On the Forefront of Hematology and Oncology

On the Forefront of Hematology and Oncology:

A Clinical Pharmacist's Perspective

By

Clement To Chung

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FOREWORD

It is my pleasure to write this brief foreword for Clement Chung, PharmD, MS, BCOP, BCPS. As a practicing pharmacist Clement is notable for the regular publication of mechanistic and forward-looking articles that highlight advances in the care of individuals with cancer. Along with his interest in the science of medicine/pharmacy, Clement is also engaged in enhancing the delivery of direct patient care to individuals and improving pharmacy operations to support these efforts.

Thus this collection of articles ranges from reviews into the mechanisms of the multiple myeloma microenvironment and apoptosis signaling to interdisciplinary care and stewardship of oncology practice. The article collection is pertinent and timely in its support of the practicing pharmacist, oncology specialized or not, and the administrator of an oncology service. I would encourage you to review the table of contents and start where your current interests lie but to consider reading even those that may not appeal to you right away as I think you will find value in all.

Joseph Bubalo, PharmD, BCOP, BCPS

ACKNOWLEDGMENT

Like all works by human minds, this one undoubtedly falls short of its goal. Yet I am grateful to God for His grace in my career which has spanned over two decades. I am thankful for the continuing support from my wife Emily, and the upbringing and nurturing my father Peter YP, and my mother Sylvia H gave me. My daughter Deborah also gave me fresh perspectives on editing. I am also indebted to Dr. Joseph Bubalo for his foreword in this book.

BIOGRAPHY

Clement Chung (full name: Clement To Chung) currently works as a senior oncology clinical pharmacy specialist at Houston Methodist West Hospital, one of the six community hospitals within Houston Methodist, a major health system in Houston, Texas, United States. He is currently board certified in oncology pharmacy and pharmacotherapy. Of Chinese descent, Clement is well-versed in both Chinese and English. He held a long-time interest in literature and history, graduated from King's College in Hong Kong, studied medicine for a year, then moved to the United States where he completed his undergraduate and graduate professional (Doctor of Pharmacy) programs at the University of Washington (Seattle). He lived in Seattle for over two decades prior to moving to Houston in 2013 with his wife and daughter.

In his career as an oncology clinical pharmacist, he constantly strives to advance the quality, safety, and value of oncology pharmacy. He was instrumental in developing and implementing an interdisciplinary oncology program in the Seattle area from 2005-2012, a computerized physician order entry system for chemotherapy in a safety net health system in Houston, Texas from 2015-2016, and most recently, a multidisciplinary treatment-related toxicity detection and reduction program for cancer patients. In the past 10 years, he has precepted over 50 students/residents and served as the first author for over 30 peer-reviewed articles, some of which influenced the shaping of future practice in clinical oncology pharmacy. He was a 2021 recipient of the "I CARE" award, i.e. the highest service award given to a Houston Methodist employee that demonstrates integrity, compassion, accountability, respect, and excellence.

PART I

PERSONAL PERSPECTIVES

CHAPTER ONE

FORMATIVE YEARS

"Blessed is the man
who does not walk in the counsel of the wicked…
But his delight is in the law of the Lord,
and on his law he mediates day and night.
He is like a tree planted by the streams of water,
which yields its fruit in season
and whose leaf does not wither.
Whatever he does prospers." (Psalm 1:1-3)

The notion of being born into an overseas Chinese (in Pinyin*, Hua Qiao*) family never occurred in the back of my memory during my elementary and middle-high school years in Hong Kong where I grew up, until one day, my dad took my whole family to where he was born, Thailand. On that trip, I took a glimpse of my grandparents' home and visualized for the first time the tough time that my dad grew up. But it took the next twenty years or longer for me to slowly realize the forgotten traits of my parents (namely, diligence, responsibility, and tenacity) started to become part of my gene and play an influential role in my career, especially during times of uncertainty and adversity. I understand however long I enjoy my career; it can never be too long for growth and progress.

