Currents in Military Pharmacy

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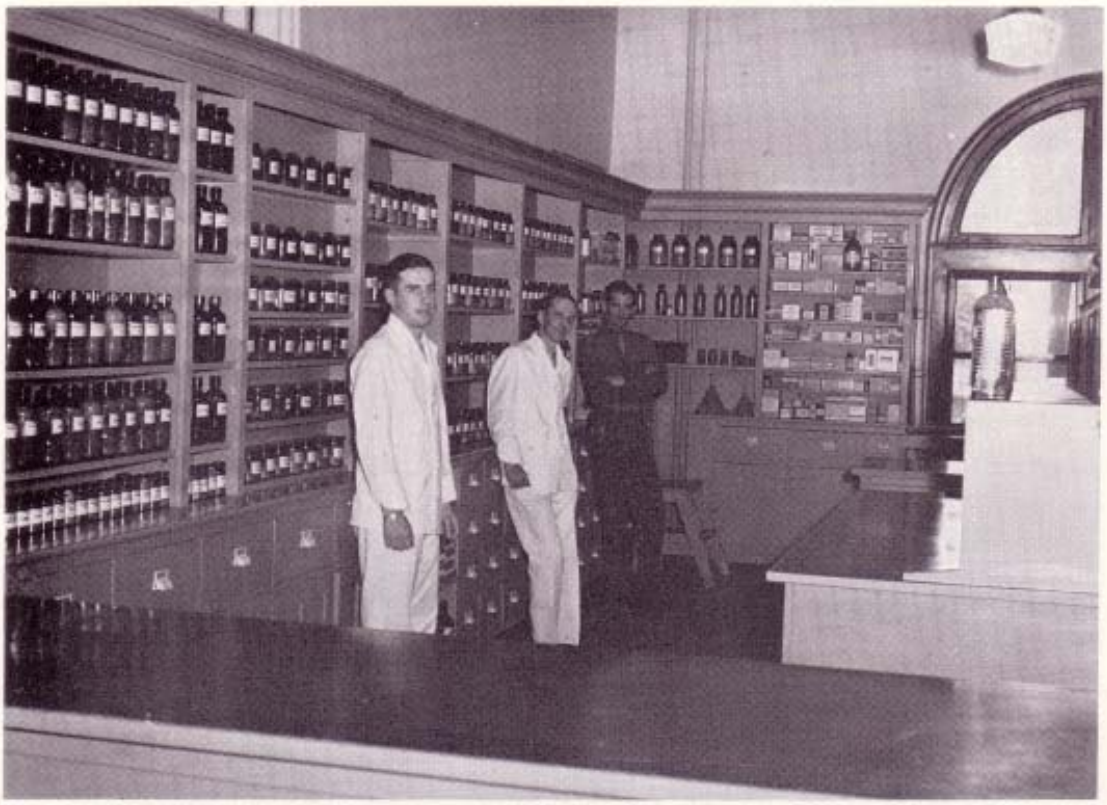

FIGURE 38.—Well-stocked pharmacy at Percy Jones General Hospital, Battle Creek, Mich.

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Letter from the SAFP President

Maj Forsythe

Greetings Society of Air Force Pharmacy members! I hope everyone had a wonderful and successful 2014. Your Officers worked very hard and the Society had a successful year. One of the biggest tasks we took on was reestablishing the SAFP journal and I am very proud that it is here! The journal is a perfect way to recognize and share all the amazing and wonderful things all of us are doing in the world of Air Force Pharmacy. So, please get involved and contribute to the journal!

I am honored to serve as your President for 2015 and I am excited about the year ahead. We will continue to work and find ways to make the Society thrive despite the current fiscally constrained environment. One of my main goals is to increase participation of the members through the journal and webinar style meetings. Please feel free to reach out to me and any of the other officers with your ideas and suggestions. Ultimately, I believe the Society should benefit each member and Air Force Pharmacy as a whole. I urge each and every one of you to jump on board and help us make the Society stronger than ever!

Proud to be Your President,

Stephanie Forsythe

Letter from the Associate Corps Chief for Pharmacy

Col Sprenger

Pharmacy Colleagues,

This past year has certainly been notable from the perspective of change. We've seen changes in the pharmacy benefit with implementation of the TRICARE for Life refill prescription pilot, DoD pharmacy policy standardization, and AF pharmacy manning shifts to name just a few. Although much of the change has resulted in significant and essential cost savings, transitions often come with significant challenge.

With the standup of the new Defense Health Agency (DHA), the DHA Pharmacy Operations Division together with the Services focused on pharmacy policy standardization, formulary management, Service provider communications, contract pharmaceutical purchases and automation. We've seen recapture of prescription workload from retail business in many AF pharmacy operations. We now have consistent policy regarding the transfer of prescription refills between Service pharmacies. Air Force pharmacy has consistently led the charge towards maximizing contract compliance for pharmaceutical purchases and we have stepped forward into the era of accepting electronic prescriptions from civilian providers.

