



Currents in Military Pharmacy

Volume: 23 Issue: 1



Caption: On March 13, 1821, sixty-eight pharmacists signed the Constitution of the first pharmaceutical association in the United States. The Philadelphia College of Pharmacy, as known now, was officially formed.

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Letter from the SAFF President



Maj Jarnot

The Society of Air Force Pharmacy has branched out into social media. Social media is a critical way to provide important information quickly to our membership in today's digital enhanced age. Now you can follow the society on Facebook as well as Twitter with the handle @SAFFPharmacy. Connecting with the society will allow you the ability to receive the newest information hot off the presses. The society has also taken suggestions from membership to enhance and improve the functionality and capability of our www.af-pharmacists.org website. Two new webmasters, Capt Brian Welch and Maj David Valentine, will join our SAFF Journal Editor Maj Rohin Kasudia, to enhance the user experience and ensure SAFF members find value in using the SAFF website. In addition to design changes and improvements to the viewer aesthetics, tons of new information will be loaded to the website to provide a one-stop shop for utilizing the benefits of membership such as the SAFF Journal and Certificate Program reimbursement. Additionally, improvements are

being made to the SAFF Shop to make it easy for members to shop for SAFF swag.

As the TDY restrictions ease slightly SAFF is researching the possibility of bringing back the SAFF Jerry Ross Awards Banquet/Social at Joint Forces Pharmacy Seminar in October 2016. SAFF is also researching the logistics for a SAFF Mid-Year Meeting event in 2017. Before the dreaded CARD system made these type of functions difficult to attend, members who have been around can remember how amazing these events were. There is no replacement for learning, networking, and mentorship than a live event. SAFF Vice President Maj Jennifer Baker is taking the lead and if you are interested in helping out please contact her ASAP.

Check out the website and social media pages for the latest information over the next few months and provide feedback for what you as a member would like to see from SAFF. If you are on social media connect with us today! If you are not on social media, what a great reason connecting with SAFF is to get you to throw away that flip phone and join the rest of the 21st century ;)

Letter from the Associate Corps Chief for Pharmacy



Col Sprenger

Pharmacy Team,

As my time wearing the Air Force uniform draws closer and closer to an end, I am reminded daily how amazingly fortunate I have been over the past 27+ years in Air Force Pharmacy. As a young Lt, I never imagined just how good a military pharmacy career could be. Now, as a "seasoned" Colonel, I still am amazed at just how great it has been. And if I were given the chance to do it all again, I'd tell you...in a heartbeat, absolutely!

Military careers don't come without sacrifice whether they last 4 years, 30 years, or anywhere in between. We all know that right up front, before we sign on the dotted line and take the oath. Perhaps the sacrifice is really what makes our military service so rewarding. Although that may be a hindsight perspective, it is a good perspective to have, regardless. Whether you've been told recently or not, your service and sacrifice really does make a difference.

I have been blessed over the years to be part of such su-

perb pharmacy teams. And as the Associate Corps Chief, I see the results of your cumulative incredible efforts to provide outstanding pharmacy service to all DoD beneficiaries. I have to tell you that I couldn't be more proud of each of you and what you all do.

Recently, I was notified that I am the 7th recipient of the Society of AF Pharmacy Career Sustained achievement award. Although I am so honored and truly humbled by this recognition, it's hard for me to imagine receiving such an award when the AF has given me so much more than I believe I have or ever could give back. Each of you has somehow been part of my Air Force Pharmacy career, so in large part, really you deserve the credit for any and all achievements occurring during my service. Thank you for letting me be part of such a great experience.

As Col Melissa Howard transitions to be the next Associate Corps Chief, I wish her and all of you the very best for future success. Many thanks

Col (ret.) Sprenger

Letter from the 4POX1 Career Field Manager

“Pharmily”

What an amazing honor! This is my response to the question, “do you like your position as the Pharmacy Career Field Manager?” A simple four word answer that has been twenty-five years in the making. It includes a road steeped in nostalgia, pride, and emotions and I know many of you understand because of the many stories I get to hear each and every day. For me that nostalgia is tied to all of the great pharmilies I’ve had the privilege of being a part of. The bond with peers, the NCO’s that pushed me to develop my expertise, and the officers that entrusted our teams to accomplish the mission. That feeling of elation and adrenaline that leads to pride when you get that two in the morning phone call to come in, make those pediatric syringes for a neonate, then help load a precious loved one onto an air evacuation flight on a snowy flight line and then receive word the patient is doing well! The growth that comes from those personal and professional emotions shared with pharmily members in good times as well as bad. Simply put, an amazing honor many years in the making.

I see my role as serving all of you and it is reflected in our Air Force Pharmacy motto rarely heard today, “A Proud Heritage, A Proven Profession.” This phrase represents our commitment and it fits perfectly with the values of both the Air Force Medical Service and our United States Air Force. It’s a commitment to developing our Airmen (all Airmen and those teammates who help make our mission happen) and to working hard to ensure each of you have the tools you need to get the job

done. To make sure the lines of communication remain completely open and transparent in an effort to achieve the best for both our beneficiaries and our people. As we make this journey together I will be able define “how” each of these principles can and will be accomplished. I cannot accomplish this alone; it will be in concert with our Associate Core Chief, our Headquarters Pharmacy staff, our MAJCOM Consultants and Functional Managers, your Flight Commanders, Flight Chiefs and finally all of you!

Looking forward, I’m excited about connecting and reconnecting with as many of you as possible! I’m excited to hear your stories of success and the challenges you face implementing the institutional priorities that will help us continue to be the greatest Air Force our planet has ever known. I’m eager to work with all of you to develop our Human Capital Investment Strategy to ensure we retain the best Pharmacists and Technicians we have in the years to come! Great leaders who had passion and vision to do some fantastic things have paved our way and today there’s no shortage of talented individuals that believe in doing the same. With such a great team of proven professionals leading the way there’s nothing left to say but, “What an amazing honor!”

