ANTICOAGULATION THERAPY: PAST, PRESENT, AND FUTURE

MANAGEMENT SYSTEMS

By

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To the faculty of Washington State University:

The members of the committee appointed to examine the ICN Research requirements and manuscript of Coreen (Cory) M. Siobig find it satisfactory and recommend that it be accepted.

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Someone once said, seventy percent of success in life is showing up. These last four years of interactive long distance WHETS schooling has involved people coming, people going; with some people staying a while, and some leaving footprints on my heart.

Thank you, Sue Rogers, for showing up with me during this journey of knowledge. I will never forget the footprints we walked in Spokane for advanced H&P assessment and our free continental breakfast. Remember Ms. Budd…. never rattle your potato chip bag, then fall asleep and snore in a live lecture.

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To my husband, Troy and our girls; Audra and Tori that have cooked dinner, cleaned the house, folded the clothes, took care of me, the dogs, the chicken, & each other during this journey of knowledge. Thank you, I love you…..

Yours are the footprints........................
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Abstract

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The number of patient’s under oral anticoagulation therapy has markedly increased (Meschengieser, Casais, Sanchez & Lazzari, 2000). The demand for anticoagulation management has in turn increased (Parry, Fitzmaurice & Raftery, 2000). Cardiac indications for the use of coumadin are listed in table 1. Morbidity and mortality from atrial and venous thromboembolism has been significantly reduced with anticoagulation therapy.

Patient’s taking anticoagulants must make daily decisions involving their diet, medication dosage, blood test monitoring, and keeping appointments. Patients need to experience success in their self-care performance and effectively interact with the healthcare system to obtain the necessary support to manage their anticoagulation therapy.

The focused care available through specialized anticoagulation clinic services enhances patient compliance and offers a more accessible monitoring process. Clinical guidelines that specifically outline anticoagulation therapy initiation, patient assessment, patient education, and cost analysis are being scrutinized through retrospective clinical trials. Developments of standard
pharmacokinetic anticoagulation protocols to perform anticoagulation dosage management, dosage adjustment, and excessive anticoagulation management need to be agreed upon.

Future anticoagulation management with in-home blood testing accompanied by practitioner oversight has yielded high patient satisfaction and more therapeutic INR results. Successful anticoagulation management begins with providing the patient with the skills they need to attain within range INR results to avoid hemorrhage or thromboembolism complications. Consistent motivated oversight of anticoagulation management is an important factor in positive outcomes with anticoagulation therapy.
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Introduction

The number of patient's under oral anticoagulation therapy has markedly increased (Meschengieser, Casais, Sanchez & Lazzari, 2000). The demand for anticoagulation management has in turn increased (Parry, Fitzmaurice & Raftery, 2000). Cardiac indications for the use of coumadin are listed in table 1. Morbidity and mortality from atrial and venous thromboembolism has been significantly reduced with coumadin therapy.

Patients taking anticoagulants must make daily decisions involving their diet, medication dosage, blood test monitoring, and keeping appointments. Patients need to experience success in their self-care performance and effectively interact with the healthcare system to obtain the necessary support to manage their anticoagulation therapy.

Successful aging calls for effective adaptation, which in turn implies flexible use of coping strategies to optimize personal functioning and well-being (Slangen-de, Midden & VanWagenberg, 2001). In the same sense, the fundamental message of self-efficacy theory for those involved with task accomplishment is that they experience success in their self-care capabilities. Self-efficacy can predict how people function in terms of behavior, effort expenditure, persistence, thought patterns, and emotional reactions (Van Der Bijl & Shortridge-Bagett, 2001). Self-efficacy can be measured in terms of successful medication management (Alijasem, Peyrot & Rubin, 2001).

This article will explore performance improvement of past and present specialized models of coumadin management; the effectiveness of that
management, as well as initiation of anticoagulation therapy. Anticoagulation dosing management, dosing adjustment, and management of excessive anticoagulation is offered via tables and algorithms. Patient assessment and patient centered education concerning bleeding and thromboembolism are reviewed. A cost analysis of past versus present anticoagulation oversight is offered. Future trends in anticoagulation management are presented.

Monitoring of Anticoagulation

The majority of people with chronic conditions are living normal lives, but are faced with the threat of recurrent exacerbation, higher health care costs, more days lost from work, and the risk of long term limitations and disabilities (Hoffman, Rice, and Sung, 1996). In the past, patients prescribed an oral anticoagulant were traditionally sent to a laboratory for International Normalized Ratio (INR) blood testing that involved a fragmented, labor-intensive, and time consuming coordination of their anticoagulation instructions.