In response to Government directed Service manpower reductions, the Air Force implemented Force Management programs which had significant impact on Air Force Pharmacy manning for both pharmacists and technicians. Over the past four to five years, pharmacy manning numbers had risen to meet the workload demands but actually reached levels which exceeded our end strength authorizations. Manpower reductions are always difficult as adjusting to this change has such a big impact on many members' lives. It results in changed plans for the future for some and concern about future careers for many others. Although the transition is difficult, I remain confident in our team's strength, commitment and our outlook for the way ahead.

The years that I have served as an Air Force pharmacist have been amazingly rewarding both personally and professionally. The best part of all has been the people I have been blessed to serve with and for. It truly has been like a big family. It is an honor and a privilege to serve as your Associate Corps Chief and your representative to the Air Force Surgeon General on pharmacy issues. A special thanks to each member of our Air Force Pharmacy family who work hard each and every day to provide the very best service for all our beneficiaries.

Career Management in Our New Air Force

By: Maj Stephanie Forsythe, Capt Rohin Kasudia, MSgt June White

Introduction:

For any new Airmen, the Air Force offers a plethora of leadership, developmental and assignment opportunities. Navigating these prospects is daunting, and determining how to posture our careers successfully is a great challenge. There is the constant struggle between meeting mission requirements (AKA - 'daily grind') and all the other military requirements. With new changes to performance reports and force shaping, there is an ever-greater need to actively manage your military career. There are some common themes that any Airmen should be aware of that will ensure their continued growth.

Excellence always:

Most of us have at some point heard the advice of setting long term and short term goals. These goals can span between our personal and professional targets. In the military environment, some tend to view "goals" as being confined within the bounds of our current assignment. As a result, some may feel there is very little opportunity at the current assignment. Hence, there is a tendency to professionally stagnate and fail to realize significant opportunities of growth.

You should believe in the opposite, every assignment has the potential for you to grow and learn. There will be challenging problems you will need to tackle. Sure, you can wait until you or someone else PCSes, but someone else is just going to have to deal with that problem later. By navigating through road bumps and finding solutions no matter what the obstacle, you and those around you will professionally grow and develop.

So, set realistic goals that allow you to tackle problems head on, both personal and professional. These issues may not be resolved in a day, a week, or even a year. But by leading your teams and families through such challenges, you will grow more than you could imagine.

Stop Selling Yourself Short:

As pharmacists and technicians, we have a tendency to sell ourselves short. There as so many things we do on a daily basis to lead, manage, maintain and grow our operations that we forget to take credit! We have all sat down with our Airmen and have helped them answer the question of what they really did during the year when writing an award package or performance report.

Tips:

Here are some quick tips that we think will help folks out no matter what command they reside in:

1) Quantify everything you do. If you are unsure how to quantify what you are doing, then ask the questions like: How much is the process worth? How much have we saved in terms of dollars, time, steps, man-hours, resources, etc.? Can other bases use our process? Is it a future 'AF Benchmark' program? How does what I did affect the mission? (The "So What" question)? Did we improve quality? (i.e. The 'Best,' 'Most-Successful')
2) Do not repeat the same thing in the current performance report that was in the previous report. Repeat performances tend to diminish in value.
3) Write a draft performance report after 6 months and then figure out what opportunities you need to be exposed to in order to make it as strong as possible.
4) Don't peak too high, too fast. Set yourself up for the next job so when your promotion board hits, you show the board that you are progressing. This goes for stratifications too; a #1 stratification years before your board meets can set you up for failure.
5) Focus on leadership and seek leadership opportunities. The Air Force needs followers, but promotes leaders. Performance reports should indicate potential to the next grade. If you are a SrA then learn to be a SSgt. If you are a Captain then learn to be a Major.
6) Don't write in functional language. The more acronyms and pharmacy jargon we use, the more difficult it is years later for someone to understand what you did.
7) Don't fall victim to the "Pride of Authorship." There will always be something wrong with the bullets you write, give your supervisors an 80% product before close out rather than a 100% product late.
8) Your push lines are the most important lines of any enlisted or officer report. They tell the reviewer what the Air Force should do with this Airman. Make sure you SHOW the reviewer why you are an All-Star and not just tell them.
9) Review your SURF, update your Airman Development Plan and let your supervisor/mentors know your career aspirations.
10) Your record needs to reflect sustained excellent performance as a leader in every job and opportunity that you have.

How to Stand Out From the Rest:

1) Always find ways to lead. Don't just be a member to an organization (IE Booster Club, Top III, CGOC), but be one of the executive officers.
2) Find volunteers opportunities, get other folks involved, be the example and lead the event.
3) Know your peers, what they do and work with them. Equal contribution to a shared project is better than doing it alone.
4) When someone tells you about an "opportunity" no matter how impossible the task, commit to it.

Final Thoughts:

We hope this short article helps start the next conversation between you and your supervisor or mentor. Our Air Force is only as great as our Airmen and pharmacy has some of the hardest working Airmen. The prescriptions never stop. So make sure you pull your head out of the sand, take care of yourself, your career and your troops.