My dad is a Hakka person (literally translated as "guest people"), an ethnic Han Chinese group that historically had been labeled as migrants with ancestral roots traced back to northern China thousands of years ago. Over the centuries, they successfully integrated their lives with the "locals" through arduous work and a strong sense of family. I could still recall the myriad of life's sorrows and joys when I skimmed through the chronicles of my ancestors that documented successive waves of migration: through tumultuous times of social unrest, famine, and life's hardships. Though I may not have all the good connections like the "legacy kids", "don't settle for mediocrity" is what has gotten me through changes in the past two decades.

My mom was also born and raised in an overseas Chinese family. Her family migrated to a southeast Asian country in the early 1920s. Both of my parents went back to China to study in the late 1950s, a time when the nation attracted millions of young souls with beaming hopes. My parents lived in Beijing for nearly two decades, where my older sister and I were born. A new page of life was ushered in the early 70s when my dad decided to leave for Thailand, but we settled down in Hong Kong instead, changing my mesmerizing memories of snow flurries and distinct four seasons into the balmy breeze of the South China Sea.

Photograph 1: Childhood family picture in Hong Kong (Author at far right)

During my childhood years in Hong Kong, I slowly morphed from a skinny boy with an improvised toy gun into an introspective, lonely but inquisitive soul, who thoroughly enjoyed the self-initiated production of "Pictorials for the Little Ones", a biweekly collection of cartoons, fictions, history and science articles that featured my curiosity about the origin of life. I was oblivious to my sister's hobby of craft-making and her small circle of friends but immersed myself in the books of history, literature, and many other subject matters that helped cement my interest in medicine and astronomy (the ultimate why). The ferocious academic competition and the uninspiring didactics in my preteen and teenage years did not do much to throttle my curiosity; instead, I started writing and publishing

poetry. I spent a lot of time writing poems, and reading and practicing anatomy on my own, which propelled my later interest in pathology.

Photograph 2: A class picture during middle/high school years in King's College, Hong Kong (Author at first left, second row)

My passion for human anatomy and the yearning to become a medical doctor drove me to apply to medical school at the end of high school. Unfortunately, the short stint of my medical school ended abruptly in the late 80s due to a health issue and the decision of my parents to send me abroad. I am still nostalgic about the good, old days when I studied gross anatomy and histology, and the delightful moments of conversing with dozens of aspiring young minds in medicine. Yet I embarked on a new journey in the United States in 1988, forever changing my interest from morphological science to the molecular mechanisms of life. I focused on microbial pathogenesis in my graduate school study and turned to oncogenesis after completing pharmacy school and entering the clinical pharmacist field. My passion for cancer care took the center stage in my life over the last twenty years. This approach helped me to take charge of my profession, and to bring my practice in line with the real needs of cancer patients.

I remember a passage written by William Zellmer in his book entitled "The conscience of a pharmacist", which states that "if we apply our collective minds and energies to the task, we can indeed change the conditions under which we practice. The time has come for us to stop complaining about the injustices in the profession and act to do something constructive about them." [1] This piece of advice is vividly imprinted in the footsteps I treaded in my formative years and will continue to serve as a guidepost for future clinicians.

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CHAPTER TWO

THE GOLDEN YEARS

"In the end, it is not the years in your life that count. It is the life in your years." (Abraham Lincoln)

During my early career as a clinical pharmacist, I came across differences in practices between oncology pharmacists who work in community hospitals versus those who work in academic medical centers. While I tried to avoid the generalization of these two practices, pharmacists in these practice sites manage operational and non-operational tasks (e.g. clinical responsibilities such as patient education, review of treatment plans, and offering pharmacotherapeutic consultations or interventions) differently.

Generally speaking, those with greater autonomy or buy-in for more services are given more administrative, clinical, or teaching tasks. These practitioners typically work in academic medical centers or community hospitals. On the other hand, those with limited resources or manpower, not supported with state-of-the-art technology, are often assigned a disproportionately greater number of operational activities such as order verification, inventory keeping, final product checks, and even compounding of premedications and antineoplastics. Perceivably, one may assume that employee dissatisfaction rates are higher in community hospitals than in academic medical centers. However, this is often not the case when academic centers have a high patient load, more diverse services, and more stakeholders (including physician trainees). Workflow issues in both settings impact the efficiency as well as the quality of care perceived by patients.