Chief Daniel McCain

Strategic Manning—A Functional Perspective

By: SMSgt Jacey McDuffie

As the Air Mobility Command Pharmacy Functional Manager, I have the great opportunity to impact pharmacies at 10 different bases with around 130 enlisted personnel. My job is to serve as a liaison between them, the Career Field Manager and the Air Force Personnel Center (AFPC).

I have served as AMC’s Functional Manager for the last 8 months and the number one concern I keep hearing from the field is manning. Manpower has been a great challenge over the last few years, not only within the 4P career field, but the entire Air Force. By the admission of the Chief of Staff of The Air Force, General Mark Welsh, the force has been cut too much too fast. The Pharmacy Career Field has been hit hard by these cuts

as well. Today, 80% manning has become the new 100%. The days of being 100% manned are gone. So, with that said, what can we do?

Communication is critical to success in the efficient use of resources. Expanded use of technology and innovation will impact work in ways not yet seen. It is important to focus on new perspectives, ideas and technology. I ask you to not become complacent in your operations, be open minded and reach out to other locations to see and learn different ways to run an operation. Pharmacies will have to work together to develop more efficient ways to overcome periodic manning gaps.

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Strategic Manning—A Functional Perspective

Effective and economical management of manpower will always be a number one priority.

As 4P Functional Managers, we do our best to meet and accommodate all of the manning needs within the commands. I encourage everyone to look at their manning through a more strategic lens. If you find your Pharmacy is continually struggling with manning I suggest doing the following: commission a Manpower study through the HAF, bring back any matrixed bodies, look for ways to innovate and be more efficient, network with other Pharmacies to find best practices and submit unfund-

ed request for additional hires. Our Career Field is one of three medical AFSC's with an approved workload/manning standard. This standard supports our ability to gain the personnel we need to get the job over others. We will do everything within our power to ensure you have available resources that will assist you with your team's continued success. Finally, keep those communication lines open and never hesitate to reach out to your Functional Manager, it's our job to serve you!

SMSgt Jacey McDuffie

Reflections of a New Senior Non-Commissioned Officer

By: MSgt Leah Lewis

As I think back on my Air Force career so far there have been many ups and downs, challenges and triumphs. I joined the Air Force as a pharmacy technician when I was 20 years old with the intent of serving for four years and then getting out and going to school.

In 2010 after being in the Air Force for about 8 years, I deployed to Kuwait as a pharmacy technician with the CASF for 6 months, and again in 2014 to Ramstein AB as a part of the CASF mission there. Those two deployments were some of the most rewarding and challenging experiences I have had in my Air Force career so far. When I was deployed to Ramstein AB, the biggest part of our mission was to transport our wounded warriors to Landstuhl for further care and then back to the United States once they were stable enough to fly.

It was challenging for me to see so many young men and women coming home with such debilitating physical and mental injuries. What I learned from that experience was that even on my worst days, when I have meetings to attend, EPR's to write, employees calling off, angry patients to deal with and a million other things going on, I am truly blessed. Many of those heroes

didn't make it home and the ones that did have challenges that put mine to shame.

As a leader I think it is important to remind our Airmen that they will face many challenges throughout their careers and life in general, however they can overcome them with persistence and determination. Challenges grow us and help up to become the best possible version of ourselves. Help your Airmen identify their strengths and weaknesses and encourage them to tackle their weaknesses head on and to share their strengths and encourage others. Surround yourself with people who inspire you and encourage you to chase your dreams and to make them a reality. It's ok to feel like you can't do something or that you're not ready...trust me I felt both of those things when I found out I had made Master Sergeant. Just because you feel like you can't do something doesn't give you the option to quit or to not do it. Sometimes it takes a little push and some encouragement from others to help us to see what we are truly capable of. Don't sell yourself short...you are capable of whatever you put your mind to. Continue to face the challenges that you have in your life head on and you will succeed.

MSgt Leah Lewis

Not Just Any Pharmacy Technician—AFSOC/4P

By: MSgt William McDuffie

My time as a 4P in the Air Force Special Operations Command (AFSOC) was one of the best experiences to date in my career. The training was un-matched and invaluable. A few months into my assignment at Hurlburt Field AFB I was assigned to a Unit Type Code that was extremely unique. The

overall mission capability read like this: *Provides additional medical support personnel to a SOF IW/SSTR medical team. Provides additional medical personnel to execute missions in...*

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Not Just Any Pharm Tech—AFSOC/4P

support of irregular warfare (IW) and stabilization, security, transition and reconstruction (SSTR) operations. May collocate with partner-nation forces and other us DOD forces to support theater combatant commanders during missions and operations. Can be deployed in total or increments to meet operational mission requirements.

The training that I received was second to none. The Air Force Special Operations School at Hurlburt Field provided real world training and the staff was extremely knowledgeable and professional. It all started with Introduction to Special Operations (ISOC). Next on the list was Introduction to Special Operations Medicine (ISOM). Then we had to qualify on the M9 and M4. After those qualifications you perfect those skills at Field Skills Training (FST), which was magnificent. This course consisted of around 15 people who had to become experts on the M4, we shot 30,000 rounds in 15 days.