Thoughts on a Thankless Job

By: MSgt Jason Christianson

MSgt Christianson

Each day as the windows roll up, it begins again. Our days do not differ much. The faces may change, but the process stays the same. We watch as the other areas close for "Official Functions" and we wave to the staff that is headed out the door while we take care of the patients we still have. We are the faces that the patients know, because we are the professionals that address the vast majority of their questions. We are a versatile group whose abilities are leaps and bounds beyond those that work in the civilian sector. WE are Pharmacy Technicians in the United States Air Force.

In the 20 years in which I have served in the Air Force, I have worked in nearly every area in which we task our technicians with working. One thing that I have always made clear to the technicians and pharmacists alike is the wide scope of knowledge that we as technicians are expected to know. Whether it is a call from a patient asking if one of the several hundred items on the formulary is stocked, explaining to the patient at the window what type of symptoms they may experience if their potassium levels are off or interpreting the squiggly lines faxed over for an inpatient order, our technicians will know the answer. A pharmacy technician in the civilian sector is not authorized to perform a fraction of the duties and tasks that our technicians perform routinely and without a second thought. They are not able to counsel patients, check each other's work or make a judgment call about a dosage form. A few years back I deployed on a humanitarian assignment in support of PACANGEL. When I returned I was bragging to a civilian pharmacy technician who was a friend of mine. They could not believe that I was able to perform my work without a pharmacist present to check it. AF technicians do this daily.

The job of a pharmacy technician has never been a glamorous job. While the patients will stop to thank the provider that discovered their tumor, or heart condition for saving their life, they may berate the technician for taking so long to "slap a label on it." It is imperative that our technicians know that although they may receive a barrage of complaints, they are just as important to the process as the provider prescribing the medication. We are the last person the patient generally sees at our clinics, the last chance to ask a question and the last check to make sure that all the interactions/allergies/dosage issues are covered for the patient. I have often told the technicians that work with/for me that "Without us taking care of the patient, it is nothing more than people with a piece of paper on their wall telling people that they are sick."

As Air Force pharmacy technicians, we have come to learn that our hours and days may be longer than our clinic counterparts. We, at times, have come to dread the ringing phone 2-3 minutes before we are supposed to close. That call saying that Dr. Whomever still has patients that they have not seen yet. We have come to understand that when we look out the doors in the morning, a line will have formed and we will be running from the moment we open. We accept these challenges and march forward with a smile for our patients.

It is imperative that our senior pharmacists make sure that the junior officers coming in realize the impact that their technicians will have on their career. Much of the time our techs are performing work that in the civilian sector would only be performed by a credentialed pharmacist. Our technicians are well trained by an extraordinary school house staff and then receive in depth, hands on, on the job training from the best pharmacy technicians in the world.

Much of my career I had looked at my job as thankless but necessary. I understood that I would probably never be glorified for saving a life or shooting down enemy planes, but nonetheless accepted that what I was doing mattered. I assumed, incorrectly that we, in the pharmacy field were the only people that truly appreciated the scope in which we operated. One day in 2010 that changed for me though. The CSAF, General Schwartz, was visiting Osan, AB in Korea. Our hospital had the nicest briefing room on the base at that time, so the base leadership brought him there for their meeting with him. He was on a tight schedule and supposed to leave the briefing room and head directly to his car. As he left the briefing room, he stopped to watch me speak to a patient. I heard his aides inform him that they really needed to keep moving. He told them to give him a minute and came to my window and waited for the patient to leave. He stuck his hand out and introduced himself. He informed me that "You have a thankless job. But, I want you to know that the people at the top know what you do and how much work is involved and that you are appreciated." He smiled, pointed at me and said, "You remember that." He did not stop at any of the other windows in the lobby, nor did he speak to any other people on his way out. That has stuck with me. So, my fellow technicians, it is my turn to reiterate that you are all appreciated and have a job that won't get you thanked all of the time. You will however touch every life that leaves your clinic in one way or another. You remember that…

SAFP 2014 Awards Call

Maj Forsythe

As reiterated by our Associate Corps Chief, Col Sprenger, recognizing our outstanding performers is one of the many things that the Society of Air Force Pharmacy has traditionally done very well. With the reduction of pharmacy specific recognized awards within the AFMS annual awards and the elimination of Team Awards this year, the SAFP Annual Awards provide an especially important opportunity to highlight our amazingly talented AF pharmacists and technicians. Please consider nominating your superior performers. If those performers are not members, then ensure a membership application and dues are submitted in conjunction with the awards package. For more information on becoming a member go to http://www.af-pharmacists.org/.

The deadline has been extended to 13 February 2015 by COB to help ensure that all categories receive nominations.

Award Categories:

1) **The SAFP Senior SNCO Pharmacy Technician of the Year Award.** Nominees must in the grade range of MSgt through SMSgt and be assigned as a 4P0XX.
2) **The SAFP Maxine Beatty Field Grade Pharmacy Officer of the Year Award**. Nominees must be an AF pharmacist (Maj - Lt Col, military or civilian equivalent) who has demonstrated distinguished service to Air Force pharmacy over the last year.
3) **The SAFP Fred Coleman Company Grade Pharmacy Officer of the Year Award**. Nominees must be an AF pharmacist (company grade military or civilian equivalent) who has significantly contributed to Air Force pharmacy over the last year. Award recognizes outstanding performance and achievements in a practice setting.
4) **The SAFP Ed Zastawny Clinical Pharmacist of the Year Award**. Nominees must be an AF pharmacist (Capt - Lt Col, military or civilian equivalent). Award honors outstanding performance and achievements in clinical pharmacy.
5) **The SAFP Civilian Pharmacy Technician of the Year Award**. Nominees must be employed in the GS-661 designation.

