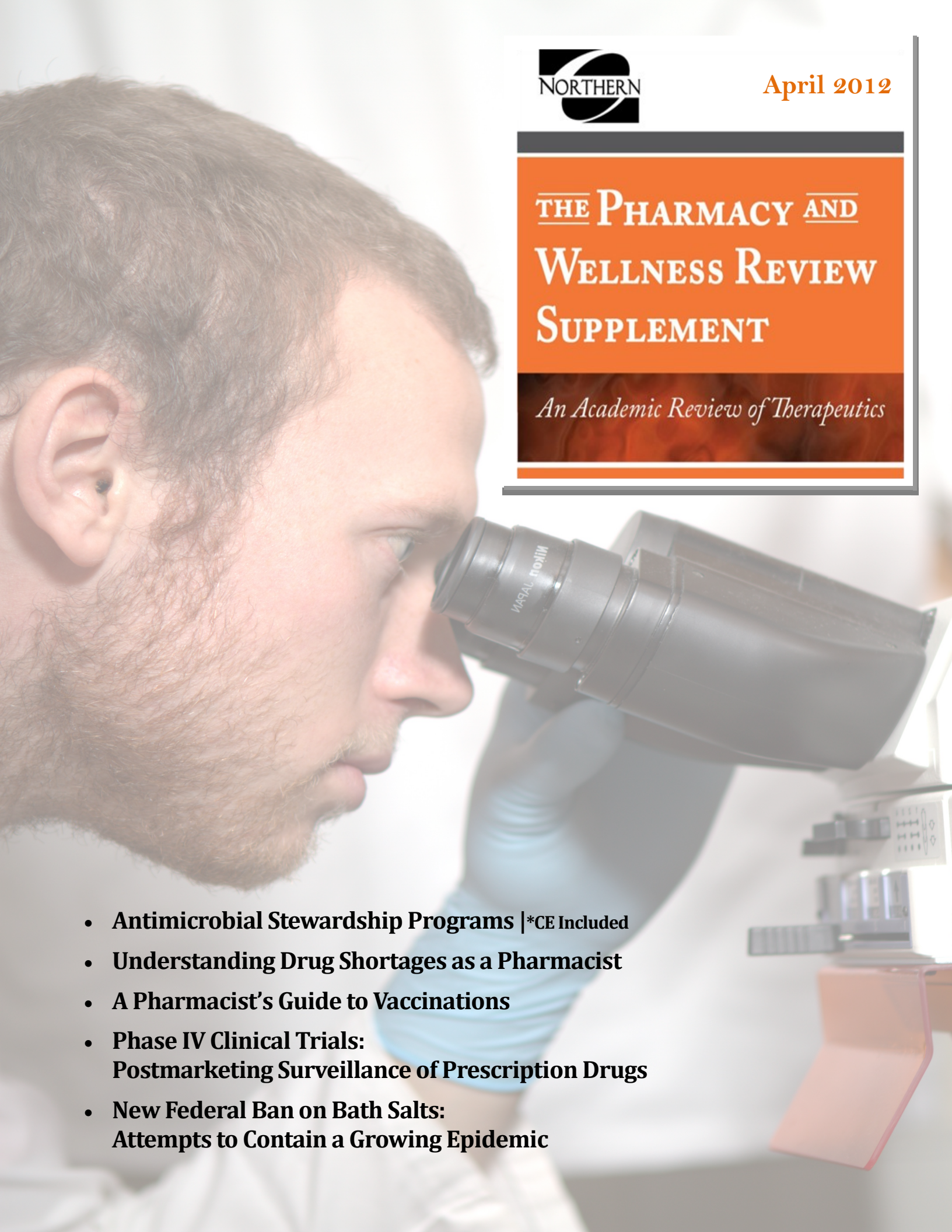


NORTHERN

April 2012

The Pharmacy and Wellness Review Supplement

An Academic Review of Therapeutics

- **Antimicrobial Stewardship Programs |*CE Included**
- **Understanding Drug Shortages as a Pharmacist**
- **A Pharmacist's Guide to Vaccinations**
- **Phase IV Clinical Trials: Postmarketing Surveillance of Prescription Drugs**
- **New Federal Ban on Bath Salts: Attempts to Contain a Growing Epidemic**