Coumadin management is in the midst of a transition. The INR developed by the World Health Organization in the early 1980's was designed to eliminate problems in oral anticoagulant therapy caused by variability in the sensitivity of different commercial sources and different lots of thromboplastin to blood coagulation factor VII. The INR is used worldwide by most laboratories performing oral anticoagulation monitoring, and is routinely incorporated into dosage planning for patients receiving coumadin (Riley, Rowe & Fisher, 2000).

The INR is the mathematical correction to normalize (standardize) the results of the prothrombin time test. The International Sensitivity Index (ISI)
expresses the sensitivity of a particular thromboplastin reagent. The ISI is determined by direct or indirect calibration against a standard reagent with a known sensitivity to the antithrombotic effect of oral anticoagulants. The higher the ISI, the less “sensitive” the thromboplastin. The calculation is: $INR = \frac{\text{patient PT}}{\text{mean normal PT}} \times \frac{1}{\text{ISI}}$ (Ansell et al., 1997; Nadeau et al., 2000; Tiede et al., 1998).

Technological advances in Coumadin Management in 1989, produced a Point Of Care (POC) capillary blood-testing machine that offers INR blood determination within minutes and at the patient’s fingertip. POC INR measurement offers simplified management of oral anticoagulation by allowing the practitioner to give dosing advice in person within a small amount of time (Ansell 1999; Ansell et al., 2001; Nadeau et al., 2000).

Today, several computer-based and Web-based management systems for anticoagulation monitoring are on the market. Some of the software packages are record keeping systems only, while others also include clinical decision-support tools, such as testing and dosage recommendations. There are also anticoagulation decision-support systems for the Palm and compatible handhelds; but they generally do not provide a patient tracking function.

Some of the more popular software options are CoumacCare (at www.coumacare.com), CoagClinic (at www.standingstoneinc.com/coagclinic.htm), Dawn AC (at www.4s-dawn.com/dawnac), Anticoagulation Information Manager (at www.wellersoft.com/AIM.html), Clever Clog (at www.clevclot.freeserve.co.uk), and INRstar (at www.anticoagulation.com/inrstar.htm).
All these programs provide patient-tracking capability and some provide clinical decision-support capability. Some companies charge a flat fee for software, while others charge per number of patients. All software automate the tedious details of patient tracking and documentation (WSMA, 2002).

History of Coumadin Use

Oral anticoagulants emerged from 1920's veterinary medicine research on a hemorrhagic disorder afflicting cattle that consumed spoiled sweet clover hay. Sweet clover contains a chemical known as coumarin. Several chance encounters led Karl Link and his University of Wisconsin team to the identification of dicumarol as the offending agent in 1939. Because the Wisconsin Alumni Research Foundation (And Raisin Incubator Nose) supported much of the work; the acronym warfarin was established. Link later developed warfarin as a rodenticide, but therapeutic applications were not initially recognized. In 1955, President Dwight D.Eisenhower's post MI treatment brought coumadin to the forefront. Coumadin consumption is at number fourteen on the list of prescription selling drugs (Duxbury & Poller, 2001; Fihn, 1995; Mueller & Scheidt, 1994).

Clinical pharmacology

The pharmacokinetics, drug, and dietary interactions of coumadin are intricate. The potential benefits from prevention of stroke, DVT, PE, or even death must be carefully weighed with the costs/risks of a bleed complication. Both bleeding events and thromboembolic events occur when the INR is found outside the therapeutic range (Chafin, Ritter, James & Self, 2000; Nadeau et al., 2000).
Ansell et al., (2001) and Meschengieser et al., (2000) describe two important determinants of therapeutic effectiveness and of reducing hemorrhage risk: intensity of therapy and time in the therapeutic range. Ideally, the INR should be kept in the therapeutic range, as determined by patient diagnosis and risk factors. Many factors influence the attainment of this goal. These include physiologic and pharmacological factors, such as interacting drugs or illnesses that affect the pharmacokinetics or pharmacodynamics of coumadin, dietary or gastrointestinal (GI) factors that affect the availability of vitamin K1, or physiologic factors that affect the synthetic or metabolic fate of the vitamin K-dependent coagulation factors.