Call for Future Articles

Capt Kasudia

As we all know, the Society of Air Force Pharmacy (SAFP) Journal / Newsletter is long overdue. The SAFP team has worked hard to put this edition together with the hopes that we will continue to help connect pharmacies across the Air Force. The Society welcomes original articles that promote the Pharmacy and Military Health Profession. Its aim is to describe advances and developments to the practice of pharmacy and military medicine. The articles may introduce new or emerging themes related to pharmacotherapy, technology, research, drug safety, informatics, management, public health, patient case studies and military medicine.

Currently, the only publication format is this newsletter. In 2014, we took major strides to become recognized by the Library of Congress (ISSN: 2331-7604). This was an important first step in ensuring that our future publications will be available to the entire pharmacy community nationwide through websites such as PubMed, EmBase, Google Scholar, etc. We are anticipating our Journal to go live sometime in 2016 as we continue to gain traction and interest. The website for the Journal of Air Force Pharmacy is at <https://safpjournal.org/index.php/safp> .

But we need your help to make this a success. We will continue to need new articles and article reviewers. If you have any questions, then please reach out to myself via the Global or <JAFP.EditorInChief@Gmail.com>.

The Editorial Team looks forward to your submissions!

Currently Accepting Articles for the 2nd Quarter Newsletter

Submission Deadline: 8 May 2015

Email Submissions to: JAFP.EditorInChief@Gmail.com

Atrial Fibrillation and Anticoagulation Therapy

By: Brandy L. Renner, Capt, USAF, BSC, Pharm D.

Learning Objectives

1) **Compare the $CHADS_2$ and CHA_2DS_2-VASc risk assessment tools.**
2) **Estimate a patient's risk of stroke and bleed as they relate to anticoagulation therapy for the treatment of atrial fibrillation (AF).**
3) **Evaluate the safety, efficacy and pharmacologic properties of conventional anticoagulants and new oral anticoagulants used for the treatment of AF.**
4) **Analyze the clinical trial data for the treatment of AF with new oral anticoagulants**
5) **Provide accurate and appropriate counsel as part of the treatment team**

PIM Postgraduate Institute for Medicine

Released: 1 February 2015
Expiration Date: 31 January 2016
Time to Completion: 1.0 Hour

Jointly provided by Postgraduate Institute for Medicine and the Society of Air Force Pharmacy

This activity has been designed to meet the educational needs of pharmacists involved in the care of patients with Atrial Fibrillation.

Background

Atrial fibrillation (AF) is the most common form of arrhythmia.[1] It is a tachycardic dysregulation of the atrium of the heart, impairing the outflow of blood from the heart. Due to the impaired outflow of atrial blood, stasis occurs, potentially causing thrombotic events.[2] Endothelial damage and coagulation properties also are integral players in the formation of thrombosis in atrial fibrillation.[3] According to the American Heart Association, 15% of strokes or thrombotic events are caused by untreated AF and about 2.7 million Americans are diagnosed with AF.[4] The incidence of stroke related to atrial fibrillation increases with age and a number of other factors.[5] Risk stratification tools for assessing the risk of stroke in patients with AF have been established and their use is recommended. Two widely accepted schemes are the $CHADS_2$ and CHA_2DS_2-VASc. Based on the risk estimated by these tools, initiation of antithrombotic or anticoagulation therapy may be recommended.

Anticoagulation decreases the risk of thrombotic events, therefore, reducing morbidity and mortality. Warfarin, a vitamin k antagonist, is the oldest and cheapest anticoagulant currently available. However, approximately 50% of eligible patients do not receive treatment with warfarin but instead with antiplatelet medications such as aspirin and clopidogrel or go untreated altogether.[5,6] Due to the need for alternative anticoagulant options, the novel oral anticoagulants (NOACs) have become available. The NOACS include apixaban, dabigatran, and rivaroxaban. Dabigatran and apixaban were shown to be superior to warfarin in the prevention of stroke or systemic embolism, with fewer bleeds, in clinical trials, through the RE-LY and ARISTOTLE trials respectively.[7,8] Apixaban also proved to reduce the rate of mortality.[8] While rivaroxaban was not superior to warfarin clinical trials it did prove to be comparable to warfarin in stroke or systemic embolism prevention and bleed rates.[9] The NOACS provide an anticoagulation alternative to warfarin with less bleed rates, less monitoring and fewer drug interactions.[5] The purpose of this article is to review treatment of atrial fibrillation with anticoagulation therapy.