Honestly, it was through exposure to these two diverse types of practice that my career gained toughness and maturity. I learned that while I could not change what I initially faced, I could have discussed options for changing my workflow in a way that would not affect my morale or mental health. Simply put, shouldering too many responsibilities with no room left to grow and rest is a vicious cycle that will not help resolve

work-related problems. Instead, a happier work environment is where the whole team shares some amount of workload effectively. Based on individual differences in skill sets, employees in a workplace can manage their tasks collaboratively.

My career blossomed in the last four years, thanks to excellent communication and good teamwork. Through camaraderie and multidisciplinary collaboration, I was able to implement a program for reducing treatment-related adverse effects for patients receiving active cancer treatments in an ambulatory infusion center. [1] Discretion in planning, tactful communication with stakeholders from different departments, dedication in working with patients/clinicians to improve patients' symptoms, and proactive development and modification of treatment plans (most could be attributed to individualized considerations based on patient's tolerability, pharmacogenomics, predictive biomarkers, or other factors) constitute the important elements to drive a successful career.

In retrospect, I found out a successful oncology clinical pharmacist should possess a few key qualities below, in addition to the basic qualifications of certification, education, and experience:

1. Proper understanding of customer needs (patients, nurses, physicians), institutional goals, and departmental challenges and successes. To achieve or optimize the goal of care, all these key considerations should be connected like a chain. The chain is only as strong as the weakest link. Understanding the shifting and changing priorities requires constant realignment of strategies and an open-minded approach to help move the chain efficiently.

2. General clinical skills or clinical literacy. This is the ability to integrate real-world scenarios such as detecting and reducing treatment-related adverse effects for cancer patients, working with patients and clinicians toward a common clinical goal, and keeping up with clinical literature, guidelines, or areas of interest/expertise. It requires a pharmacist's astuteness, effective strategic planning, and sound judgment.

3. Core ability. The real core of being a clinician lies in the skills to work efficiently not only as an individual but also as a team member. People skills, proper work ethics, and decisions that

demonstrate maturity, integrity, and respect all shape and determine how far a clinical pharmacist can go.

Reference

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CHAPTER THREE

PROBLEMS AND SOLUTIONS

"And all the time we talked you seemed to see
Something down there to smile at in the dust…
Afterward I went past what you had passed
Before we met and you what I had passed."
(Robert Frost)

The practice model of clinical pharmacy in the United States is constantly evolving and varies widely across many different organizations and care settings. The professional life of a clinical pharmacist likewise follows this paradigm. Although oncology clinical pharmacists participate in the selection, modification/management of patients' cancer therapies (and their treatment-related adverse effects), provide patient education, decrease non-adherence rate, detect drug-drug/drug-disease interactions, and reduce medication errors, [1-3] their different levels of engagement with collaborating physicians and institution-specific workflow/logistics contribute to different outcomes.

Furthermore, traditional pharmacy core programs such as drug therapy monitoring, drug use review, formulary management, therapeutic interchange, and collaborative drug therapy agreements must align with organizational goals to improve patient safety, reduce cost, and improve care quality. Likewise, the workflow of oncology clinical pharmacists requires a delicate balance of many different responsibilities, such as the review of different cancer treatment plans (including the development, revision, or modification of computerized electronic treatment plans), involvement in the drug distribution process, and participation in direct patient care activities. Oncology stewardship and supportive care for cancer patients create tremendous opportunities to advance the practice of oncology pharmacy and shape the development of new practice models and cost-saving strategies.

Herein are a few examples that illustrate how frontline oncology clinical pharmacists address workflow problems. Solving these problems requires time, observation, and honest communication.