Patient-specific factors such as adherence to a therapeutic plan are also important. Lastly, the provider’s ability to make appropriate dosing and follow-up decisions will have a profound impact, if such decisions are incorrect. The comprehensive management of these variables requires a knowledgeable provider, an organized system of follow-up, reliable prothrombin time (PT) monitoring, and good patient communication and education (Ansell et al., 1997, 1999, 2001; Hirsh et al., 1999).

Coumadin acts by inhibiting the synthesis of vitamin K dependent clotting factors, which include Factors II, VII, IX, and X, and the anticoagulant proteins C & S. Half-lives of these clotting factors are as follows: Factor II – 60 hours, VII – 4-6 hours, IX – 24 hours, and X – 47-72 hours. The half-lives of proteins C and S are approximately 8 hours and 30 hours, respectively (PDR, 2002).
Because thrombi are held together by small amounts of fibrin, anticoagulants are used to prevent this fibrin deposit. Oral anticoagulants block the regeneration of vitamin K, thus depleting the amount of vitamin K proteins available for coagulation reactions (Dahlback, 2000). This in turn interferes with synthesis of coagulation factors II, VII, IX, and X. Prothrombin is converted to thrombin via the vitamin K prothrombin complex (Xa- Va- Ca2+). Thrombin, the key enzyme in coagulation, has many roles including converting fibrinogen to fibrin, activating platelet activating factor V and factor VIII, combining with thrombomodulin to activate protein C. Downregulation of formation of the vitamin K enzymes, especially the amount of available thrombin through anticoagulation therapy, has a major influence on the coagulation cascade.

Coumadin has a reasonably predictable onset and duration of action. The anticoagulation effect of coumadin is due to the decrease in the activity of Factor VII. The antithrombotic effect of coumadin is due to the decrease in the activity of Factor II. In addition, a simultaneous decrease of Factor II will decrease protein C; which can create a hypercoagulable state resulting in a risk for a bleed. A single dose of coumadin has a duration of action of 2 to 5 days. Coumadin has no effect on an already formed thrombus, and will not reverse the damage to ischemic tissue. Coagulation inhibition via coumadin therapy can be affected by many variables that exist between individuals taking the same dose of treatment, including liver function in the synthesis of the clotting factors, enhancement of the effect of other medications, and dietary intake, and absorption of vitamin K. The goal of anticoagulation treatment is to stop the cascade of additional
thromboembolic events. Anticoagulants can control many conditions, but they do not cure them (Tiede et al., 1998; Weitz & Hirsh, 2001).

**Traditional Anticoagulation Management Systems**

Advising patients on oral anticoagulants has involved a labor-intensive paper shuffling process, a time delay (e.g., 6 hrs) to receive lab (INR) results, and telephone communication of those results to the patient. Advising patients via telephone invites confusion, is time consuming, and envelops a large amount of non-reimbursable practitioner time (at a time when reimbursement percentages are decreasing).

The typical medication surveillance regimen for an anticoagulated patient begins with a formal education session. A consent is signed, documenting the agreement between the provider and patient to follow the prescribed treatment plan. Review of the indications for coumadin therapy, the definition of anticoagulation, and INR goals need to be explained. Frequency of clinic visits and INR blood testing should be reviewed. Factors influencing coumadin therapy and when the patient should seek medical care due to adverse effects should be discussed. The patient should also be offered information regarding obtaining a medic alert tag and pill box (Kroner 1998).

Ansell et al., (1997) found the amount of information presented to the patient beginning anticoagulation therapy could be overwhelming. Research has shown that, on average, 40% of patients forget the information given to them. Written information reinforces verbal information, helps patients remember important facts about therapy, and enhances knowledge about their disease.
Since therapy is often long term, and the patient and disease characteristics are not static, periodic reassessment should be part of the educational program.

Elderly patients with multiple medications, atrial fibrillation, history of stroke, and low educational ability may not be able to follow directions. They may find it difficult to understand written materials and dosing instructions; thus not fully comprehending the risks and benefits of anticoagulation. Brochures should be written at or below the 6th grade reading level (Estrada, Hryniewicz, Higgs, Collins, & Byrd, 2000; Fulmer et al., 1999).

The traditional anticoagulation services involve a standing lab order with ICD-9 diagnosis coding, a venous blood draw from the lab of choice, a time delay for lab (INR) results, and one or more phone calls back to the patient. Results, dosage titration, and next test recommendation need to be conveyed to the patient. Oral anticoagulation therapy is a complex and labor-intensive therapeutic modality, where not only good dosing decisions, but attention to detail and communication can make the difference between success and failure (Ansell et al., 2001).