Short Pharmacy Facts

A Brief Look at Some Fun Facts from the Rich History of the Profession of Pharmacy

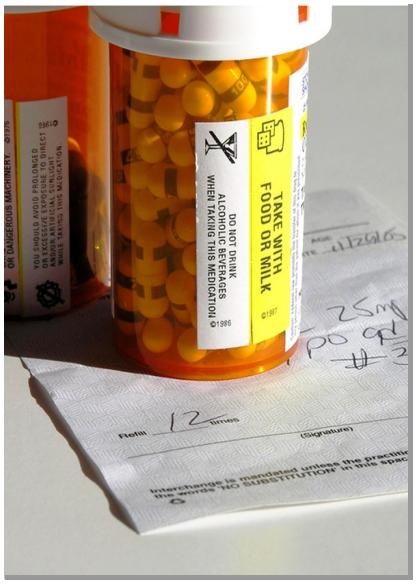
Lauren Desko, fifth-year pharmacy student from Perrysburg, Ohio; Amanda Lovell, fourth-year pharmacy student from Lexington, KY

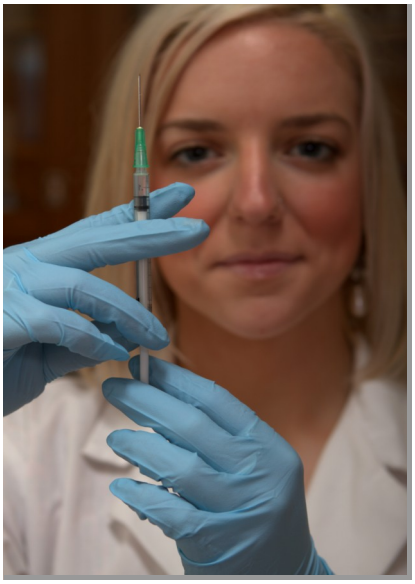
The first female pharmacist in the United States was named Susan Hayhurst. She was an 1859 graduate of the Woman's Medical College of Philadelphia, and went on to be a staff member there. For many years she was in charge of the college's pharmaceutical department. At the age of 63, she became the first woman to graduate from the Philadelphia College of Pharmacy in 1883. Until this point in history, women were not a part of the profession of pharmacy because they were not considered physically strong enough to properly crush substances used in compounding.[1]

Benjamin Franklin had an important role in developing the profession of pharmacy in the United States. He was responsible for appointing an apothecary to the Pennsylvania Hospital, which was a key step in separating the preparation and dispensing of medications from the physicians' role.[2]

The symbol R_x is a key part of the profession of pharmacy, and there are two theories as to how the symbol came about. First is the theory that R_x was derived from the lines in the Eye of Horus, which was considered a symbol of health in ancient Egypt. The second theory is that R_x comes from the Latin word recipere meaning "take." The R_x symbol would come before the physician's recipe for making the medication.[3]