We would shoot in different scenarios to include night ops. The anticipation of completion was overshadowed by more shooting. We also had to become familiar with any weapon that we may come in contact with while detached to a SOF team. This included: 50 cal, M 240, and the standard AK-47. We perfected the art of clearing rooms and houses in a standard shoot house. This course also provided defensive driving as well as maneuvering to a safe position from a convoy attack and a Hummer driving course. Our instructors were 3 Army Green Berets with combat experience in Afghanistan. After FST we had Evasion and Conduct after Capture (ECAC), this was very intense. This course was taught by a retired par-rescue member who was in the Battle of Takur Ghar (Roberts Ridge), the deadliest entanglement of Operation Anaconda. In this training, we learned the art of evasion as well as land navigation and survival. We practiced escapes, kidnapping and hostage scenarios. I also took body language courses taught by a rep from the Central Intelligence Agency. Finally I completed a Tactical Combat Casualty Care Course (TCCC) at Ft Bragg taught by 68W's (whiskeys) the Army Combat Medics. I would do most of my training with Army because we were very similar to their Special Ops Civil

Affairs and Psychological Operations units. Unfortunately, due to the sensitive nature and classification of other training I received, they cannot be shared in this forum.

Once proficiency was achieved, all I wanted to do is put my new skills to use. I had deployed numerous times all over the world before this assignment but I wanted to use my newfound training. I finally got selected for a joint training deployment with the Army in associated with a Combined Joint Task Force. My official role was an Air Force Special Ops Irregular Warfare

Team Member. I served in remote Middle Eastern town helping teach Mass Casualty Care to foreign nation partners. My team and I also conducted Health Care Assessments throughout the region to include some small detail of Pharmacy work, this was not without danger. The local town near the camp was not very receptive to Americans and in recent news has become very pro ISIS. I and another medic wound up look-

ing down the barrel of an AK-47 while serving as a paying agent for the team. At the time we had no weapons or uniforms, all I had was \$5k cash and a passport. Luckily, we were able to escape that situation, help save another team from entering the area, and departed that area of the country the next morning under heavily armed escort. Despite the rigorous training and dangerous encounters, the overall experience of being 4P in AFSOC was amazing. I would encourage other 4P's who get assigned to the command to take advantage of the unique opportunities of a career and possibly a lifetime.

There are unique opportunities within the 4P career field and this was just one example. I have been fortunate throughout my career to be selected for similar things. There are plenty of chances to participate in these types of assignments. You have to work hard, be proficient at what you do and let leadership know you will do whatever it takes to complete the mission. You need to be able to be trusted working solo and be able to hold your own in a joint environment. If you possess these attributes the opportunities will open up for you.

MSgt William McDuffie

A Pharmacy Technician's Thoughts on Deployment

By: TSgt Kristine Butler

Deployments are stressful; Deployment as a stand-alone pharmacy technician is intimidating. Even with 13 years of pharmacy technician experience, I still felt uneasy managing operations as a stand-alone technician without a pharmacist. Standing side by side with your pharmacist gives any pharmacy technician relief and reassurance that operations will be clinically safe and sound. My confidence set in, as I set foot in a tiny Al Dhafra Air Base pharmacy in 2013. I used my technical experience from Langley Air Force Base and put them into practice. If there is one advice I can suggest to any pharmacy technician, it would be to know your job, inside and out. This will ease any stress you may have from any deployment, at any time, anywhere in the world.

My deployment was not set up for trauma operations but primarily outpatient support for the entire populace of approximately 2,500 Airmen, Seamen, Soldiers, Marines of Al Dhafra Air Base, as well as 17 Forward Operating Bases, extending to the Horn-of-Africa. It was intimidating to think about, however, the day-to-day operations was easily managed with the experience I brought from my home base. Knowing your job inside-and-out means learning your primary duties as well additional duties whenever possible. There is no such thing as too much information. Do not wait until you need specific training to learn the job; you must seek the knowledge. For example, although you were not appointed the Primary Narcotics Custodian, it is still your responsibility to learn the processes that comes with movements of controlled substances. Other knowledge I gained that eased my mind are pharmacy calculations, extemporaneous compounding, and Logistics management i.e. DMLSS to name a few. Progressing technically is our responsibility. These tasks helped me tremendously when I was alone at Al Dhafra.

Although my deployment was primarily outpatient, my experiences and knowledge I gained through inpatient also gave me the confidence to tackle any calculations from simple IV's and extemporaneous compounding. Trust me, when your formulary is limited, your flight doctors can become creative. Memories of "what you want over what you have," "weight/weight x volume/volume" and little trinkets you feared you lost from you CDC's will come out. This is only true if you truly practiced them prior to your deployment. This is why I say, learn and know your job before you need to know your job.

My patients walked up to my window, trusting that my level of knowledge and skills will safely dispense their medications. Whenever I came across a clinical issue that is beyond my realm, I used my lifelines:

1. I phoned a Friend. I called Langley Air Force Base all the time to speak to a pharmacist after hours. I also called them to speak to another technician that can help me solve a problem.
2. I asked the audience. I referred to my SGH, whom, by trade, is my acting pharmacist if a pharmacist is not available. The SGH is a great resource for lots of your clinical questions.
3. Ask an expert. I also utilized Al Udeid Air Base pharmacy for assistance. The pharmacy team, 4 hours away from me, assisted me with alternative medications and other logistical issues I'm dealing with.

To survive a stand-alone deployment is to remember that you are not alone. You don't have to know everything but you do need to know your resources at all times and know your job.

TSgt Kristine Butler

Remembering Our Newly Minted Airmen

By: SrA Michael Branch

Today in ALS class, I had the very humbling experience of watching 14 people walk to the front of the class and mark down exactly how much they cared about their commitment to their job and, by extension, the Air Force. I won't say I was surprised by the way our little care-continuum turned out, as this subject tends to elicit either a very positive or very negative response from our junior Airmen. A response that, you, the supervisor, NCOIC, or even commander probably see every day in your respective shops. Our deep, intrinsic moti-

ations are a very sensitive subject, and I feel privileged that those 14 other people were willing to share. I'm not going to delve too deep into exact specifics, however I would like to share some over-arching themes common among my classmates and the other individuals outside my career field whom I had the pleasure of interviewing.