In a longitudinal inception study on outpatient anticoagulation clinic implementation, Norton & Gibson (1996) contrast anticoagulation management by individual physicians to management by an outpatient anticoagulation clinic. From a population of 1,000 coumadin patients at Overlake Hospital in Bellevue, WA., the researchers found individual physicians customarily manage their oral anticoagulation patients through a handful of disjointed steps, as described above. Removed from this management process are visual patient/provider
interaction and practitioner reimbursement. Added to this management system are increased chances for error in communication.

Coumadin instructions by phone may contain environmental distractions, obscure an already anxious patient's history giving, and add confusion with dosage changes and test frequency. Telephone practitioners rely on their own and the patient's sense of hearing for verbal clinical descriptors (Devore, 1999; Hoare, Lacoste, Haro, & Conyers, 1999).

Most clinical laboratories report their INR results in a batched form. This creates a large list of INR results to be communicated via return phone call to providers, usually near the end of the workday. This can create a domino effect for high capacity call times and can add pressure and elevated prioritization to daily telephone coumadin management and triage responsibilities. Telephone calls remain a non-billable service.

Complication rates are increased among coumadin patients when inconsistent patient supervision occurs (Pubentz, Calcagno and Teeters, 1998; and Sawacki, 1999). Deficient accounting of patient adherence and lack of patient education, result in higher treatment failures.

**Specialized Anticoagulation Management Systems**

Systematic outpatient anticoagulation management services were first established in the United States in the late 1960s (Witt & Tillman, 1998). These services may be defined as a system of care designed to coordinate and optimize the delivery of anticoagulation therapy and evaluate patient-specific risks and benefits. The management of anticoagulation dosing and prescription
attainment evaluates INR results, diet, concomitant drug therapy, and most important the patient's clinical evaluation (Ansell et al., 1997).

In 1991, a clinical pharmacy specialist in Colorado began monitoring coumadin therapy for a group of Internal Medicine patients. In 1994, requests to expand the service brought a retrospective analysis reviewing the benefits and feasibility for expansion of those services to all anticoagulated patients (Witt & Tillman).

The American Society of Health-System Pharmacists and some state pharmacy societies have developed anticoagulation traineeship programs for pharmacists. However, these programs do not extend to other healthcare practitioners (Ansell et al., 1997). Currently, there is no recognized means of ensuring the competency of anticoagulation therapy to all providers.

Outpatient anticoagulation clinics continue to develop, bringing together patient results and dosing recommendation through streamlined point-of-care fingerstick capillary blood testing with computerized decision support systems. This type of anticoagulation management service will impact patient and provider satisfaction, in-range INR consistency and time management.

Wong, Norton and Wittkowsky (1999) have demonstrated, in a longitudinal retrospective review of anticoagulation management, that attention must be directed toward coumadin dosing regimen to avoid confusion, dosing errors, missed doses or missed lab tests for out of range INR variability. The study compared 109 same day dose patients with 177 alternate day dose patients.
The study established baseline information for future studies on anticoagulation service outcomes.

A Colorado clinic retrospective outcome comparison between an anticoagulation service directed by physicians and nurses, and a service by a clinical pharmacy service, found more in-range therapeutic INR's with the primary pharmacy group (Witt & Tillman, 1998). The specific size of the groups was not stated. The stability of this anticoagulation service was related to a more dedicated monitoring service among the pharmacy group. The pharmacy group had a paging service, a cellular phone, and a laptop computer with modem, and was available 24 hours a day.

**Initiation of Anticoagulation Therapy**

Oral anticoagulant therapy has been traditionally initiated with fixed loading doses, which are larger than those required for maintenance of an adequate anticoagulant effect (Ginsberg, Crowther, White and Ortel, 2001). Historically, loading doses, as large as 1 mg/kg were used to produce prothrombin times exceeding the lower limit of the therapeutic range within 24 to 36 hours of the first dose.

The risk of major bleeding is highest during the first month of therapy (Beyth & Landefeld, 1995). This is a period when many patients are making the adjustment from inpatient to outpatient settings and when multifactorial system illness, concurrent treatment, and the anticoagulant effect of warfarin may fluctuate.
Currently, the average maintenance dose of coumadin, 5 mg, is recommended as the initial starting dose (Ansell et al., 2001; Goolsby, 2002; Harrison et al., 1997; Mandani et al., 1999). Elderly patients with co-morbid liver or nutritional disorder or who are at increased risk of bleeding should be started at a lower dose. Regardless of the starting dose, INR should initially be monitored daily, until the therapeutic range is verified on two consecutive days, at which time monitoring can then be decreased to two or three times a week for up to two weeks. If the level remains stable, the monitoring rate can be further decreased (Ansell et al., 2001).