continued inside back cover





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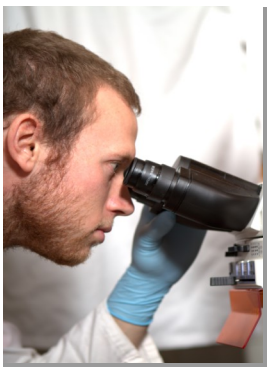
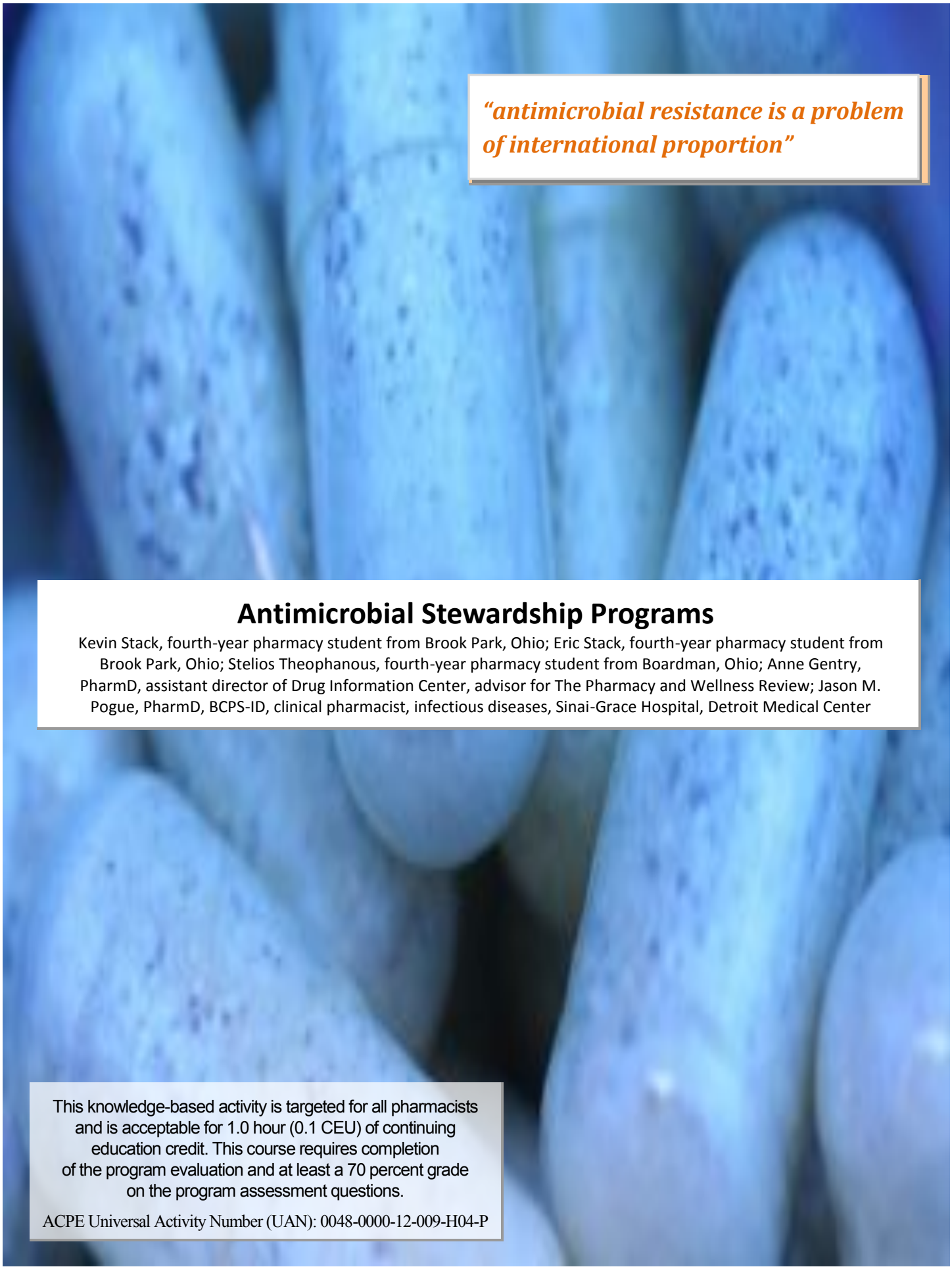


On the Cover

Antimicrobial Stewardship Programs (ASPs) are becoming increasingly prevalent in the United States as concerns continue to mount regarding antimicrobial resistance and the lack of new, novel antibiotics being introduced. While antimicrobial resistance is a problem of international proportion, each health care institution remains responsible for assessing its own protocols pertinent to antimicrobial usage. ASPs have the potential to reduce antimicrobial resistance evolution and therefore improve patient outcomes.



"antimicrobial resistance is a problem of international proportion"

Antimicrobial Stewardship Programs

Kevin Stack, fourth-year pharmacy student from Brook Park, Ohio; Eric Stack, fourth-year pharmacy student from Brook Park, Ohio; Stelios Theophanous, fourth-year pharmacy student from Boardman, Ohio; Anne Gentry, PharmD, assistant director of Drug Information Center, advisor for The Pharmacy and Wellness Review; Jason M. Pogue, PharmD, BCPS-ID, clinical pharmacist, infectious diseases, Sinai-Grace Hospital, Detroit Medical Center

This knowledge-based activity is targeted for all pharmacists and is acceptable for 1.0 hour (0.1 CEU) of continuing education credit. This course requires completion of the program evaluation and at least a 70 percent grade on the program assessment questions.

ACPE Universal Activity Number (UAN): 0048-0000-12-009-H04-P

Objectives:

After completion of this program, the reader should be able to:

1. Identify ways in which Antimicrobial Stewardship Programs (ASPs) are utilized to decrease microbial resistance.
2. Comprehend the multiple and interconnected roles of various health care professionals associated with ASPs.
3. Recognize the significant decrease in current research and development of antimicrobial agents by major pharmaceutical companies and its impact on the need to properly utilize available antibiotics.
4. List strategies that can be established to create and run an effective institutional ASP.
5. Examine how the quality of patient health has been improved as a result of successful implementation of ASPs in a variety of health care settings.

Abstract

Antimicrobial Stewardship Programs (ASPs) are becoming increasingly prevalent in the United States as concerns continue to mount regarding antimicrobial resistance and the lack of new, novel antibiotics being introduced. There are a multitude of factors that have contributed to the escalation in antimicrobial resistance, with some of the more common concerns being overly broad antimicrobial coverage and prolonged antimicrobial treatment amongst others. While antimicrobial resistance is a problem of international proportion, each health care institution remains responsible for assessing its own protocols pertinent to antimicrobial usage. ASPs have had unparalleled success in achieving their goals due to the collaboration of health care personnel, informatics, data collection, and effective policies being employed. While the pharmaceutical industry struggles with the development of novel antimicrobials, ASPs are a critical component to promote the continued efficacy of currently available antimicrobials.

ASPs have had unparalleled success in achieving their goals due to the collaboration of health care personnel, informatics, data collection, and effective policies being employed.

A considerable number of strategies have been established to implement and manage an effective institutional ASP, including educational programs, the development of institutional antimicrobial and disease state guidelines, prior approval for certain broad-spectrum agents, post-prescription review, and computer-based decision support. However, resources are often limited thus creating barriers for institutional ASP success. Some common barriers include a lack of fundraising, inadequate or absent diagnostic facilities, poor data collection, variation in data collection, a lack of communication among various health care professionals and a lack of cooperation among health care facilities.

ASPs have the potential to reduce antimicrobial resistance evolution and therefore improve patient outcomes. The involvement of multiple health care professionals, including pharmacists, is imperative to the success of an ASP.