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Remembering Our Newly Minted Airmen

Picture yourself scouring your bedroom looking for just where in the Sam Hill you put the dang car keys. Just as you're checking the pants you wore yesterday for the 4th time, little baby Junior decides now is the time to start bawling at the top of his lungs. Even though you're stressed and don't have time for this because, "Where heck are those stupid keys?" babies cry because somehow their needs aren't being met. That need could be food, burping or (most likely) upsies.

Human beings are the same way: we cry when our needs aren't being met. Now, granted, most of us don't start crying our eyes out when we need something. Thus; it's difficult for people in leadership positions to understand why their Airmen are "crying" mostly because the reason usually (according to the people I spoke to) lies with the leadership itself. Our tactical/strategic leaders walk into work every day with a deep and intimate focus on how their team can make sure the Air Force's needs have been met. While that's certainly an appropriate and admirable mind-set to have; the crux of the issue comes when that dedication isn't reciprocated. The most common theme as to why our junior Airmen are unhappy is because their supervision never made an effort to find out why the new body added to the manning roster was even there. These Airman felt as if they were never aware of options such as space available traveling, overseas special duties, and the various roads to commissioning. For a great majority of our Airmen, retraining into another career field might make their life more in tune with the original reason they joined. As these disgruntled Airmen rise to the rank to E-4, they start to realize all the opportunities missed out. The individuals I spoke to professed that this loss of trust in the system sort of "settled and congealed" into an overall feeling of dissatisfaction.

Fortunately, there's a very simple solution to this. If supervisors incorporated the base, underling reason why their troop joined the Air Force into their initial feedback, the supervisor can set reasonable milestones into their training plan. If, right off the bat when they enlist, a person can see the Air Force is making every attempt to give as much as it takes, they will be more likely to reciprocate.

The second most common reason why our Airmen lose faith in the system goes much deeper into the intrinsic properties of their all too human supervisors. There were several responses, particularly from our maintenance and security forces wingmen, about supervisors that just didn't care to motivate or mentor their troops. While the exact reason for this varied, the end result boiled down to Airman basically fighting the "Good ol' Boy" system where their enlisted leadership favored people who "just shut up and color" as opposed to challenging the status quo. This is where our commissioned corps come into play. Officers and commanders represent the "balance" portion to how the EPR system implements checks and balances. Without a knowledgeable and impartial leader signing off on EPRs, the inflated and bias "check" the NCO does will represent the totality of how the Air Force see that Airman.

I understand the difficulties with this, however. Not many Air Force entities interact with their officers to the extent that would allow for meaningful evaluation. Changing the evaluation system to accommodate an informed opinion from the commander or designated reporting official might seem radical and undoable, but it's important to remember that there is precedent for it. Our current evaluation system is the product of multiple failures and, even now, is in the process of revision. It's important to recognize and remember how important our voice is

Pharmacy Practice SIG Update

The Pharmacy Practice SIG rotates leadership every few years. I am happy to announce that Col Sprenger has selected Major(s) Jason Bingham from Columbus AFB as the next Pharmacy Practice SIG leader. Maj(s) Bingham brings a wealth of operations expertise to the position and has been actively engaged in managing PPSIG projects over the past several years. He has obtained his Lean Six Sigma Green Belt and is in the final steps to achieving his Black Belt certification. Transition will occur over the summer months and be completed in time for Joint Forces Pharmacy Seminar this fall. Managing the PPSIG is an

incredible experience and provides great learning into Air Force Pharmacy operations as well as networking with our Army and Navy counterparts. Maj(s) Bingham's selection as SIG leader was in no doubt related to his active involvement in the SIG. If you are interested in becoming a future SIG leader...get involved today!

Active projects currently underway with the PPSIG are an analysis of Patient Safety Reporting (PSR) data to provide standardization recommendations for evaluating prescription error data by pharmacies.

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Pharmacy Practice SIG Update

Also, a systems downtime team is working to develop standardize operating instructions to assist pharmacies determine scope of operations during systems outages.

As always PPSIG projects begin with ideas from PPSIG members. If you have an idea, please send a message to SIG leaders Maj(s) Jason Bingham and MSgt Rosland Upshaw. Also, check out the PPSIG information page on MilSuite at <https://www.milsuite.mil/book/groups/air-force-pharmacy-practice-subject-interest-group-sig>. Thank you for improving patient care every single day!

Maj David Jarnot

Readiness SIG Update

Your Readiness SIG leaders are Maj Anthony Dargush and SSgt Stephen Iles. We are responsible for ensuring the 43Ps and 4Ps have the proper tools for readiness operations in the AOR and in garrison. One of the most common question the SIG receives is regarding how to stay up to date on Inpatient Pharmacy Operations training. We realize the majority of Air Force Pharmacies do not have the capabilities or resources to train their own folks so they are prepared to complete the inpatient mission down range. One option is to create a local partnership with either a downtown or Sister Service facility in your area. Create a MOA to allow you folks to rotate in at that site to practice Inpatient Operations Skills, most importantly Intravenous Compounding Skills and common inpatient emergency medications. Another option if you have a short notice tasking is to reach out to our larger facilities within the Air Force for a TDY to help spin your Airman up. This will require you coordinate unit funding.

One project your Readiness SIG is working on to help alleviate problems achieving these skills is creating virtual training modules to improve readiness skills that are not easily trained in garrison. SSgt Iles has worked hard on a sterile technique videos to help remind you when it is your turn to head down range. Below is the link to a few of those videos. Please take a look and incorporate into your training routines. Other modules in the pipeline include emergency medicine and Logistics/Antivenins.

https://www.youtube.com/channel/UC2i__ngSyUrABTaUk9T110A?nohtml5=False

Please contact us with any questions or if you are interested in participating with the Readiness SIG.