The optimal therapeutic range for oral anticoagulant therapy was reviewed by the Committee on Antithrombotic Therapy of the American College of Chest Physicians (ACCP) and the National Heart, Lung, and Blood Institute in 1986, 1989, 1992, 1995, and again in 1998. The recommendation made at the earlier conferences, that the intensity of coumadin treatment should be reduced for many indications, continues to be upheld. Whenever a more intense international normalized ratio (INR) is compared directly in a randomized trial, with an INR of 2.0-3.0, the less intense INR is as effective and safer. Maintaining the INR level within the therapeutic range is achieved by targeting the mid-level of the INR range (eg., 2.5 for a designated range of 2.0-3.0 and 3.0 for a designated range of 2.5-3.5). Establishing a targeted INR range entails careful assessment of the indication for therapy. The Committee on Antithrombotic Therapy of the ACCP recommends an INR of 2.0-3.0 for all indications except mechanical prosthetic heart valves, for which an INR of 2.5-3.5 is recommended.
Anticoagulation Dosing

Studies in primary care settings have found lack of experience in dosing and recognition of individual patient trends with coumadin medication can be overcome when computerized decision support systems are in place (Fitzmaurice et al., 2000). A computerized dosing schedule can be implemented to encompass nearly every milligram dose of varying pill size. Coumadin is available in color-coded doses of 1 mg, 2 mg, 2 1/2 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7 1/2 mg, and 10 mg.

Each computer generated patient page should include phone number, reason for anticoagulation, INR goal, special circumstance comments, INR results, schedule of dosing recommendation and next test date. Table 2 offers an example of a computerized anticoagulation dosing schedule without the patient data. The total weekly milligram dosing is divided up per week (Yakima Heart Center, 1996; Yakima Valley Memorial Hospital, 1999).

Anticoagulant Dosage Adjustments

Ginsberg et al. (2001) notes algorithm guided coumadin initiation, results in a more rapid achievement of a therapeutic INR, than simple practitioner guided coumadin management. A dosage assessment algorithm dependent on the INR lab result is presented in Figure 1. The dosing is based on the weekly milligram-dosing schedule presented in Table 2. The algorithm and table are used
together to coordinate closer patient medication review (Wilson-Norton & Gibson, 1996; Witt & Tillman; Wieland, Ewy & Wise, 1998).

Management of Excessive Anticoagulation

Bleeding is the leading complication of oral anticoagulation. Ginsberg et al. (2001); Hirsh et al. (2001); Taylor, Cohen & Ebramhim, (2001); and Turpie Weart & White, (1998) found a strong relationship between the risk of bleeding and the INR level, with this risk rising sharply when the INR exceeds 5.0. Bleeding that occurs when the INR is less than 3.0 is frequently associated with an obvious underlying medical cause or an occult gastrointestinal or genitourinary lesion. Patients should be instructed to notify their health care provider, if they experience any change in dietary pattern, medication regimen, or bleeding. Any such change will require more frequent INR monitoring. A provider should consider monitoring for potential hemorrhage with both the fecal occult blood test and hematocrit measurement (Kajubi, 2000).

Anticoagulation specialists agree that therapy to reverse anticoagulation is often too aggressive in patients with a high International Normalized Ratio (INR). This is due to small increases in coumadin availability cause large increases in the INR. Before initiating treatment with vitamin K, it is essential to assess the risk of bleeding and its source (Turpie, Weart & White, 1998).

Current guidelines (Table 3) suggest that if the INR exceeds a therapeutic threshold, but is between 5 and 9 without significant bleeding, coumadin should be held for 1-2 doses and consider giving vitamin K orally. When the INR is >9.0 with serious bleeding, rapid reversal of anticoagulant effect can be obtained by
giving 10 mg vitamin K by slow IV infusion, or giving fresh frozen plasma, or prothrombin complex concentrate (Ansell et al., 2001; Hirsh et al., 2001; Nadeau et al., 2000; Turpie, Weart & White, 1998).

**Patient Education with Anticoagulation**

The Veterans Administration Pittsburgh Healthcare system developed a patient education form (table 4) that highlights patient-specific indications for coumadin. The provider should review the form with the patient and make sure the patient knows the strength and color of their coumadin tablets. Patients should be provided with pamphlet information to obtain a Medic Alert tag, pill cutters, pill boxes, telephone numbers to the clinic and the education booklet, "A Patients' Guide to Using Coumadin" provided by DuPont Pharma (Kroner, 1998). Patients should have an understanding that life-threatening bleeding can occur from an overdose of coumadin. Table 5 presents key patient education points. Patients must take the medication exactly as prescribed and have the blood tests on the days instructed (Kroner, 1998; Nadeau et al., 2000; Turpie, Weart & White, 1998).

**Cost Analysis**

Because of improved outcomes with fewer hospitalizations and emergency department visits, the management of anticoagulation therapy by an anticoagulation management service may prove to be cost effective (see table 6). Chiquette, Amato & Bussey (1998) found savings of $1,621 per patient year of therapy in their comparative study due to a significant reduction in hospitalizations and emergency department visits. Wilt, Gums, Ahmen & Moore
(1995) found an extremely high rate of savings of $4,072 per patient year of therapy due to reduced utilization of services. These observations need to be validated by large scale randomized studies (Ansell et al., 2001; Chiquette et al., 1998; Wilt et al., 1995).

In a prospective, cohort study, Mandani et al. (1999) found lower total hospital costs through a bivariant analysis with a pharmacist-managed anticoagulation service, as compared to traditional care. This observational study from the Detroit Medical Center compared 49 traditional anticoagulation management care patients with 48 pharmacist-managed anticoagulation group patients. The study found clinical and economic gains through lower total hospital costs when compared with traditional care.

Hamby, Weeks and Malikowski (2000) emphasize that establishing an anticoagulation clinic is only the first step toward reducing complications related to anticoagulation. They identified twelve patients in a four-month period that experienced coumadin related adverse effects.

Future Management

Ansell, (1999) describes two point-of-care instruments recently approved for anticoagulation patient monitoring home use, the CoaguCheck and ProTIME Monitor. The actual management of oral anticoagulation in the home setting can be performed in one of two ways: 1.) Patients can measure their PT-INR and call in results to their provider for coumadin dose adjustment or 2.) Patients can be instructed in self-dose management within certain parameters, based on their own PT-INR measurement.
Several studies have shown the value of patient self-testing (McConnell, 2000; Murray, Fitzmaurice & Hobbs, 1999; Pubentz, Calcagno & Teeters, 1998). In a three month, randomized controlled study of 50 patients, Cromheecke et al., (2000) showed that patient self-testing yielded adequate therapeutic control and a high level of patient satisfaction. In a randomized, controlled trial of 325 elderly patients with a variety of indications for anticoagulation, Byeth and Landefeld showed a 52.5% reduction in major bleeding events in the first 6 months of therapy in the patient self-testing group.

As demonstrated with other education and self-management programs (eg., self-management of insulin-dependent diabetes) anticoagulation patients are capable of self-management with more accurate range INR's and increased patient satisfaction. A limiting factor for self-management is visual impairment. A potential disadvantage of self-management could be poorer regulation of oral anticoagulation due to less professional guidance. Also, self-management may theoretically be associated with increased anxiety of patients or even preoccupation with their disease. Proper self-management of oral anticoagulants should not be done without a structured, extensive teaching program.

Conclusion

Successful aging calls for effective adaptation, which in turn implies flexible use of coping strategies to optimize personal functioning and well-being (Slangen-de et al. (2001). In the same sense, the fundamental message of self-efficacy theory for those involved with task accomplishment is that they experience success in their self-care performance. Self-efficacy can predict how
people function in terms of behavior, effort expenditure, persistence, thought patterns, and emotional reactions (Van Der Bijl & Shortridge-Bagett). Self-efficacy can be measured in terms of successful medication management (Alijasem, Peyrot & Rubin (2001).

The focused care available through specialized anticoagulation clinic services enhances patient compliance and offers a more accessible monitoring process. Clinical guidelines that specifically outline anticoagulation therapy initiation, patient assessment, patient education, and cost analysis are being scrutinized through retrospective clinical trials. Developments of standard pharmacokinetic anticoagulation protocols to perform anticoagulation dosage management, dosage adjustment, and excessive anticoagulation management need to be agreed upon.

Future anticoagulant management with in-home blood testing accompanied by practitioner oversight has yielded high patient satisfaction and more therapeutic INR results. Successful anticoagulation management begins with providing the patient with the skills they need to attain within range INR results to avoid hemorrhage or thromboembolism complications. Consistent motivated oversight of anticoagulation management is an important factor in positive outcomes with anticoagulation therapy.
<table>
<thead>
<tr>
<th>Indications</th>
<th>INR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prophylaxis of venous thrombosis (high risk surgery)</td>
<td>2.0-3.0</td>
</tr>
<tr>
<td>Treatment of venous thrombosis</td>
<td>2.0-3.0</td>
</tr>
<tr>
<td>Treatment of pulmonary embolus</td>
<td>2.0-3.0</td>
</tr>
<tr>
<td>Prevention of systemic embolism</td>
<td>2.0-3.0</td>
</tr>
<tr>
<td>Tissue heart valves</td>
<td>2.0-3.0</td>
</tr>
<tr>
<td>Anterior myocardial infarction (to prevent systemic embolism)*</td>
<td>2.0-3.0</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>2.0-3.0</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>2.0-3.0</td>
</tr>
<tr>
<td>Mechanical prosthetic valves (high risk)</td>
<td>2.5-3.5</td>
</tr>
<tr>
<td>Bileaflet mechanical valve in aortic position</td>
<td>2.0-3.0</td>
</tr>
</tbody>
</table>

*If oral anticoagulation therapy is elected to prevent recurrent MI, an INR of 2.5-3.5 is recommended, consistent with United States Food and Drug Administration recommendation.

### Warfarin (Coumadin) Dosing Schedule

**Please Take Your Anticoagulant Medication As Follows:**

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Sunday</th>
<th>Monday</th>
<th>Tuesday</th>
<th>Wednesday</th>
<th>Thursday</th>
<th>Friday</th>
<th>Saturday</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Total # of tablets for the week</td>
<td>Dose of Medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Consider lowering milligram</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Consider lowering millgram</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2</td>
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Yakima Heart Center (1996); Yakima Valley Memorial Hospital (1999)
## Table 3

### Managing warfarin in patients with high INR values

| INR > therapeutic range but <5.0, no significant bleeding, rapid reversal not indicated for reasons of surgical intervention. |
| Decrease or omit the next dose; resume at a lower dose when INR approaches desired range. If INR is minimally above therapeutic range, dose reduction may not be necessary. |
| INR >5.0 but <9.0, no clinically significant bleeding |
| When there are no additional risk factors for bleeding, omit the next 1-2 doses, monitor INR more frequently, and resume at a lower dose when the INR is in therapeutic range. When there is an increased risk of bleeding, omit the next dose, and give vitamin K1 (1.0-2.5mg P.O.). Patients requiring more rapid reversal before urgent surgery or dental extraction: give vitamin K1 (2-4mg P.O.): if the INR remains high at 24 h, give an additional dose of 1-2 mg. |
| INR > 9.0, no significant bleeding |
| Give vitamin K1 (3-5 mg P.O.): closely monitor the INR; if the INR is not substantially reduced in 24-48h, the vitamin K1 dose can be repeated. Serious bleeding or major warfarin overdose (INR>20.0) requiring rapid reversal of anticoagulant effect: give vitamin K1 (10mg by slow IV infusion), with fresh frozen plasma transfusion or prothrombin complex concentrate; depending upon urgency, vitamin K1 injections may be needed q 12 h. |
| Life-threatening bleeding or serious warfarin overdose |
| Give prothrombin complex concentrate, with vitamin K1 (10 mg by slow IV infusion); repeat if necessary, depending on INR. |
| Continuing warfarin therapy indicated after high doses of vitamin K1 |
| Give heparin, until the effects of vitamin K1 have been reversed and the patient is responsive to warfarin. |

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<tr>
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<td>Indication of warfarin (Coumadin) therapy</td>
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<td>Frequency of clinic visits and INR test</td>
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<td>1. Appointments range from 1-6 weeks based upon the patient's INR</td>
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<td>2. Maximum time between appointments is 6 weeks</td>
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<td>1. Patient compliance - take only as directed; education on what to do for missed doses, etc.</td>
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<td>2. Avoid Alcohol</td>
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<td>3. Diet - be consistent when eating foods high in vitamin K</td>
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<td>4. Drug interactions - patient to make all providers aware that the patient takes warfarin</td>
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<td>Adverse effects from warfarin therapy - when to seek medical care</td>
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<td>Patient given or mailed a Medic Alert pamphlet</td>
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Patient Education

Why do I take Coumadin?