Introduction

Atrial fibrillation (AF) is a major cause of thromboembolic events, is the most common type of dysregulation of the heart and is one of the leading causes of stroke. It is characterized by rapid irregular echocardiograph waves and causes discordance between atrial and ventricular contraction.[1] In fibrillation, the outflow of blood from the heart is impaired causing stasis of the blood. Thromboembolic events such as stroke, occur as a result of blood stasis, endothelial damage and coagulation properties.[3] AF increases the risk of not only stroke but also morbidity and mortality.[10]

The lifetime risk of having AF is 1 in 4 Americans over the age of 40.[1] In a study by Heeringa J et al, the prevalence of AF increased with age and was higher in men than in women in each age group. However, the high lifetime risk for AF differed little between genders.[11] AF increases risk of stroke by 60% or approximately by a factor of 5 and that risk increases with age.[1,5] The estimated economic burden of stroke in 2010 was $54 billion and is expected to climb in the upcoming years as Americans continue to live to older ages.[1] Factors other than age can also increase the risk of stroke in patients with nonvalvular AF. These factors include the following: hypertension, diabetes, heart failure and a history of stroke or transient ischemic attack (TIA). Although studies show inconsistencies, according to the ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation) study, women have a 1.6 fold higher incidence of ischemic stroke and peripheral thromboembolism over men.[1] However, the most powerful predictor of stroke is a history of previous stroke or TIA.[10]

Discussion

Risk Assessment Tools

Due to the increased risk of stroke in patients who have AF and other comorbidities and risk factors, risk assessment tools have been developed. The $CHADS_2$ and CHA_2DS_2-VASc are risk assessment tools used to identify AF patients who are at increased risk of stroke. The $CHADS_2$ assessment of risk is most commonly used in the United States guidelines while the CHA_2DS_2-VASc is used in European guidelines. The $CHADS_2$ (see table 1) **Cont…**

	$CHADS_2$ Risk	Points
C	Congestive Heart Failure	1
H	Hypertension (> 140/90 mmHg or treated)	1
A	Age ≥ 75 years	1
D	Diabetes	1
S_2	Prior Stroke or TIA	2

Table 1. $CHADS_2$ Scoring Chart

Atrial Fibrillation and Anticoagulation Therapy

By: Brandy L. Renner, Capt, USAF, BSC, Pharm D.

assessment of risk assigns one point for each of the following risk factors: congestive heart failure or left ventricular dysfunction, hypertension, age greater than or equal to 75 years, and diabetes; and assigns two points for a history of stroke or TIA.[10] Scores can range from zero to six and can help determine if oral anticoagulation therapy is indicated. In those with low risk (score of zero), no therapy or aspirin is recommended. With an intermediate risk (score of one) oral anticoagulation is preferred or combination of clopidogrel and aspirin, while in the high risk (score of two or greater) group, oral anticoagulation is preferred.[12] However, the $CHADS_2$ scheme has been criticized due to perceived pitfalls in that it left many in the intermediate risk group of oral anticoagulation or aspirin and does not stratify many into the no therapy or very low risk group. It also does not account for other risk factors, such as female gender, vascular disease, or age 65-74 years.[12] Due to this criticism and perceived pitfalls, the CHA_2DS_2-VASc risk assessment tool was designed.

The CHA_2DS_2-VASc (see table 2) risk assessment tool stratifies patients risk on a scale of zero to nine. Utilization of the CHA_2DS_2-VASc risk assessment tool, recommends that a larger population of those with nonvalvular atrial fibrillation be on oral anticoagulation therapy by stratifying fewer patients with AF into the low thromboembolic risk group. The benefit of using the CHA_2DS_2-VASc risk assessment tool is to identify those who truly are at low risk and therefore those with increased risk are provided appropriate thromboprophylaxis therapy.[13] While vascular disease does increase the risk of stroke and is accounted for separately in the CHA_2DS_2-VASc risk assessment tool, it contributes little to reclassifying stroke risk, considering those who have vascular disease are either of older age, have hypertension or have diabetes, therefore they are already stratified to receive anticoagulation therapy.[14] Reclassification based on a $CHADS_2$ score is due to being of the female gender or the age stratification.[14] In a Danish nationwide cohort study, including 47,576 patients, the CHA_2DS_2-VASc was found to identify truly low risk patients who do not need any antithrombotic therapy. By doing so they showed that utilization of the CHA_2DS_2-VASc provides better risk stratification.[13] Both risk assessment strategies provide a recommendation for oral anticoagulation therapy that requires clinical judgment of the risks versus the benefits of therapy for the individual patient.[14] One consideration for those who require anticoagulation is to determine the bleed risk.

	CHA_2DS_2-VASc Risk	Points
C	Congestive Heart Failure	1
H	Hypertension	1
A	Age ≥ 75 years	2
D	Diabetes	1
S	Stroke/ TIA/ Thromboembolism	2
V	Vascular Disease	1
A	Age 65-74 years	1
F	Female	1

Table 2. $CHADS_2DS_2$-VASc Scoring Chart

The bleed risk can be assessed using the HAS-BLED assessment. The HAS-BLED (see table 3) risk score assigns one point for each of the following criteria: hypertension, abnormal renal and/or liver function, previous stroke, bleeding history, labile international normalized ratios, elderly, and concomitant drugs and/or alcohol excess. A score over three indicates a high risk of bleed and should be considered when initiating anticoagulation therapy.[15] The risks of anticoagulation therapy or not anticoagulating versus the benefit must be weighed and treatment must be individualized for each patient.