Maj Anthony Dargush

Technology SIG Update

The TechSIG is currently involved with multiple projects. 1) The largest and most applicable to most pharmacies is the Automation and Workflow modernization refresh. While Phase 1 is complete, the Large Refill Site and Phase 2 are still with contracting. One significant change in Phase 2 is removing 21 sites from Phase 2 and switching these 21 pharmacies from a replace refresh to an upgrade refresh. What this means is the sites will keep some automation and all licensing fees but will replace all workstations, servers, and some equipment. The 21 sites have already been identified and most of these sites have already started work on their upgrade. 2) The Pyxis refresh is still underway. Any site that was refreshed within the first six months knows that BD did not install the correct software and had to return to fix their mistake. By the end of April all re-visits should be complete and new site up-grades will resume. 3) Queuing Standardization project is proceeding on both an AF and DHA level. The AF SME is Maj(s) Karl Bituin for the DHA initiative. Additionally, the AF is working with both Q-Flow and QMATIC to enhance the patient experience though standardization. 4) The Patient Centric Label initiative is finalizing the label design and should be available on the Kx in the next month. All 21 sites receiving the upgrade refresh will migrate to the AF Patient Centric Label. 5) The Kx continues to receive updates - please follow the Kx and visit on a regular basis for continued TechSIG updates.

If you need anything else please let me know.

Maj Justin Lusk

Annual Award Winners

2015 SOCIETY OF AIR FORCE PHARMACY **CAREER SUSTAINED ACHIEVEMENT AWARD**



COLONEL SCOTT A. SPRENGER

PHARMACY CONSULTANT TO THE AF/SG

Colonel Sprenger entered the United States Air Force in 1988. As a Company Grade Officer, Col Sprenger served as OIC of inpatient pharmacy and pharmacist liaison to critical care nursing, contributing to Wilford Hall Medical Center's first every "Outstanding" rating on the Health Services Inspection and Inpatient Pharmacy recognition as a "model for all Air Force pharmacies". Col Sprenger was competitively selected to obtain his Doctor of Pharmacy and utilized his clinical expertise to co-author the ASHP accreditation package for the Air Force Pharmacy Residency Program. As a Field Grade Officer, Col Sprenger served in variety operational assignments, as MAJCOM Pharmacy Consultant for 3 different MAJCOMS, as well as pharmacy department chair for the San Antonio Military Medical Center. He was handpicked to serve as the senior pharmacy analyst to the Air Force Surgeon General staff and implemented a \$25 million optimization project to standardize operations across the Air Force. Additionally, he was selected for Squadron Command at Lackland AFB, and Group Command at Eielson AFB, prior to reaching the summit of his career as the USAF Pharmacy Consultant and Associate Chief for Pharmacy at the Defense Health Headquarters. A life member of the Society of Air Force Pharmacy, Col Sprenger served as President, Board Member, and advisor during his career. His over 27 years of service to the United States Air Force is testament to his leadership and brings great credit upon himself and the United States Air Force.

Annual Award Winners

2015 SOCIETY OF AIR FORCE PHARMACY

MAXINE BEATTY FGO OF THE YEAR



MAJOR JENNIFER L. BAKER

MISAWA AFB

Major Baker led the Misawa AFB pharmacy to provide around the clock care to 10 thousand patients, directing 6 thousand call hours, and resolving 240 urgent medical needs in less than 20 minutes. As Deputy Commander, she was vital to the leadership of 9 flights and \$153 million in assets. She served as the Air Force Clinical Subject Matter Expert and provided input for 2 Defense Health Agency committees. Additionally, she developed an IV training program that enhanced training for 1.6 thousand members. Her leadership was evident as she led her flight to 3 Group/Wing annual awards, 11 Squadron/Group/Wing quarterly awards as well as PACAF #1 rankings in accuracy, satisfaction, and individual medical readiness. Major Baker's leadership reflects great credit on herself on the United States Air Force.

Annual Award Winners

2015 SOCIETY OF AIR FORCE PHARMACY

FRED COLEMAN CGO OF THE YEAR



CAPTAIN ADAM K. COOPER
MOUNTAIN HOME AFB

Captain Cooper guided the installation disease containment exercise providing flu vaccine to 485 patients and contributed to a Wing 88% Individual Medical Readiness rate. He led Mountain Home AFB to pilot a new clinical screening program for the Department of Defense supporting patient safety screening for 587 Military Treatment Facilities and 9.6 million beneficiaries. Finally, he spearheaded a medical health initiative to implement 75 prescription changes and saved the Air Force \$208 thousand. His leadership and commitment to improving processes reflect great credit on himself and the United States Air Force.

Annual Award Winners

2015 SOCIETY OF AIR FORCE PHARMACY SNCO PHARMACY TECHNICIAN OF THE YEAR



MSGT ROSLAND K. UPSHAW **MACDILL AFB**

MSgt Upshaw led the Air Force's largest clinic pharmacy as Pharmacy Operations Section Chief. In this role she was responsible for 60 staff, \$28 million operations budget, and oversaw the dispensing of 646 thousand prescriptions to 215 thousand patients. In addition, MSgt Upshaw served as the Medical Group interim First Sergeant and Squadron Superintendent providing guidance to 760 personnel. As the enlisted leader for the Air Force Pharmacy Practice Subject Interest Group, MSgt Upshaw teamed with career field experts to author a 120 page practice guide setting the practice standard for 828 pharmacy technicians. She earned a professional manager certification, served as President of the Medical Group Top 3, facilitated a leadership development seminar, and emceed the Wing SNCO Induction ceremony for 250 attendees. MSgt Upshaw's leadership reflects great credit upon herself and the United States Air Force.

Accreditation Statement



Postgraduate Institute for Medicine is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Credit Designation

Postgraduate Institute for Medicine designates this continuing education activity for 1.0 contact hour(s) (0.1 CEUs) of the Accreditation Council for Pharmacy Education.