First, the resolution of drug-related problems hinges not only on the traditional and distributive roles of staff pharmacists but also on the skills of clinical pharmacists. In fact, the distributive and clinical roles of pharmacists may affect the clinical outcomes of patients. Needless to say, the knowledge and skills of oncology clinical pharmacists add value to the organization only if they are integrated with the care of the patients (primary role) and the daily operations of the pharmacy department (secondary role). Conversely, a true oncology clinical pharmacy program will not exist without direct patient care driven by oncology clinical pharmacists. Dedicated time for pharmacists involved in the care of patients is pivotal to the success of the multidisciplinary oncology program. It takes effective humanistic skills (e.g. awareness, insight, wisdom, vision) and administrative leadership/support for oncology clinical pharmacists to function well in their clinical and non-clinical roles (e.g. operations, teaching, and administrative workload). Appreciation of the full spectrum of these roles is important to understand where oncology clinical pharmacists need to make progress in their workplace.

One distinct example is how to manage drug distribution for ambulatory cancer patients, in particular, how to balance operational efficiency versus cost consideration for pre-medications (i.e. medications given before administration of antineoplastic agents to prevent infusion-associated reaction as well as acute chemotherapy-induced nausea or vomiting). Preemptive preparation of pre-medications ideally improves the efficiency of nursing workflow and patient satisfaction but may generate waste if cancer treatment is subsequently canceled or interrupted for a variety of reasons. On the other hand, “just-in-time” preparation of pre-medications, albeit cost-saving, is detrimental to efficient nursing workflow and patient satisfaction. Strategically, pre-medications may be prepared and made available in certain dose ranges. They can be recycled if not used. Further, If the service of a clinical pharmacist in an ambulatory care setting is solely defined by his/her role in drug distribution, he/she will have little time to review and clarify problematic orders, interact with patients, physicians, and nurses, thereby devaluing the clinical role of the pharmacist, leading to burnout, job dissatisfaction, and safety compromise.

Second, problems of cancer care often demand the efforts of multiple stakeholders and departments to resolve them systemically. Although the conventional wisdom of keeping the status quo appears reasonable to foster familiarity, appease harmony, or minimize inconvenience, the maintenance of the status quo may eventually compromise patient safety. One distinct example is the handling of certain pharmacologic agents that requires specialized knowledge and experience, such as the use of intrathecal cytotoxic agents. If the pharmacist involved is not familiar with the process, he or she may not appreciate the rationale of monitoring the frequency and schedule of these medications. As expected, a change in the schedule of the intrathecal chemotherapy (e.g. from induction to maintenance) or its route of administration (e.g. from intrathecal to intraventricular route) may cause a sentinel event if the hospital personnel continues to disregard these safeguards. Similarly, many fatal events involving the preparation of vinca alkaloids had occurred because of institutional barriers to implementing changes (i.e. preparing the drugs in mini-bags rather than in syringes). [4]

Third, problems may arise when there is a discrepancy between standard-of-care and physician-driven preferences. For example, a physician may decide to give one dose of trastuzumab-pertuzumab preoperatively to a patient (patient A) who has completed the full course of neoadjuvant therapy but is awaiting surgery. However, this course of neoadjuvant therapy (including the extra dose of trastuzumab-pertuzumab) will be deemed treatment failure if the pathology from patient A's resected tumor demonstrates residual disease, necessitating a different treatment based on current practice (i.e. ado-trastuzumab emtansine). On the contrary, another physician may choose to defer treatment until surgery is completed and pathology is confirmed from the resected tumor in patient B, who (with similar clinicopathological characteristics) underwent the same treatment as patient A. This type of physician-driven variation is very common in the real world. It illustrates clearly that the practice of medicine, although grounded in science, is very much an art shaped by many influences. A solution to this apparent discrepancy demands transparent and honest communication between physicians and oncology clinical pharmacists.

In summary, life on the frontline can be both rewarding and challenging. Mature thinking requires input and perspectives from all stakeholders (nursing, pharmacy, medical staff, administration, and/or

others). It is worth taking incremental steps to address problems with a long-term solution.

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CHAPTER FOUR

LOOKING AHEAD

"Exuberant years of life will not return,
The morning of the day does not repeat itself.
Seize your time and brace yourself,
For time does not stop to wait for you."
(Tao, Yuanming)

It is easy to project what the future holds for oncology clinical pharmacists when there is a surge in demand, driven by economic or other influences (e.g. oncologists' demand for more clinical support, availability of institutional resources to improve patient care, departmental initiatives to reduce cost or implementation of new clinical pharmacy programs). Conversely, an economic downturn, a decrease in the institutional reimbursement rate for government-subsidized programs, or a lack of support in oncology stewardship may foreshadow an adverse impact on the employment outlook of oncology clinical pharmacists.

