Minazio P, Perrier A, Bounameaux H. Resistance to activated protein C in an unselected population of patients with pulmonary embolism. *Lancet* 1996;347:1374-5.
- Manten B, Rudi G, Westendorp J, Koster J, Reitsma PH, Rosendaal FR. Risk factors profiles in patients with different clinical manifestations of venous thromboembolism: a focus on the factor V Leiden mutation. *Thromb Haemost* 1996;76:510-3.
- Martinelli I, Cattaneo M, Panzeri D, Mannucci PM. Low prevalence of factor V: Q⁵⁰⁶ in 41 patients with isolated pulmonary embolism. *Thromb Haemost* 1997;77:440-3.
- Ridker PM, Glynn RJ, Miletich JP, Goldhaber SZ, Stampfer NJ, Hennekens CH. Age-specific incidence rates of venous thromboembolism among heterozygous carriers of factor V Leiden mutation. *Ann Intern Med* 1997;126:528-31.

(Accepted 8 September 1997)

A memorable patient

Déjà vu

It was a dark winter afternoon in January 1981. The friendly Dublin porter at the top of the formidable entrance steps to the Mater Hospital pointed to the corridor where the membership examination was being held. The old high ceilinged wards were dim, and the lights outside brightened the gloom. The long case was behind the screens in the corner of the ward and my well rehearsed approach of history taking followed by examination started. He was an active lively 13 year old, more streetwise for his years than me, with a broad Dublin brogue which his rapid delivery made it almost impossible to follow. Communication was a major problem, and his attention was swiftly slipping.

Unable to obtain any history my anxiety and despair quickly rose. The only interest he had in matters medical was my stethoscope, which in desperation I gave to him and proceeded anxiously to start the examination with his pulse, conscious that the allotted time was ticking by. Following a short period of fruitless examination, I retrieved the stethoscope after a struggle and realised that part of the struggle was due to his difficulty releasing it, and the presence of myotonus was revealed. The diagnosis now became clearer, and the examiners were satisfied that a proper history and examination had taken place.

Ten years later as a membership examiner I arrived in the same hospital to see the minor cases before the examination started. The harassed registrar showed the examiners the minor cases, but apologised that the one with dystrophica myotonia had failed to arrive. At that moment a young man sauntered into the ward with his can of coke and paper folded at the racing page. A relieved registrar told us that the final short case had arrived. Slowly the sense of strange familiarity, accompanied by a distinct sense of unease and déjà vu, was confirmed by his broad, still almost unintelligible diction. Thanking him for his help with the examination, I asked if he had attended before and he replied, "Oh yes Doc, for a brave number of years."

It was a unique but unsettling experience to examine on a case that I had previously been examined on.

Timothy Beringer, consultant physician in care of the elderly, Belfast

We welcome articles up to 600 words on topics such as *A memorable patient*, *A paper that changed my practice*, *My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk.