REFLECTIONS ON MONOCLONAL ANTIBODIES AS THERAPY FOR GASTROINTESTINAL POLYPS

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INTRODUCTION

Participating in the Biomedical Sciences (BMS) graduate program has greatly shaped and contributed to my view of the overall healthcare system while helping me pursue my personal goals. The start of the program consisted of preclinical courses that included "Pharmacology," "Anatomy," and "Immunology & Infectious Disease." It was beneficial to have taken these courses before delving more into the clinical shadowing experiences because I was able to establish a connection between class content and clinical conditions. The curriculum during the fall and spring semesters has helped me expand my current clinical knowledge while learning more about advanced scientific and healthcare topics from a different perspective. By studying material on more of a molecular and physiological level, I am better able to grasp not only information seen in the clinical setting but understand the deeper science behind it as well. Throughout this paper, I provide examples of what I have experienced since joining this program. The overall sections include "Classroom to Clinic," "Framing a Clinical Question and Interrogating the Literature," "Reflection on Communication and Healthcare," and "Reflection on Psychosocial Determinants of Health." The inclusion of each section serves to demonstrate what I have learned both in the classroom as well as experientially through my shadowing experiences. Ultimately, each section consists of specific components of the BMS program that have allowed me to develop and grow as an individual pursuing a career in healthcare.

Contents

From the Classroom to the Clinic

During our "Immunology & Infectious Disease" module, we learned that passive immunity involves the administration of antibodies produced by an infected individual to a non-immune individual. (Vaillant *et al.*, 2024). After this transfer, the uninfected individual will thus have antibodies that can recognize and respond to the specific antigen that can cause illness. Monoclonal antibodies are an example of passive immunity that can be used to treat a variety of conditions, not just those resulting from infection. For example, we discussed monoclonal antibodies during the "Genetics" module when reviewing how they can be used to mitigate the impact of the abnormal activation of an oncogene. When an oncogene is either overexpressed or becomes activated from a mutation in a normal cellular gene, signaling from tyrosine kinase receptors (TKRs) can become abnormal or excessive. This process has cancer-causing potential due to the TKR-induced signaling that promotes cell division. Monoclonal antibodies that target TKRs can be studied as future therapies to treat aberrant TKR signaling and the malignancies that might result from this abnormal receptor expression (FAUVEL & Yasri, 2014).

During a shadowing experience, a physician shared how monoclonal antibodies can be used in the treatment of nasal polyps and how they may play a large and significant role in healthcare in the future. After hearing this, I reflected on my shadowing experience in gastroenterology. On the physician's procedural days, he performed many colonoscopies in which he was looking for the presence of colonic polyps. If a polyp was detected, it was removed and sent to the lab to be examined for the presence of cancer. These two experiences led me to investigate the use of monoclonal antibodies and how effective they might be in the treatment of polyps.

In a 2023 review, a variety of monoclonal antibody treatments for colorectal cancer were discussed, giving some insight into their mechanism of action (Heidari *et al*., 2023). The article states how advancements in colorectal cancer treatment are needed to improve the low five-year relative survival rate, which is approximately 65%. The review highlights the development of monoclonal antibody therapies targeted to receptors for growth, differentiation, division, metastasis, and transformation. It then goes on to discuss specific antibody treatments alone as well as their administration in combination therapy. To give a brief example, cetuximab is an antibody that targets the epidermal growth factor receptor (EGFR) domain that is overexpressed in many human cancers, including colorectal cancer. From its competitive binding activity, pathways such as mitogen-activated protein kinase (MAPK), Janus kinases (Jak), and signal transducers and activators of transcription (Stat) pathways can be inhibited/altered. By blocking the EGFR receptors and subsequently inhibiting different pathways that have roles in gene expression, proliferation, and differentiation, specific monoclonal antibodies can be used as a therapy to maintain the regulation of cell division to stop cancer progression. The article furthermore details the use of cetuximab in conjunction with a regimen that includes 5-fluorouracil, folinic acid, and irinotecan (FOLFIRI). When analyzing the results for patients with wild-type mutations in a group of oncogenes known as RAS that commonly contribute to the development of human cancers, patients with these wild-type tumors saw significant improvements when the antibody was added to the treatment plan with the FOLFIRI regimen. While the benefits of monoclonal antibody treatment are highlighted in this review, the importance of understanding the complexity of cancers should still be considered when deciding treatment options, especially when antibody treatments are specific to certain targets and can be individualized.