The drive for precision medicine and results of translational clinical trials (including basket trials) are poised to change the practice of oncology from clinicopathologic-driven prognostic variables (such as tumor stage, tumor grade, prognostic biomarkers) and morphologic characteristics to a more individualized genomic-based approach. Oncology clinical pharmacists are expected to be familiar with the genomic aspects (e.g. rationale, methodology, clinical efficacy, and limitations) associated with this new methodology but must also be able to manage the supportive care associated with these therapies. It is time for oncology clinical pharmacists to expand their niche and take advantage of this new opportunity. [1]

Looking back on my twenty years of working in the frontline, a few landmarks stood out:

First, advances in the understanding of malignancies as well as the emergence of new drug therapies accelerate the development of new practice opportunities for oncology clinical pharmacists. The future workforce must be competent in subject matters that encompass molecular biology, basic pathology, clinical hematology/oncology, and genomic applications. However, most pharmacy schools in the United States and other countries fall behind in curricular development and recruitment of qualified clinical practitioners that are well-grounded in these disciplines. This dearth of knowledge and manpower has caused hardship for clinical preceptors to impart key therapeutic concepts to students. Pharmacy schools or administrators must respond to this call urgently. Educators and legislators must wake up to the fact that a clinically competent pharmacist must be familiar with common disease states and appreciate the complexities of cancer diagnoses and treatments.

Second, a successful clinical pharmacist must possess both emotional and intellectual maturity. It is often easy for academically capable students or clinically astute clinicians to grasp complex subject matters, but skills in discernment, empathy, and teamwork typically take a much longer time to develop. Similarly, painful life lessons, hardships, and inadequate people skills often take a longer time to learn and correct. Briefly, qualities such as accepting criticism without blaming others, acknowledging mistakes and utilizing them as a learning opportunity, and thriving in difficulties help both new and seasoned practitioners to avoid complacency and improve self-awareness. In a larger sense, humility consists of a thorough understanding of the subject matter but also awareness of one's limitations. It is natural to gravitate toward what most excites a professional intellectually, but it is equally important to develop the willingness to get along with peers and management, even when one feels wronged. [2] Sometimes, a professional may feel trapped in his or her career path. However, if one is curious and passionate about a particular subject matter, it should not be difficult to find a niche where he or she can contribute. In other words, "run your passion".

Third, learning never ends. Life is a function of learning new things, modifying the status quo, and gaining lessons from the past. A bright career future in hematology and oncology belongs to diligent and well-prepared professionals.

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PART II

SELECTED ARTICLES IN ONCOLOGY PHARMACY PRACTICE

CHAPTER ONE

DEVELOPMENT AND IMPLEMENTATION OF AN INTERDISCIPLINARY ONCOLOGY PROGRAM IN A COMMUNITY HOSPITAL

COAUTHORS: ANGELA COLLINS AND NANCY CUI

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The inherent risk of chemotherapy agents is very high due to their lower therapeutic index and safety margin compared with those of other medications. In addition, the dose, route, and administration schedule may vary as a function of tumor type and stage of the disease. Even a minor error has the potential to cause serious harm. Common examples of chemotherapy-related errors include administration to the wrong patient, underdosing or overdosing, incorrect route or rate of administration, incorrect sequence of administration, missing premedication, and incorrect schedule of administration. If treatment plans and chemotherapy orders are not verified during each treatment, errors may be repeated during subsequent treatments and go undetected throughout an entire course of therapy. To ensure patient safety and maintain standards of care, every institution requires standard policies and procedures that address the acquisition, storage, transcription, dispensing, transportation, administration, and monitoring of chemotherapy agents. [1-7] Despite established and accepted standards of care, [8, 9] challenges remain regarding the development and maintenance of a collaborative program for patients receiving chemotherapy treatments at both a private practitioner-based infusion suite and a hospital-based outpatient infusion unit. Such a program is especially necessary when laboratory test results and chemotherapy orders from the private practitioner-based infusion suite may be used within the hospital-affiliated outpatient infusion unit. This

article describes one facility's approach to implementing and improving the practice model of an oncology program.