	HAS-BLED Risk	Points
H	Hypertension	+1
A	Abnormal liver or renal function	+1 or 2
S	Stroke	+1
B	Bleeding	+1
L	Labile INRs	+2
E	Elderly ≥ 65	+1
D	Drugs or alcohol	+1 or 2

Table 3. HASBLED Scoring Chart

Anticoagulation Therapies

Oral anticoagulation therapy is a preferred therapy in the prevention of stroke in AF patients due to its proven risk reduction of approximately 39%, with a decrease in stroke incidence of 64% as compared to antithrombotic therapy incidence reduction of 22%.[1] Oral anticoagulation therapy provides better benefit in preventing thromboembolic events and has a similar bleed risk as antithrombotic therapy; therefore, antithrombotic therapy should only be used if oral anticoagulation is not suitable or the patient refuses.

Warfarin, a vitamin K antagonist, has been the standard for care for over 50 years.[16] It interferes with the synthesis of vitamin K dependent clotting factors II, VII and IX, by inhibiting the C1 subunit of vitamin K epoxide reductase enzyme complex (VKORC1), thereby reducing the regeneration of vitamin K epoxide and subsequent factors by 30-50%.[17] It prevents the formation of thromboembolism for those with AF however it does nothing for an already formed thrombus. Warfarin has shown to be effective in clinical trials, particularly in comparison to antithrombotic therapy, in reducing the risk of stroke.[5] While warfarin is the gold standard, it has several short comings. Warfarin has a narrow therapeutic **Cont...**

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index and requires a significant amount of monitoring and dose adjustments to maintain the optimal level of anticoagulation. Higher levels increase the risk of bleeding while lower levels increase the risk of thromboembolic events. An INR <2 increases the risk of stroke while and an INR of >4 increases the risk of bleed.[1] Warfarin therapy also has multiple drug interactions and food interactions that affect patients' ability to comply with therapy. Genetic variations in CYP 2C9 and VKORC1 also interfere in an individual's response to warfarin therapy, however genotyping for warfarin therapy is not recommended.[1] Tight control of INR is needed to prevent the risk of stroke. Approximately one-third of patients who are indicated for anticoagulation therapy go untreated.[10] The difficulty of maintaining patients in the narrow therapeutic range (INR 2.0 to 3.0), frequent monitoring, and major bleeding highlight the need for newer anticoagulant therapies.

There are three novel oral anticoagulants (NOACs) on the market; a direct thrombin inhibitor, dabigatran, and two direct factor Xa inhibitors, rivaroxaban and apixaban. Direct thrombin inhibitors exert their activities by blocking the catalytic and fibrinogen binding sites to prevent the formation of thrombin.[18] Dabigatran is a prodrug converted to its active form by estrases. According to A. Amin's review of oral anticoagulants, dabigatran has a "Rapid onset of anticoagulant effect, predictable pharmacodynamics, and few drug-drug interactions".[1] The half-life of dabigatran is 12-17 hours versus 20-60 hours with warfarin and is renally cleared. Therefore, renal dosing is necessitated for those on dabigatran with a CrCl <30ml/min and not recommended for CrCl <15ml/min. Its efficacy and safety was established through the RE-LY trial (Randomized Evaluation of Long-term Anticoagulant Therapy), a multicenter, multinational, randomized parallel group trial. The study randomized 18,113 people into treatment groups and compared two doses of dabigatran to open label warfarin. Through the study, dabigatran proved to be superior to warfarin in preventing ischemic and hemorrhagic stroke with less bleeding.[18] (See table 4)

Factor Xa inhibitors, rivaroxaban and apixaban; exert their actions by blocking the binding site of factor Xa without the need of co-factor III. Rivaroxaban's half-life is 5-9 hours while Apixaban's is approximately 12 hours. Both factor Xa inhibitors are metabolized by CYP 3A4 and are not recommended in moderate to severe hepatic dysfunction.[8,19]

Safety and efficacy was established for rivaroxaban through the ROCKET AF trial (Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial). It was a multinational, double-blind, noninferiority study to assess the effectiveness in reducing the risk of stroke and non-central nervous system systemic embolism in patients with nonvalvular AF. In the trial, 14,264 patients were randomized to receive rivaroxaban or warfarin therapy over a period of a median of 590 days. Rivaroxaban proved to be non-inferior to warfarin and superiority to warfarin was not demonstrated.[19] (See table 4)

Apixaban demonstrated effectiveness in the ARISTOTLE study (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation). It was also a multinational, double-blind study, where 18,201 patients with AF were randomized to receive apixaban or warfarin therapy. Apixaban was superior to warfarin in reducing the risk of stroke and systemic embolism. (See table 4) Therapy with apixaban over warfarin also provided a significant reduction in the number of major bleeds and rate of mortality.[8]