Similar to polyps found in the colon, nasal polyposis associated with chronic rhinosinusitis has also been looked at as a possible target for monoclonal antibodies. While nasal polyps that grow in the nasal and paranasal mucosa are generally benign, they can still cause discomfort and other symptoms for patients. Common symptoms of nasal polyps include nasal obstruction, a decreased sense of smell, and even a runny nose (Agarwal *et al*., 2019). Currently, intranasal corticoids or removal of the polyps through a polypectomy are two common options to treat nasal polyposis. However, they cannot inhibit the formation of future polyps, providing a need to explore other therapies (Agarwal *et al*., 2019). It is important to consider the mechanism behind nasal polyp formation to better understand the role that monoclonal antibodies might play in their treatment. Nasal polyposis contains an allergy- and non-allergy-mediated pathway. In both pathways, immune cells can release specific interleukins that then recruit vascular cell adhesion molecules (VCAM-1) and eosinophils. As a result, swelling, inflammation, and tissue damage allow for the formation of polyps (Agarwal *et al*., 2019). Presently, there are no clinically approved treatments for nasal polyposis. However, late-stage clinical trials are in progress. An interesting pharmacologic therapy being studied is dupilumab, which is an antibody that binds to the interleukin-4 (IL-4) receptor. In the clinical trials, it was found that participants receiving this antibody had improved nasal polyp scores and clinical symptoms.

Researching more into a classroom topic that I had exposure to during my clinical shadowing has helped me understand more about the treatment of monoclonal antibodies as well as conditions that involve polyps. I gained an appreciation for the detail that is required in clinical research, as just these two polyp-based conditions involved different mechanisms for cell division, differentiation, and overall lesion formation.

Framing a Clinical Question and Interrogating the Literature

For the duration of my time observing a critical care physician, I noticed that advanced congestive heart failure (ACHF) was a common condition requiring management within the Intensive Care Unit (ICU). Before this day, my limited knowledge of the diagnosis was that patients needed to be maintained on a specific diet that included fluid restriction. Restriction of fluid intake by patients is important to ensure an overall equal or negative fluid balance. Additionally, pharmacological treatments known as diuretics can also be administered to aid in the excretion of excess fluid to help lessen ACHF symptoms. These symptoms include difficulty breathing, which can worsen while lying flat or bending at the waist, and edema (swelling) in the body that is most noticeable in the legs and feet (Chen & Aronowitz, 2022).

With a desire to learn more about ACHF and how it is managed, I conducted a search using the "Population, Intervention, Comparison, Outcome (PICO)" format to find a research article about the subject of interest. The elements of each component of PICO I used for my search were: P-adult patients with ACHF, I-diuretic administration differing from the standard of care, C-standard of care for diuretic administration, and O-improvement of symptoms. Connecting each section of PICO, I was able to frame my question, "In patients 18 years or older with advanced congestive heart failure, how effective is a modified administration protocol for diuretic therapy compared to the standard of care (SOC) diuretic therapy protocol at improving diuresis and congestive symptoms?" Using the PubMed database, I found a retrospective study that compared the SOC for ACHF including loop diuretics to the SOC including loop diuretics along with the additional treatment of high-dose spironolactone to analyze if there was a significant improvement in decongestion (Kapelios *et al.,* 2018). Spironolactone is an agent commonly used to treat high blood pressure and edema as well as other cardiovascular

conditions (Patibandla *et al*., 2023). Another compelling article was a 2019 clinical trial that studied the administration of the loop diuretic, furosemide, during a continuous infusion compared to the typical standard of intermittent bolus infusions of furosemide (Frea *et al*., 2019). A noteworthy aspect of the clinical trial is that it included ACHF patients who were at risk of developing resistance to diuretics.