Introduction

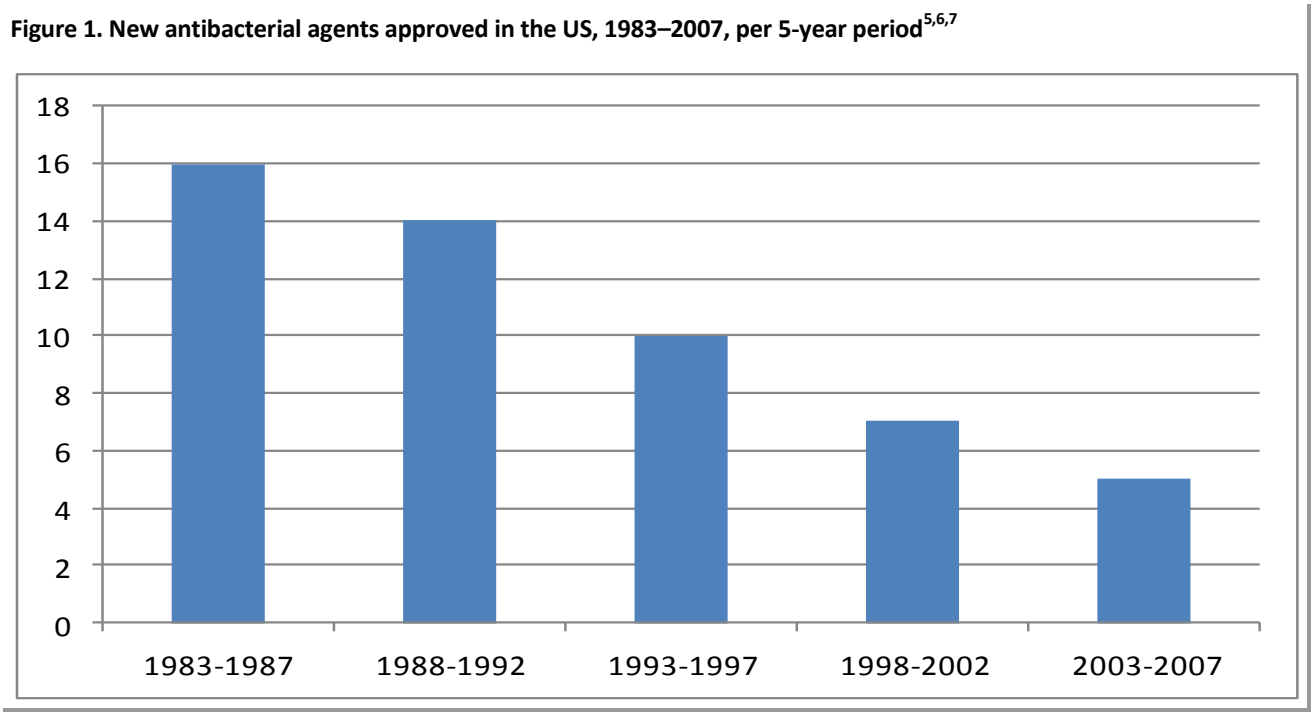
Inappropriate prescribing, overuse of antimicrobial agents and even appropriate antibacterial use have resulted in multidrug–resistant organisms, elevated medical care costs and adverse events.[1] On a universal level, there is a growing concern of increased antimicrobial resistance which has led to the development of ASPs. An ASP is defined by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) as "a system of personnel, informatics, data collection, and policy/procedures that promotes the optimal selection, dosing, and duration of therapy for antimicrobial agents throughout the course of their use."[2] Furthermore, the World Health Organization (WHO) defines optimal antibiotic prescriptions as "the cost-effective use of antimicrobials which maximizes their clinical therapeutic effect, while minimizing both drug-related toxicity and the development of antimicrobial resistance."[3] As seen by the definitions of ASPs and optimal prescriptions, preventing antimicrobial resistance truly involves all sections of health care, especially pharmacy.

Nonetheless, there exists a significant gap between the presence of novel candidates in the latter stages of the "US drug-development pipeline" and the increasing number of resistant microorganism strains.

Impetus for the Development of ASPs

Pharmaceutical advancements in drug development of novel antimicrobials have been steadily declining. The number of new antibacterial drugs approved for marketing in the United States continues to decrease[7] (Figure 1). It is important to recognize that it is not only the number of antimicrobials in the drug-development pipeline, or the number of antimicrobials that have been recently approved, but also the quality of novel drugs developed with new mechanisms of action.