Coumadin is an oral anticoagulant that slows down the clotting ability of the blood. Vitamin K helps your blood to clot.

What is anticoagulation?

Oral anticoagulants block the regeneration of Vitamin K, thus depleting the amount of Vitamin K proteins available for coagulation reactions. Coumadin is available as scored pills in 9 different strengths and colors.

Laboratory tests and the INR

The International Normalized Ratio is a blood test calculation that measures how slow or fast the clotting ability of the blood is.

How often do I check the INR?

Initially, you may need daily blood tests, until the therapeutic range and dosing is established. Then the frequency of your blood testing may decrease, depending on your INR.

Taking your Coumadin

Take the medicine exactly as prescribed. Call your provider if you forget a dose. Don’t take extra pills to catch up. Do not stop taking your coumadin without your practitioners approval.
Avoid Alcohol

High alcohol intake tends to result in higher INR levels and may result in a greater risk for bleeding.

Diet

Eat consistent amounts of foods containing Vitamin K on a daily basis but avoid eating large amounts of foods high in Vitamin K. These include leafy green vegetables, certain beans, peas, and vegetable oils.

Drug Interactions

Make sure your health-care team knows what medications you are taking. Many drugs interact with coumadin and alter its effect. Unless otherwise specified, patients taking coumadin should avoid aspirin and ibuprofen, and any products containing these ingredients.

When to seek Medical Care

Report any bleeding that is not normal. Symptoms to report include:

- bloody urine
- black stools
- bruising more easily than usual
- spontaneous bleeding from the nose or gums (unless common)
- severe pain in a single joint or localized area
- abdominal pain or swelling
- blurred vision or bleeding in eyes
- confusion
- dizziness or lightheadedness
- fainting, sudden weakness
- numbness or paralysis in the arms, legs or face
- women with periods that are heavier or longer than usual.

Pregnancy

Coumadin can harm your unborn child.

Table 6

Cost Savings due to Hemorrhage/Thromboembolism in Patients Managed under Present Anticoagulation Management in comparison to Past Anticoagulation Management

Wilt et al., (1995) Reduced utilization of medical services savings of $4,072 (per 100 pt-yrs)

Chiquette et al. (1998) Reduced hospitalizations/E.R. visits savings of $1,621 (per 100 pt-yrs)

Cost of Preventable Coumadin-Related Adverse Events for patients Not rerolled in Anticoagulation clinic

Hamby, Weeks & Malikowski (2000)

Bypass leg graft thrombosis = $10,927*

*Due to coumadin stopped for liver biopsy, with failure to restart warfarin

Intra-abdominal bleed = $18,115**

**Due to being discharged on coumadin & not monitored, pt died

GI bleed = $33,487***

***Due to patient not being monitored
Figure 1

COUMADIN Dosage Adjustment Protocol
(use in conjunction with Table 2)

GOAL RANGE INR 2.0 - 3.0

- INR in-range
- INR < 2.0
  - Hold 1 day
  - Hold no more 2 schedule, UP 1 schedule, recheck INR 1-2 schedule, recheck INR 1-2 wk

- INR > 3.0 - 3.5
  - DOWN 1 schedule, recheck INR 1-2 wk
  - UP 1 schedule, recheck INR 1-2 wk

- INR > 3.5
  - Hold 1 day
  - UP 1 schedule recheck 1-2wk

- INR > 5.0
  - Hold no more 2 days, recheck INR.
  - UP 1-2 schedules, recheck 1-2wk

GOAL RANGE INR 2.5-3.5

- INR in-range
- INR < 2.0
  - Hold 1 day
  - Hold no more 2 schedule, UP 1 schedule, recheck INR 1-2 schedule, recheck INR 1-2 wk

- INR 2.0-2.4
  - RELOAD 1-15mgX1.
  - DOWN 1-2 schedule, recheck INR 1-2 wk

- INR >3.5-5.0
  - Hold 1 day UP 1 schedule recheck 1-2wk

- INR > 5.0
  - Hold no more 2 days, recheck INR.
  - UP 1-2 schedules, recheck 1-2wk

Wieland, Ewy & Wise (1998); Wilson-Norton & Gibson (1996)
References


Wilmington, D.E. Dupont Pharmaceuticals


Gerontological Nursing, 25, 7-15.