The most common adverse reaction for the NOAC medications are bleeding related, but dabigatran can also cause gastritis like symptoms. These medications have two black box **Cont...**

	Dabigatran	Apixaban	Rivaroxaban
Action	Direct Thrombin Inhibitor	Factor Xa Inhibitor	Factor Xa Inhibitor
Dose	150 mg twice daily	5 mg twice daily 2.5 mg twice daily	20 mg daily 15 mg daily
N=	18,113	18,201	14,264
$CHADS_2$	2	2	3.5
Follow up	2 years	2 years	2 years
Discontinuation	21.20%	25.30%	23.70%
INR Therapeutic	64.00%	62.20%	55%
Stroke or SEE	Superior	Superior	Non-Inferior
Bleed	Similar	Significant decrease	Similar
Mortality	Not Significant	Significant decrease	Similar
Trial	RE-LY	ARISTOTLE	ROCKET AF

Table 4. Novel Anticoagulants

Atrial Fibrillation and Anticoagulation Therapy

By: Brandy L. Renner, Capt, USAF, BSC, Pharm D.

warnings cautioning against the premature discontinuation of anticoagulation therapy with these agents and use of neuraxial anesthesia or a spinal puncture while on these medications. Premature discontinuation increases the risk of thrombotic events, while use with neuraxial anesthesia could cause long-term permanent paralysis. The dosing for dabigatran is 150 mg orally twice daily for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), prevention of recurrent DVT and PE and for the prophylaxis against thromboembolic events in patients with non-valvular atrial fibrillation for those with a CrCl > 30 ml/min.[18] Dosing of apixaban is based on the indication for use. In DVT prophylaxis following hip or knee replacement surgery apixaban should be initiated 12 -24 hours after surgery at the dose of 2.5 mg twice daily. Prophylaxis of recurrent DVT and PE is 2.5 mg twice daily and the treatment of DVT and PE is 10 mg twice daily for seven days followed by 5 mg twice daily.[8] Therapy with rivaroxaban for the treatment and prevention of recurrent DVT and PE is 15 mg orally once daily with the evening meal. Prevention of thromboembolic events for patients with nonvalvular atrial fibrillation is based on CrCl. For those with a CrCl > 50 ml/min, the dosing is 20 mg once daily with the evening meal and for those with a CrCl 15-50 ml/min the dosing is 50 mg with an evening meal.[19]

These new agents do not require monitoring the INR and are more predictable and consistent anticoagulants.[7] Dabigatran and apixaban have been shown to be superior to warfarin in the prevention of stroke, while rivaroxaban is just as effective as warfarin. All three NOACS cause less bleeding and a better side effect profile compared to warfarin. A head to head trial of all three NOACS would be beneficial.

Conclusion

The biggest risk of developing stroke in AF is a history of previous stroke. Therefore, prevention of stroke is a primary goal of therapy and should be individualized for the patient. Anticoagulation therapy provides greater benefit in reducing the risk of stroke compared to alternative therapy. The utilization of available tools, $CHADS_2$ and CHA_2DS_2-VASc, can provide an objective measure as to the risk of stroke and determine the appropriateness of anticoagulation therapy. However the risks of anticoagulation therapy and nontherapy vs the benefits must be weighed. Warfarin, the gold standard of care, and the novel oral anticoagulants provide stroke risk reduction in patients with atrial fibrillation. Consideration and monitoring of anticoagulation therapy for patients has heightened importance due to the narrow therapeutic window of the medications, making them more prone to having medication mishaps. The Joint Commission National Patient Safety Goals were established to help facilities better address patient safety issues. National Patient Safety Goal 03.05.01 states, "Take extra care with patients who take medicines to thin their blood."[20] In order to take extra care, the recommendations of therapy must be understood and the risk versus benefit for the patient must be taken into account. Through identifying the risk of stroke in nonvalvular atrial fibrillation and the recommendations of therapy, the overall burden on the patient and the healthcare system can be reduced.[1]