Figure 1. New antibacterial agents approved in the US, 1983–2007, per 5-year period[5,6,7]



The decrease in research and development for antimicrobial agents by major pharmaceutical companies has not gone unnoticed, and is highlighted when current treatment options become susceptible to resistant microorganisms. The IDSA and the Antimicrobial Availability Task Force (AATF) have expressed concern over this issue.[4] Nonetheless, there exists a significant gap between the presence of novel candidates in the latter stages of the "US drug-development pipeline"[4] and the increasing number of resistant microorganism strains. For example, the quantity of β-lactamases has greatly increased—in 1970, there were 13 of these enzymes known, 282 in 1999, and 532 in 2004.[4]

The Role of ASPs

Approximately 60 percent of hospitalized patients in the United States receive at least one dose of an antimicrobial agent. In 2002, there were approximately 1.7 million health care-associated infections (HAIs) in the United States, which resulted in about 98,987 fatalities. Many of the HAIs were caused by pathogens resistant to antimicrobial agents.[2] Alarmingly, more people now die of MRSA infection in U.S. hospitals than of HIV/AIDS and tuberculosis combined.[5] Additionally, many of the therapeutic options for these pathogens are limited, sometimes forcing prescribers to use older drugs often associated with increased risk of toxicity. Furthermore, the number of elderly patients, individuals undergoing surgery, transplantation, and other procedures continues to increase making the average patient more susceptible to these infections due to their immunocompromised status.[5]

"More people now die of MRSA infection in U.S. hospitals than of HIV/AIDS and tuberculosis combined."

As it becomes clear that antimicrobial resistance is an increasingly troublesome reality, the roles of ASPs today become ever more significant in the health care world. The primary goal of ASPs is to increase the quality of patient care, while the secondary goal involves reducing health care costs.[2] Additionally, ASPs are aimed at being able to successfully use current antimicrobial agents in the future by limiting overuse and misuse of antimicrobials today, thus minimizing antimicrobial resistance.[1] The use of ASPs can decrease medication errors pertaining to antimicrobials, such as preventing duplicate antimicrobials or avoiding the prescribing of unneeded antimicrobials.[8] Ultimately, infections that arise from multidrug-resistant (MDR) pathogens increase the length of illness and hospital stays.[9] Efficient ASPs should monitor the proportions of antimicrobial agents used in patient populations to ensure there is some diversity in the prescribed drugs for specific indications. This monitoring will aid in avoiding the development of resistance to antibiotic classes as a whole.[1] Additionally, ASPs encourage the streamlining or the de-escalating of therapy in the earliest possible stages of a treatment, the transfer to oral treatment from parenteral treatment, the administration of antimicrobial agents over the correct length of time and the administration of the correct dose. In many institutions without ASPs, the ability to tailor a medication regimen from the initial broad-spectrum therapy is neglected even when microbiologic data becomes available. Similarly, "spiraling empiricism" occurs when broad-spectrum antibiotics are quickly and haphazardly administered when a patient does not improve health after the initial therapy. Likewise, the probability of encountering a MDR pathogen is enhanced when antimicrobial treatment is administered for too long of a time period. As a result of ASPs, these issues can be minimized.[2] Inevitably, lower medical costs are

another "bottom-line"[1] goal of ASPs without compromising the standard of care administered to the patient.[1]

In order for an ASP to be effective in achieving the goals described above, it is imperative that appropriate health care professionals are actively involved. There can be several combinations of participants that prove to be effective, but the fundamental staffing involved in an ASP usually includes an infectious disease physician, clinical pharmacist, and infection control personnel. The ASP pharmacist works closely with the microbiology laboratory who provides patient-specific cultures and vital susceptibility information.[1] An emergency medicine clinical pharmacist (EPh) can play a significant role in an antibiotic stewardship program, by reconsidering empiric antimicrobial treatment before the patient leaves the emergency room (since a patient is normally started on an IV broad-spectrum antibiotic after arrival in the emergency room before a culture is taken).[10]

Several strategies have been established to create and manage an effective institutional ASP, but there are basic principles that are crucial for success. Some common, baseline items that are present in the majority of successful ASPs include educational resources, the development of guidelines incorporating both local and national concerns, prior approval, post-prescription review and computer-based decision support.[1] Also, ASPs are most effective when they incorporate local guidelines into national guidelines by taking into consideration the prescribing and resistance patterns of antimicrobial agents in a certain region. Two proven strategies for incorporating ASPs are the "back-end"[2] and "front-end"[2] approaches. The "front-end"[2] approach includes formulary restriction and preauthorization (e.g., phone calls to the stewardship team) for restricted antimicrobial agents. The negative effect of this strategy is a possible delay in the administration of "stat" antimicrobials. The "back-end"[2] approach, also known as the prospective audit, involves the antimicrobial support team, including the infectious disease clinical pharmacist, to give feedback with suggestions to the prescriber based on institutional guidelines, patient specific information and culture results.[2] Common interventions include de-escalating or discontinuing one or more medications, switching from an intravenous to oral dosage form, and recommending a short-term duration of therapy. Additional strategies include educational programs, antimicrobial order forms, and computer systems with clinical decision support (such as computerized physician order entry). Overall, it is important for each institution to build an effective ASP based on available resources, personnel and various local factors. [2]

Although many health care settings have successfully implemented an ASP, there are a number of barriers that may be encountered including a lack of fundraising and physician participation, an insufficient number of infectious disease physicians and pharmacists, inadequate or absent diagnostic facilities, poor data collection, variation in data collection, a lack of communication among various health care professionals and a lack of cooperation among health care facilities.[8,11] An underlying issue that has a prominent role in the lack of physician participation is that only approximately 18 percent of infectious disease physicians that participate in ASPs are reimbursed for their services.[1] These sorts of obstacles are especially true for smaller institutions with limited budgets and personnel. In order to overcome these problems, it is suggested that executive planning and continued education programs be implemented to increase the cooperation among health care professionals to augment their clinical knowledge base dealing with steps to decrease and prevent antimicrobial resistance.[11] Therefore, educational programs directed at health care professionals can have a significant impact on the awareness of antimicrobial resistance, and the necessary procedures that need to be considered in their area of practice.

Impact of ASPs

There are numerous examples of successful implementation of ASPs to combat certain drug resistant pathogens and to improve the quality of patient care in a variety of specific health care settings. For example, an ASP was initiated in 2002 at the Vanderbilt University Hospital surgical trauma and intensive care units. The data collected as a result of this ASP spanned over an eight-year period. Over this time period, there were 1,794 Gram negative pathogens isolated. As a result of the initiation of the ASP, the percentage of infections due to MDR pathogens decreased from 34.7 percent in 2002 to 8.5 percent in 2008. Because resistant Gram negative infections are associated with about three times the health care costs compared to antimicrobial susceptible Gram negative infections, the implementation of the ASP resulted in decreased overall health care costs.[12]

Similarly, at John Hopkins Children's Medical and Surgical Center, a 175-bed hospital, an antimicrobial stewardship campaign was implemented. As a result, there was an 11.6 percent decrease in the number of doses of restricted antimicrobial agents dispensed. In addition, there was a 40 percent reduction in the number of telephone calls from the pharmacy when restricted antimicrobial use occurred. This was in large part due to the increased communication and educational programs offered to prescribers of the antimicrobial stewardship campaign. Additionally, there was a $370,069 decrease in the projected costs associated with restricted antimicrobial agents.[13]

A clinical trial evaluated the effectiveness of an ASP by comparing an intervention group (a pharmacist involved in antimicrobial stewardship) compared to a control (no antimicrobial stewardship pharmacist). The role of the stewardship pharmacist was to utilize prospective audit for the basis of interventions, to monitor the cultures of the patients, and to educate health care personnel of the program. In this study, there were 442 antibiotic orders for 160 patients. A total of 168 interventions by the antimicrobial stewardship pharmacist were performed, with a 91 percent acceptance rate by the prescribing physician. Compliance of all quality indicators, as a result of the ASP, rose to 54 percent compared to the baseline 16 percent of the control group. The quality indicators, together forming the primary outcome measure of this study, included documented indication for antibiotic therapy, appropriate cultures collected, appropriate empirical therapy and antimicrobial selection based on institutional and national guidelines, and appropriate de-escalation.[14]