(Universal Activity Number - 0809-9999-16-322-H01-P) - Pharmacists

Type of Activity

Application

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Tyrosine Kinase Inhibitors (TKIs) for Chronic Myelogenous Leukemia (CML)

By: Nina Tachikawa, Maj, USAF, BSC, Pharm D

Goal

- 1) To familiarize pharmacists with the pathophysiology and treatment options for CML.

Learning Objectives

- 1) Explain the significance of the Philadelphia chromosome
- 2) Describe the clinical presentation and diagnosis of CML
- 3) Summarize current treatment options for CML
- 4) Modify and discuss treatment alternatives pertinent to the patient
- 5) Identify and manage toxicities associated with first line treatments



Postgraduate Institute for Medicine

Released: 1 June 2016
Expiration Date: 30 January 2017
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 CML.

Abstract

Chronic myelogenous leukemia (CML) is just one type of hematologic malignancy. The main etiology, translocation between chromosome 9 and 22 creating the Philadelphia chromosome, has guided drug therapy. Tyrosine kinase inhibitors (TKIs) are the hallmark of CML therapy utilized as first, second, and third line. Pharmacists can influence the clinical management of CML by providing effective medication counseling, ensuring that treatment is tailored to the patient, and monitoring or making recommendations in managing for toxicities.

Introduction

Over 40 oral antineoplastic agents now exist on the market. For 2016, there is an estimated 8,220 newly diagnoses patients and 1,070 deaths from CML.¹ Leukemia is a cancer of the blood and bone marrow further subcategorized into 4 groups: acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), chronic myeloid leukemia (CML), and chronic lymphocytic leukemia (CLL). As more oral antineoplastic agents become available, familiarization of the gold standard medication and others in that class are important. This article focuses specifically on chronic phase CML and the standard treatment – tyrosine kinase inhibitors.

Etiology and Pathophysiology

Chronic myelogenous leukemia is caused by an oncogenic protein produced by the Philadelphia chromosome found in over 90% of patient cases.^{2,8,16-20} The Philadelphia chromosome first described in 1960 was the first karyotypic abnormality specifically implicated in the pathogenesis of cancer.³ The Philadelphia chromosome is the consequence of breaks in chromosomes 9 and 22.

A translocation occurring from the Abelson murine leukemia (ABL) portion on chromosome 9 to the breakpoint cluster region (BCR) on chromosome 22 results in the formation of BCR-ABL hybrid fusion gene which produces an oncogenic protein, p210.^{3,6,8}

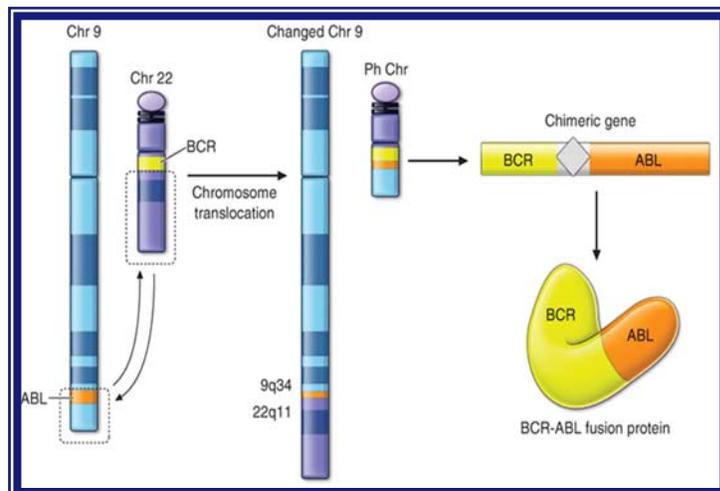


Figure 1: Creation of the Philadelphia Chromosome

Source: Pharmacotherapy: A Pathophysiologic Approach, 9e. Eds.. Harrison's Principles of Internal Medicine, 18e. Eds.

CML is further stratified into 3 phases: chronic phase (90% of newly diagnosed cases), accelerated phase (AP), and blast crisis (BC).^{3-6,16} Chronic phase (CP) CML left untreated will eventually progress

Criteria for Accelerated Phase and Blast Crisis Phase			
	World Health Organization (WHO) Criteria ^{a,b,c}	European Leukemia Net (ELN) Criteria ^{b,c,5}	Modified MD Anderson Cancer Center/ International Bone Marrow Transplant Registry ⁴
Accelerated Phase			
Spleen	Persisting or increasing splenomegaly unresponsive to therapy		
WBC	Persisting or increasing WBC (>10 x 10 ⁹ /L) unresponsive to therapy		
Blast Cells	10-19%	15-29%	≥15% and 30%
Basophils	≥20%	≥20%	≥20%
Platelet Count	>1000 x 10 ⁹ /l uncontrolled by therapy	<100 x 10 ⁹ /l unrelated to therapy	<100 x 10 ⁹ /l unrelated to therapy
Clonal Chromosomal abnormalities	Present	Present	Present
Blast Crisis			
Blast Cells	≥20%	≥30%	≥30%
Extramedullary involvement	Yes	Yes	Yes
Other	Large foci or clusters of blasts in the bone marrow biopsy		

a-ELN guidelines included both the WHO and ELN criteria
b-ESMO guidelines included both the WHO and ELN criteria
c-NCCN guidelines included both

Table 1: Three Phases of CML

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Cont... to the other aggressive phases in which median patient survival is mere months.³

Presentation and Risk Factors

Signs and symptoms of CML can include, but are not limited to malaise, fatigue, night sweats, low grade fever, and weight loss. Pain in the upper left quadrant of the abdomen can occur in patients experiencing splenomegaly (>50%).^{1,4,6,17} These signs and symptoms are frequently constitutional. In approximately 40% of diagnosed cases, patients are often asymptomatic until annual lab work shows abnormalities in complete blood count differentials with leukocytosis (basophilia and immature granulocytes) and thrombocytosis.^{6,17} The median age of diagnosis for CML is mid-sixties with only known risk factors being ionizing radiation exposure (atomic bomb survivors). No hereditary, familial, geographic, ethnic, or economic risk factors are known.³

Diagnosis

As stated previously, abnormal lab values are the hallmark of diagnosis. Definitive diagnosis occurs with cytogenetics from bone marrow biopsy (preferred) or blood smear for Philadelphia chromosome presence.^{2,3,17}

Cytogenetic testing includes chromosome banding analysis (CBA) utilizing bone marrow samples or fluorescence in situ hybridization (FISH) when bone marrow samples are unavailable. FISH determines the presence of the Philadelphia chromosome. Qualitative reverse transcriptase polymerase chain reaction (RT-PCR) testing requires bone marrow biopsy samples

and detects cells with the abnormal BCR-ABL protein. Specifically, the qualitative RT-PCR test is sensitive to detect one abnormal protein among one million cells and is significant in evaluating treatment response or further disease progression.

Treatment

Tyrosine kinase inhibitors (TKIs) are first-line therapy in the treatment of CML.^{4,16} Imatinib (Gleevec®), still the gold stand-

ard, was first studied in the 1990's with approval by the FDA in 2001 for use in chronic myelogenous leukemia.^{3,6,18,19} Once quoted as the cure for cancer, today there are over twenty TKIs available on the market justifying their effectiveness and place as a therapy mainstay.⁶ These agents are not only utilized for more familiar hematologic malignancies, but also in breast cancer, non-small cell lung cancer, thyroid cancer, renal cell cancer, and gastrointestinal stromal tumors. Tyrosine kinase inhibitors prevent tyrosine kinase from catalyzing the transfer of phosphates from ATP to tyrosine residues in polypeptides.⁶

Tyrosine kinase inhibitors utilized in CML inhibit further up-regulation of myeloid line cell progression by inhibiting the BCR-ABL kinase activity, inhibiting growth of BCR-ABL positive cells and inducing apoptosis.^{3,7} While imatinib was the first TKI approved for CML, second generation TKIs such as nilotinib (Tasigna®), dasatinib (Sprycel®), bosutinib (Bosulif®), and ponatinib (Iclusig®) were developed to overcome resistance (TABLE 2).⁷ Guidelines for first line treatment of chronic phase recommend: Imatinib 400mg daily, nilotinib 300mg twice daily, or dasatinib 100mg daily.^{4,5,16,17}

Imatinib was first shown to be statistically significant in the first line treatment of CML during the IRIS study.^{8,9,19} This trial compared 400mg imatinib with interferon alfa and low-dose cytarabine combination therapy. Prior to TKI therapy, interferon alfa and low-dose cytarabine combination therapy demonstrated cytogenetic response superiority.^{3,8}

Mixed results of survival outcome significance, frequent injections, and side effects from the combination therapy further made imatinib an attractive treatment option in addition to the statistically major cytogenetic response, complete cytogenetic response, and freedom from disease progression at 18 months demonstrated. Further IRIS study follow-ups at eight years demonstrated imatinib's overall survival prolongation at around 85%.⁹

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Medication	Usual Dose for CP	Mutation Activity	Drug-Interactions	Drug-Food Interactions	Clinical Pearls
Imatinib ^{3,11} (Gleevec®)	400mg QD		CYP3A4 inhibitors or inducers	Take w/large glass of water and meal; Avoid grapefruit juice	
Dasatinib ^{10,12,18,19} (Sprycel®)	100mg QD	Most imatinib resistance mutations, not T135I, F317V	H2 antagonists, PPIs, CYP3A4 inhibitors or inducers	Avoid grapefruit juice	350-fold higher potency than imatinib
Nilotinib ^{10,14} (Tasigna®)	300mg BID	Imatinib-resistant mutations	CYP3A4 inhibitors or inducer, CYP2C8 and CYP2D6 substrates, H2 antagonists, QTC prolonging agents	Empty stomach required	
Bosutinib ^{10,14} (Bosulif®)	500mg QD	16/18 mutations, not T135I or V299L	H2 antagonists PPIs, CYP3A4 and P-glycoprotein inhibitors or inducers	Take with food	
Ponatinib ^{10,15,16} (Iclusig®)	45mg QD	T135I	CYP3A4 inhibitors or inducers	Avoid grapefruit juice	520-fold Higher potency than imatinib

Table 2: Comparison of Tyrosine Kinase Inhibitors

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Managing Resistance

Resistance caused by point mutations (>90 characterized) in the kinase domain of the BCR-ABL gene continues to be an ever increasing problem causing resistance to imatinib.^{4,5,7,10,17,19} Imatinib resistance prevalence with patients at the accelerated or blast phases after prolonged therapy is even estimated at 79-90%.¹⁰ In CP CML, 20-30% of patients who take imatinib do not have complete cytogenetic response.^{2,9,16} This issue has propagated the development and consequent use of second generation TKIs and/or combination therapy as well as the progression to allogenic stem-cell transplantation (allo-SCT).^{3,9,17,20}

Second generation TKIs approved for first line therapy in newly diagnosed CP CML and use in imatinib resistant or intolerant patients are nilotinib and dasatinib.^{4,17} Nilotinib, first approved in 2007 for patients with chronic or accelerated phase and resistant and/or intolerant to imatinib, was shown to be superior versus imatinib in the Evaluating Nilotinib Efficacy and Safety in clinical Trials-newly diagnosed patients (ENESTnd).⁹ Both the 300mg and 400mg twice daily dose of nilotinib demonstrated statistical significance at almost twice the rate of major molecular response rates versus the standard 400mg daily dose of imatinib. Dasatinib, first approved in 2010 for patients with newly diagnosed CP CML, has a 325-fold higher potency than imatinib. Dasatinib was compared to imatinib for efficacy and safety in the dasatinib versus imatinib study in treatment-naïve CML patients (DASISION).¹⁸ This study demonstrated that dasatinib 100mg daily, compared to imatinib 400mg daily induced statistically significant rates of completed cytogenetic responses and major molecular responses. DASISION's two year follow up showed support of earlier findings both in efficacy superiority for complete cytogenetic response and major molecular response.¹⁹