With two articles to choose from, I remembered from the "Evidence-based Medicine and Clinical Research" module that randomized controlled trials were superior to retrospective studies. I proceeded with the article about the clinical trial that compared different protocols of furosemide treatment. To summarize the article, 80 patients were randomly divided into groups that either received a continuous infusion of furosemide or an intermittent bolus that was given every 12 hours (Frea *et al*., 2019). At the conclusion of the trial, all participants' symptoms were analyzed to determine if one method of administration provided significant relief compared to the other. The main finding from this trial is that approximately 50% of those who received a continuous infusion of furosemide were relieved from their congestive symptoms while only 10% of participants in the intermittent bolus group saw significant improvement. Secondarily, fluid output was greater and more consistent in the continuous administration group, helping to decrease the chances of a rise in serum sodium levels and therefore, a major shift in intravascular volume after the diuretic treatment was stopped. While the trial resulted in significant findings regarding a continuous infusion of furosemide, the authors did clarify that these findings may be specific to patients with a likelihood of diuretic resistance. This trial answered my original clinical question because it investigated a well-known diuretic under two different administration protocols. This article did a good job of delving into the specifics of the administration methods and what outcomes they were measuring related to these treatments. Given the explanations and

reasoning from this clinical trial, I learned more about ACHF, its symptoms/effects, and how two different approaches for the same medication can be compared for an improved clinical benefit for patients with ACHF. Despite the article providing interesting insight into different strategies for managing ACHF, it still had several limitations. One limitation was that the trial did not have enough participants and was, therefore, underpowered to analyze this subset of patients more confidently. Another limitation was that these findings may not apply to all patients with ACHF, demonstrating the necessity to check for risk of diuretic resistance before deciding on an administration approach.

Connecting these findings to my initial experience in the ICU, I believe that a continuous infusion of furosemide might provide patients with substantial benefits and relief. Given the potential for patients to excrete a greater amount of fluid while also avoiding a sudden increase in serum sodium levels leads me to wonder if continuous infusions could be utilized more frequently in the future. Perhaps treatments such as this might decrease the length of hospital stays for patients while helping them return to their normal baseline levels more quickly. However, since this study was stated to be underpowered, additional studies are warranted to justify further implementation of this protocol in the future.

Reflection on Effective Communication in Healthcare

While observing a vast variety of specialties in healthcare has exposed me to a great amount of clinically interesting content, I have been able to reflect on other aspects that contribute to the overall healthcare experience as well. I quickly noted the important role that communication plays in the healthcare system given that it is comprised of numerous interconnected disciplines working together to serve the best interests of patients. An important aspect to remember about communication in healthcare is that it is multifaceted, meaning that

communication is utilized not only between professionals but also between providers and their patients. Due to the current structure of healthcare, communication must be utilized effectively to maximize patient care. If not considered by both the providers and patients, negative consequences may result including discontinuity of care, risking patient safety, and an overall negative patient experience (Vermeir *et al*., 2015).

When reflecting on a provider-patient interaction that I observed to go well, I remember a father bringing in his two children to be examined for strabismus/pseudostrabismus. In this condition, one or both eyes appear to turn inward or outward. During this visit, I watched the provider try to appeal to the children's interests as she conducted her examinations. This observation helped me see the importance of trying to make your patients feel comfortable in the healthcare setting. Especially when working with children, doing so might make the examination go more smoothly by allowing the child to be distracted and thus less anxious about the visit. While the provider was able to effectively make her diagnoses, I witnessed that she made a clear effort to show the father exactly what the problem was. When it became time for the provider to develop a treatment plan, she began discussing the process referred to as patching. With this process, a patch is placed over the stronger eye so that the weaker eye can strengthen and thus become better aligned. In the context of these two patients, however, both of their eyes were turning outward with varying degrees of severity. Since each eye was looked at individually, each eye needed to undergo the patching process for different lengths of time. For example, if the left eye was turning outward more drastically compared to the right, then the provider would recommend patching the right eye for three hours a day and only one hour for the left eye. The increased patching time for the right eye would help strengthen the left eye and maintain its control. To account for each of the patient's individual needs and how mild or severe their