REFERENCES

1. Amin A. Oral anticoagulation to reduce the risk of stroke in patients with atrial fibrillation: current and future therapies. Clinical Interventions in Aging. 2013; 8: 75-84. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3556861/. Accessed January 31, 2014.
2. Dipiro J, Talbert R, Yee G, et al. Atrial fibrillation and atrial flutter. Pharmacotherapy: A Pathophysiological Approach, 7th ed New York: McGraw-Hill; 2008:288-290.
3. Iwasaki Y, Nishida K, Kato T, Nattel S. Atrial Fibrillation: Atrial Fibrillation Pathophysiology Implications for Management. Circulation. 2011; 124:2264-2274.
4. AHA/ASA resource page. American Stroke Association website. http://www.strokeassociation.org/STROKEORG/LifeAfterStroke/HealthyLivingAfterStroke/UnderstandingRiskyConditions/When-the-Beat-is-Off---Atrial-Fibrillation_UCM_310782_Article.jsp. Assessed January 31, 2014.
5. Mitchel S, Simon T, Raza S, et al. The efficacy and safety of oral anticoagulants in warfarin-suitable patients with nonvalvular atrial fibrillation: Systematic review and meta analysis. Clinical and Applied Thrombosis/Hemostasis. 2013; 00(0):1-13. http://cat.sagepub.com/content/19/6/619.longhttp://cat.sagepub.com/content/19/6/619.long. Accessed January 31, 2014.
6. Zimetbaum PJ, Thosani A, Yu HT, et al. Are atrial fibrillation patients receiving warfarin in accordance with stroke risk? [abstract]. Am J Med. 2010; 123:446-453. http://www.ncbi.nlm.nih.gov/pubmed/20399322. Accessed January 31, 2014.
7. Patel M, Mahaffey K, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011; 365 (10):883-891. http://www.nejm.org/doi/full/10.1056/NEJMoa1009638. Accessed January 31, 2014.
8. ELIQUIS [package insert]. Bristol-Myers Squibb Company, Princeton, New Jersey; December 2012. http://packageinserts.bms.com/pi/pi_eliquis.pdf. Accessed January 31, 2014.
9. Becker R, Berkowitz SD, Breithardt G, et al. Rivaroxaban-once daily, oral, direct factor Xa inhibition compared with vitamin K antagonism for prevention of stroke and Embolism Trial in Atrial Fibrillation. Am Heart J. 2010; 159(3):340-347.
10. Connolly S, Eikelboom J, Joyner C, et al. Apixaban in patients with atrial fibrillation. N Engl J Med. 2011; 364:806-817. http://www.nejm.org/doi/full/10.1056/NEJMoa1007432. Accessed January 31, 2014.
11. Heeringa J, van der Kuip DA, Hofman A, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J. 2006; 27:949–53. http://eurheartj.oxfordjournals.org/content/27/8/949.long. Accessed

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12. Ageno W, Gallus AS, Wittkowsky A, et al.Oral Anticoagulatio Therapy. Chest. 2012;141(2_suppl):e44S-e88S. http://journal.publications.chestnet.org/article.aspx?articleid=1159432. Accessed January 31, 2014.
13. Olesen JB, Torp-Pedersen C, Hansen ML, and Lip GYP. The value of the CHA2DS2-VASc score for refining stroke risk stratification in patients with atrial fibrillation with a CHADS2 score 0–1: A nationwide cohort study. Thromb Haemost. 2012; 107(6):1172-1179. http://www.schattauer.de/en/magazine/subject-areas/journals-a-z/thrombosis-and-haemostasis/contents/archive/issue/1547/manuscript/17495.html Accessed January 31, 2014.
14. Winkle R, Mead H, Engel G, Kong M, Patrawala R. Comparison between chads2 and cha2 ds2 -vasc score in a stroke cohort with atrial fibrillation [abstract]. European Society of Cardiology. 2013; 20(4):623-628. http://www.ncbi.nlm.nih.gov/pubmed/?term=Comparison+between+chads2+and+cha2+ds2+-vasc+score+in+a+stroke+cohort+with+atrial+fibrillation.+European+Society+of+Cardiology. Accessed January 31, 2014.
15. Lane DA, Lip GYH. Use of the CHA_2DS_2-VASc and HAS-BLED Scores to Aid Decision Making for Thromboprophylaxis in Nonvalvular Atrial Fibrillation. Circulation. 2012; 126:860-865. http://circ.ahajournals.org/content/126/7/860.long. Accessed January 31, 2014.
16. Soff GA. A New Generation of Oral Direct Anticoagulants. Arteriosclerosis, Thrombosis, and Vascular Biology. 2012; 32:569-574. http://atvb.ahajournals.org/content/32/3/569.long. Accessed January 31, 2014.
17. COUMADIN [package insert]. Bristol-Myers Squibb Company, Princeton, New Jersey; October 2011. http://packageinserts.bms.com/pi/pi_coumadin.pdf.
18. PRADAXA [package insert]. Boehringer Ingelheim Pharmaceuticals, Inc, Ridgefield, CT; December; 2013. http://bidocs.boehringer-ingelheim.com/BIWebAccess/ViewServlet.ser?docBase=renetnt&folderPath=/Prescribing%20Information/PIs/Pradaxa/Pradaxa.pdf.
19. XARELTO [package insert]. Janssen Pharmaceuticals, Inc , Titusville, NJ; December 2011. http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/202439s001lbl.pdf.
20. The Joint Commission Hospital National Patient Safety Goals 2013. The Joint Commission Web site. http://www.jointcommission.org/standards_information/npsgs.aspx. Accessed January 31,
21. Mason PK, Lake DE, DiMarco JP, et al. Impact of the CHA2DS2-VASc Score on Anticoagulation Recommendations for Atrial Fibrillation. Am J Med. 2012; 603 e1-603e6. http://anticoagulation.amjmed.com/Content/PDFs/Mason-Impact.pdf. Accessed January 31, 2014.
22. Appraisal of the ESC Atrial Fibrillation Guidelines 2010 (Part 1). The European Society of Cardiology Web site. http://www.escardio.org/communities/councils/ccp/news/Pages/Appraisal-of-the-ESC-Atrial-Fibrillation-Guidelines-2010-Part-1.aspx. Accessed January 31, 2014.

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