A meta-analysis was conducted to evaluate the emergence of BCR-ABL kinase domain mutations associated with newly diagnosed CML.⁷ Twelve studies involving 1,698 patients found that incidence of genetic mutation were highest in imatinib (9.7%) followed by nilotinib (3.3%) and dasatinib (1.7%). Imatinib associated mutations found were E255K, T135I, M351T, F359V, and G250E. Nilotinib associated mutations included E255K and F359C while dasatinib associated mutations found were T135I, V299L, F317L, and F317I. Ponatinib received accelerated approval by Food and Drug Administration in December 2012 for the treatment of CP-CML, AP-CML, BP-CML or Philadelphia chromosome positive (Ph+) in those patients who have failed or tolerate first line or TKI therapy.¹⁶ Ponatinib is the only TKI available with activity against the T135I mutation. Bosutinib is another option available for patients resistant or intolerant to prior therapy.^{4,5,17}

Treatment response is defined in three ways – hematologic, cytogenetic, and molecular.^{4,5,17} Complete hematologic response (CHR) is defined as the normalization of peripheral blood counts

and typically the first type of response seen after treatment initiation. Cytogenetic response (CgR) is the percentage of Philadelphia chromosomes detected by CBA or FISH testing. Molecular response is the amount of BCR-ABL detected by quantitative RT-PCR.¹⁷ Response should be evaluated every three months to determine continuation or potential changes in therapy.^{4,5,17}

Allogenic stem-cell transplantation (allo-SCT) remains the only curative treatment of CML, but is kept for last resort after failure of multiple TKIs because overall survival rates and complications related to graft-versus-host disease.^{3,5,10,17} In one study, two year survival rates for accelerated phase and blast crisis were cited 47% and 16% respectively after stem cell transplantation.¹⁰ The use of second-generation TKIs before and after allo-SCT has been discussed, but not commonly studied despite the above identified issue. In a single institution case series report of 12 imatinib refractory patients, treatment with second generation TKIs before and after allo-SCT showed a satisfactory outcome with 8 out 12 patients alive and 7 with complete molecular response at the 28 months median follow-up.¹⁰

Limitations of Tyrosine Kinase Inhibitors

There are several limitations of tyrosine kinase inhibitors that affect compliance and therefore response rates. Cost, intolerance, and toxicities among resistance are frequent reasons for interrup-

Medication	Toxicity	Management
Tyrosine Kinase Inhibitors ⁴	Hematologic: Absolute Neutrophil Count <0.5-1.0 X10 ⁹ /L Platelets <50 x10 ⁹ /L	Hold until resolution, dose decrease, filgrastim (Neupogen®)
	Rash	Corticosteroids, Anti-histamines
	Hepatic Hepatic transaminases 3-5X upper limits of normal (ULN) T-bili – 3X ULN	Hold until resolution, dose decrease
	Diarrhea	Loperamide (Immodium®), hold, dose decrease, discontinue
Imatinib ^{4,11} (Gleevec®)	Moderate renal impairment – CrCl <20-39ml/min	Dose decrease by 50%
	Fluid retention	Diuretics, hold, decrease, discontinue
	Muscle cramps	Calcium supplementation
	GI upset	Take with food and water
Dasatinib (Sprycel®) ^{4,12}	Fluid retention/Pericardial effusion	Diuretics, hold, decrease, discontinue
	GI upset	Take with food and water
	Pulmonary arterial hypertension	Discontinue
Nilotinib (Tasigna®) ^{4,13}	QTc prolongation >480 msec	Hold, discontinue
	Peripheral arterial occlusive disease	Discontinue
Bosutinib (Bosulif®) ^{4,14}	Fluid retention	Diuretics, hold, decrease, discontinue
	Pancreatitis	Hold, decrease, discontinue
Ponatinib ^{4,15,16} (Iclusig®)	Hemorrhage	Discontinue
	Hypertension	Manage and monitor
	Vascular occlusion	Hold, discontinue
	Cardiac (heart failure, chest pain, etc)	Hold, discontinue

Table 3: Managing Medication Toxicities

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Cont... -tions or discontinuations in therapy.^{4,5,17} Table 3 illustrates common toxicities and potential ways to manage.

Summary and Conclusion

CML is a hematologic malignancy diagnosed after an abnormal lab value with patients often asymptomatic and in the chronic phase. Without treatment chronic phase CML progresses to the more aggressive and terminal forms; accelerated phase and blast crisis. Diagnosis occurs classically with leukocytosis and confirmation of the Philadelphia chromosome by CBA or FISH. The Philadelphia chromosome, caused by a translocation error between chromosome 9 and 22, encodes an oncogenic protein, p210, which causes dysregulation of myeloid progenitor cells. Treatment, which has extended the overall survival of this malignancy significantly, includes the use of a tyrosine kinase inhibitor: imatinib, dasatinib, nilotinib, bosutinib, or ponatinib. First line therapy includes imatinib, dasatinib, or nilotinib. Second line therapy includes one of the 3 TKIs from the first line, bosutinib, ponatinib, or consideration of allo-SCT. Third line treatment results to any of the remaining TKIs or consideration of allo-SCT. Limitations of TKI therapy are cost, resistance, intolerable side effects, or toxicities. The role of the pharmacist is crucial as understanding the limitations and benefits of each agent could help decrease discontinuation of treatment, prevent response failure, assist patients in identifying or managing toxicities thus ensuring compliance, and providing alternative treatment recommendation to health care providers.

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