Background

Valley Medical Center (VMC) is the largest non-profit health care provider between Seattle and Tacoma, Washington, operating a full-service 303-bed community teaching hospital, a level III trauma center, and more than two dozen primary care, walk-in urgent care, and specialty clinics throughout southeast King County.

The hospital had 14-16 full-time-equivalent clinical pharmacists working in the inpatient setting before program implementation. During this time, clinical pharmacists shared responsibilities in the central pharmacy, which was staffed by two full-time technicians. One full-time clinical pharmacist had a distributive role (entering medication orders, dispensing, and other operative functions), and another clinical pharmacist with a staggered schedule was responsible for the final checking and dispensing of all chemotherapy agents for outpatients and inpatients. Thus, all inpatient-based clinical pharmacists served a distributive role in oncology and a clinical role in pharmacy-driven protocols. No oncology pharmacy program or oncology clinical pharmacist specialist model existed. The hospital had an outpatient-based ambulatory care treatment unit (ATU) that provided infusion services, including adult oncology chemotherapy administration to patients referred by the neighboring private-practice-based hematology-oncology clinic, which also had an outpatient infusion suite for patients receiving chemotherapy treatments. Both of these practice models had been in place since the early 1990s.

Problem

In recent years, the level of complexity of chemotherapy regimens, the use of new anti-cancer agents, and medication turnaround time have increased. Approximately 1,200-1,600 doses of chemotherapy agents for adults were administered annually in the outpatient setting and another 10-30 doses of chemotherapy agents were administered monthly in the inpatient setting at VMC.

In the past, difficulty in order review and monitoring originated from outpatients referred from the private-practice-based infusion facility to receive chemotherapy treatments at VMC. Similarly, when these patients

were referred back to the private infusion facility to continue therapy, clinic staff had difficulty determining the exact number of doses patients had received or the treatment schedule since the clinic did not share a medication administration record system that interfaced with the hospital. Accordingly, it was imperative to establish an interdisciplinary chemotherapy program to ensure patient safety. Further, the resolution of potential dosing and scheduling errors increased the workload of pharmacy, nursing, and medical staff.

Within the hospital, medical oncologists wrote 95% of all medication orders for chemotherapeutic agents, with the other 5% ordered by other providers (i.e. physician assistants, intensivists, nephrologists, neurologists, and rheumatologists) with prescribing privileges for chemotherapy agents if used for non-cancer indications. All medication orders for chemotherapy agents were manually written. Generally, ATU staff scanned all orders to the pharmacy for patients scheduled for chemotherapy one day ahead of scheduled treatment. Before 2005, evening-shift pharmacists entered all chemotherapy orders into the computer system; the night-shift pharmacist reviewed the orders shortly after midnight or after ATU oncology nurses arrived in the morning. The day-shift pharmacists were responsible for dispensing chemotherapy agents, maintaining dispensing records (monitoring forms), and communicating with the ATU throughout the day via telephone calls. Based on the results of an internal survey in 2005, pharmacists did not consistently verify the schedule of chemotherapy regimens, monitor pertinent prechemotherapy laboratory test values, or document when and why dose modification occurred.

Furthermore, the lack of effective communication between pharmacy and nursing led to inefficient patient care services. Nurses complained that clinical pharmacists did not consistently apply their skills and knowledge to answer questions on infusion rate, dosing information, and chemotherapy procedure. Clinical pharmacists, on the other hand, lacked an intradepartmental program to support oncology chemotherapy verification and improve documentation. They relied heavily on nurses to determine whether the chemotherapy schedule was correct and whether a dose would be withheld since laboratory test values were not available to pharmacists for review. Clinical pharmacists did not feel empowered to make clinical recommendations on dose modification or provide specific oncology drug information. When a miscommunication, misinterpretation, or process breakdown occurred, the near miss often resulted in the waste of the chemotherapy agent, causing financial loss and unsafe practices.