strabismus was, the provider tailored a specific plan for the patching process for each child. I was able to see how the parent was left slightly confused in trying to keep up with the details for both children. The provider was able to recognize the parent's hesitancy and tried to break up the treatment plan into simpler language that was easier to understand and would thus ensure that it would be followed correctly. After this visit, I felt the father was able to leave the visit with a clear understanding of the plans and all his questions answered. When looking at the non-medical aspects of the visit, I believe the provider did an amazing job of interacting with patients and their families from a holistic perspective. The provider was able to complete her examination efficiently but still converse with the patients and their father about school, their favorite food, and preferred television shows. This observation reminded me to work with the mindset that patients are people first. I believe that incorporating this mindset into work with patients greatly helps in establishing provider-patient relationships that are built on trust, openness, and compassion. Lastly, I think the office where I was shadowing had a great team-based approach that helped result in more positive interactions. A specific example of this observation was watching the dynamic between the provider and the scribe who was working with her. Because the scribe was able to help the provider complete her notes during the visit, the provider was able to focus all her attention on the patients and their families. I have had some experiences where it seemed like the provider's responsibility to document took away from being able to connect with the patients and have a more personal experience. However, the set-up of the healthcare team in this setting helped ensure that both the provider's and patients' needs were met so that it was a positive experience for all involved.

Conversely, a provider-patient interaction that I believe went poorly entails a physician who was informing a patient's family that he was concerned about the patient's blood sugar

levels. The patient had come in to have a procedure done and while waiting for the procedure, the staff had checked the patient's blood sugar level, given that the patient was diabetic. The blood sugar turned out to be markedly elevated. While the provider was still able to complete the procedure, it left him concerned. After the procedure was done, the provider went to talk with the patient's family and voiced his concern about the management of the patient's diabetes. The provider stressed the importance of making an appointment with the clinician managing the patient's diabetes to get the levels under better control. The family member appeared agitated and shared some negative remarks about the other provider responsible for the management of the patient's diabetes. Ultimately, the provider whom I was shadowing, and the family member fell into a heated discussion on the topic of insulin and whether it was the pancreas or beta cells that secrete insulin. Regardless of which individual was right, it was clear that the conversation lacked clear communication and rational explanations. An important note about this interaction is that it was not directly affecting the care plan and what the patient was there for that day. However, it still may have reflected negatively on the patient's and their family's outlook on the provider or even the establishment. I believe that this interaction could have been handled differently and resulted in a more positive experience for everyone involved. After the provider voiced his concern, I believe that a more conducive conversation would have been encouraged by asking more open-ended questions. By doing this, the family would have been able to share their concerns and any difficulties they may have experienced with managing the patient's diabetes. Both sides of the conversation seemed to take a more assertive approach that ultimately hindered the visit from ending on a more positive note. Rather than this conversation being filled with assertiveness, the experience could have been more productive if both sides had been

reminded to work with a spirit of collaboration so that both parties were working toward a common goal.

Shifting to a different perspective of analyzing communication between providers, I vividly remember one moment during a shadowing experience in the Emergency Department (ED). I observed the actions of another physician whom I had not directly been shadowing that day. From what I was able to gather, the physician was consulting different specialties for a few of his patients whom he described as being medically complex. As part of these consultations, the ED physician was attempting to find the correct services to perform indicated tests and procedures. In doing so, it seemed like he was receiving considerable pushback from the consulting services. This left the ED physician noticeably stressed as he was not making progress in delivering necessary care for his patients. The memorable aspect of this observation was witnessing the physician's exaggerated body language at the nurse's station while yelling curse words to himself.

While one can empathize with the high amount of stress that working in the ED can bring on an individual, I do believe that this moment could have been handled more professionally. If I was receiving pushback from multiple services who were resistant to admitting a patient to their team, I think it would be helpful to read the "Situation-Background-Assessment-Recommendation (SBAR)" for the patient to demonstrate the condition and needs of that patient accurately and concisely. The SBAR report would be a useful tool in this circumstance to improve communication between staff members while relaying important patient information to colleagues to promote overall safety (Bonds, 2018). Particularly when multiple interventions are needed for the patient, I believe that gathering all the pertinent information helps prioritize actions according to their urgency. This could especially help demonstrate to the other services

which team is most appropriate for managing the patient's treatment. Another way to navigate this predicament could have been to use other colleagues in the ED as a resource to discuss whether protocols for similar situations have already been established. This tactic could use pre-established guidelines to dispute any reasoning that the other services were using to avoid providing necessary care. Additionally, the entire situation might have been avoided if members of the different teams were able to meet on a three-way call to discuss the requirements and needs of the patient. I believe this could have promoted efficiency for all members of the healthcare team while minimizing the nuisance of continuously making calls with little progress. Further, all services would then have a clearer understanding of the plan for the patient. No matter what service the patient was admitted to, the other teams could still be involved in the patient's care until all important consults and studies were completed. If the previous approaches have had little success, it might have been productive for the ED provider to reassess the situation himself and assert his decision-making process to ensure that appropriate care of the patient is not delayed. Decisions such as these, however, do need to be made carefully so that the patient's safety is not put at risk. When dealing with situations of this nature, I ultimately believe it is important to remain collected while also reminding everyone of the common goal of providing the patient with quality treatment. Shadowing has provided me with many circumstances to learn about the importance of communication and how it is a major contributor to the experience for both healthcare providers and their patients. Undoubtedly, communication within the healthcare system remains complex, as both positive and negative factors can affect how information is shared between professionals and patients (Chichirez *et al*., 2018). Keeping this in mind, I have been exposed to various communication strategies in a multitude of settings

that have helped me decide for myself how I can effectively use communication to make an impact in healthcare.

Reflection on Psychosocial Determinants of Health

I remember one particular work experience where I was curious about a patient's social setting and how it might affect their current health status. I was one of the patient care assistants who was working in triage of the emergency department (ED) at the time. A nurse and I were taking a patient back to a triage room to get them fully assessed and checked in for their evaluation. The patient was an infant under the age of 12 months who was experiencing common cold symptoms and difficulty breathing. As I was obtaining vital signs on the patient, the nurse began asking the routine triage questions. One of the questions specifically asked was whether the patient is around the parents if they are smoking tobacco. The parents replied "no" and reiterated the part of the question that stated that the patient is not around second-hand tobacco smoke from cigarettes. I assumed that they reiterated that specific part because both parents were wearing a necklace connected to a vaping device. It was eventually clarified that the parents would still vape inside the house with the baby present. Although I was not able to learn more about the patient's story after this initial interaction, I continued to think of this social factor and how it played a role in the patient's health.

This specific example led me to investigate the potential health effects on patients due to exposure to aerosolized vaping particles. A 2019 review article highlighted the misconception regarding the byproducts of electronic nicotine delivery systems (ENDS) (Larcombe, 2019). One might be led to believe that ENDS do not have the same chemical products compared to cigarettes since they are not made of tobacco. This article refutes this misbelief and discusses how ENDS can produce aerosols similar to traditional tobacco products. It then goes on to state

that ENDS have the potential to expose infants and children to more second- and third-hand aerosols due to the aerosolized particles' ability to adhere to surfaces, furniture, and even skin. (Larcombe, 2019). This might leave the child more at risk compared to traditional cigarette use if ENDS or vapes are thought to be acceptable to be used inside, resulting in the possibility that the child is more likely to come into contact with these aerosolized particles. The article does a great job of comparing the more commonly known tobacco products with ENDS while also discussing their implications for exposing young children and infants to harmful aerosolized end products.

Having established the adverse effects of electronic cigarettes and their potential exposure to the children of users, my next question dealt with exploring the effects of these devices on child and infant health. According to a fact sheet produced by the American Nonsmokers' Rights Foundation, e-cigarettes/vapes/ENDS contain propylene glycol (PG), a compound that is found in the aerosolized particles that these devices emit (*American Nonsmokers' Rights Foundation, 2024)*. This foundation uses published articles to support its statements and stances. In one such study, participants with no respiratory history were exposed to a propylene glycol mist for one minute while they were subjected to specific training conditions (Wieslander *et al*., 2001). Before and after the exposure to PG, symptoms regarding the participant's ocular and respiratory systems were measured while a doctor also asked the subjects questions about their symptoms. After the PG exposure, the authors found that tear film production and forced expiratory volume in one second (FEV_1)—a measure of respiratory function—both decreased, while there was an increase in throat symptoms. It is also important to note that there were self-reports of difficulty breathing among some of the subjects. This article was an interesting study simulating the health effects of second-hand exposure to a chemical commonly found in e-cigarettes. Based on my understanding of the social situation and family

dynamic of this patient, many parallels between this study and the patient's background could potentially explain that patient's symptoms and need to be seen in the ED.

After looking at some of the direct effects of being exposed to second-hand smoke from vaping or smoking, there are still long-term effects to consider. With a child growing up in a home environment where both parents are vaping, possibly inside and around the child, it raises the concern of the parental behaviors influencing their child. A recent survey of 3,291 youth aged 10-15 years in the United Kingdom looked into possible associations between the smoking/vaping behavior of parents and its influence on the smoking/vaping behavior of their children. (Green *et al*., 2020). While this is a survey that reported limitations from the wording of the questions and possible confounding, the results are still worth consideration when investigating the long-term effects of smoking behaviors. The study reported that youth were more likely to smoke and/or vape if they had parents who currently vape or previously smoked. This survey was interesting because other factors were analyzed such as age, gender, and socioeconomic status. When comparing the data between youth who smoke and youth who vape, the investigators reported that older males coming from a lower socio-economic status, or single-parent households were more likely to engage in either of those activities. This article helped show the complexity of social factors and how multiple aspects of identity can influence an individual's social and health behaviors.

In the context of my patient whom I was checking into the ED, multiple factors led me to think about the health status of the infant from both a short-term and long-term perspective. My short-term consideration was the current status of the baby and how that baby's health was potentially being impacted by second-hand aerosols from vaping and possibly even smoking. The long-term implications of the family dynamic were how likely the child would initiate a

smoking/vaping habit years later, behaviors which could ultimately be associated with a multitude of other health or social factors as the patient grows older.

Concluding Section: Impact of the Program on Your Views Towards Healthcare

At the conclusion of the BMS program, I am reassured that I want to pursue a career as a physician. My goal of attending medical school has become much stronger because of my experiences inside and outside of the classroom. While I was interested in many of the courses throughout the past year, I was most intrigued by the preclinical courses, such as "Anatomy" and "Pharmacology." It was truly exciting to learn more about medicine and the human body while being able to make connections to my current experiences in healthcare. Since I have been working in the Emergency Department, the time and effort directed toward understanding the classroom material felt validated to me personally because I was finally seeing the relationship between what I was studying and what I was seeing clinically. Furthermore, I have grown more confident in my capabilities of being successful in medical school. The BMS program was valuable as it showed me that I can perform well in the healthcare professional school setting while balancing outside activities and responsibilities.

Being able to learn clinical content was an influential factor that helped me be more engaged during my shadowing experiences. I found that having a foundation of clinical knowledge was very helpful in asking questions and promoting discussions between different providers or healthcare professionals. Apart from learning about interesting conditions or illnesses, shadowing a variety of careers provided useful insight regarding working in healthcare and my future as an aspiring physician. One of the main aspects that I reflected on during each shadowing experience was the amount of interaction with patients or peers. I observed some specialties where I was excited about what I was seeing clinically but was still searching for

more interaction. On the other hand, there were moments when I was doing the opposite. Even with some of the experiences not completely catching my interest clinically, they still provided useful insight into the interconnectedness of medical disciplines. A great example of this is my time observing the fields of occupational and physical therapy. I remember thinking to myself that although working directly with patients would be fulfilling, I was missing the aspect of clinical medicine. Although I was not completely intrigued by these careers, I was able to learn more about two fields of healthcare that I previously had little knowledge of and how they play a role within the overall healthcare system.

I believe that it is important to explore different areas of healthcare because they can contribute to one's overall journey in finding a career that most resonates with them. If I had not decided to join this program, I would unlikely have had the exposure to healthcare that I now have. I am confident that this program has solidified my academic and career goals of becoming a physician who can truly make an impact in others' lives.

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