ASPs are currently being implemented in settings beyond the hospital and inpatient facilities in order to incorporate a "full cycle of care." An ASP should not end once a patient is discharged, but should transition to the outpatient setting. For example, the Cleveland Clinic formed the community-based parenteral anti-infective therapy program (CoPAT). Under this program, an infectious disease consultation is mandated for any patient that is discharged to another facility or to the patient's home. During this consultation, infectious disease clinicians review laboratory results and also schedule follow-up appointments. Follow-up visits are thought to decrease readmissions, which is a major concern since 34 percent of Medicare patients discharged from hospitals are re-hospitalized within 90 days, adding an additional $17.4 billion to overall Medicare costs. Demonstrating the importance of the follow-up visits, over one-half of these re-hospitalized patients were not scheduled for a follow-up visit. Overall, the Cleveland Clinic's initiative to expand their ASP program beyond their inpatient facility is aimed at improving patient health and is an area of future expansion of ASPs.[15]

Conclusion

Antimicrobial resistance is a major health care-associated predicament. Without proper preventative measures, such as the implementation of ASPs, patient health could be severely compromised. Likewise, the use of current antimicrobial agents must be monitored in an attempt to prevent resistance due to inappropriate prescribing, length of treatment, and over-prescribing. ASPs have been proven to be efficacious in a variety of formats, especially when institutional guidelines based on local patterns are combined with national guidelines. Additionally, the involvement of multiple health care professionals, including pharmacists, is an imperative part of an ASP improving patient care and decreasing antimicrobial resistance. There are still many barriers in the implementation of ASPs that need to be overcome in many institutions, but once conquered, the impact will continue to grow, eventually having an impact beyond the inpatient setting.

There are still many barriers in the implementation of ASPs that need to be overcome in many institutions, but once conquered, the impact will continue to grow, eventually having an impact beyond the inpatient setting.

ASK AN EXPERT

During our research on ASPs, we had the opportunity to interview Jason Pogue, PharmD, BCPS-ID, a clinical pharmacist (infectious diseases) at Sinai-Grace Hospital, Detroit Medical Center and author of several leading articles in this area of practice.[16,17]

Q: Why do you think ASPs are important to our health care system?

JP: Antimicrobial resistance has been recognized by the World Health Organization (WHO) as one of the top three current threats to human health. As the antimicrobial pipeline falls further behind the pace of antimicrobial resistance development, ASPs become even more vital to health care in order to preserve the antimicrobials we currently have.

Q: When formulating budget appropriations, do you believe health care institutions consider these developments in antimicrobial resistance to be of vital importance?

JP: Firstly, when strictly focusing on the bottom line, since infections involving multidrug-resistant organisms are so costly, antimicrobial resistance is to be avoided at all costs. Recently the government and other payers are not reimbursing treatment of health care-associated infections, leaving the institution to shoulder the financial burden. This makes health care facilities carefully consider, develop, and utilize an ASP to combat the development of antimicrobial resistance. Furthermore, drug resistant pathogens often require new, broader spectrum drugs for treatment, which are extremely expensive. Therefore, hospitals consider antimicrobial resistance as a priority concern when developing a budget. Even though all health care institutions desire to run an effective ASP, since ASPs have been proven to improve patient outcomes and lower overall health care costs, the lack of adequate resources needed up front may restrict many institutions from seeing the full effect of a complete ASP.

Q: IDSA has attempted to combat the lack of development in the antimicrobial pipeline by introducing the 10 x '20 Initiative calling for the development of ten novel antibiotics by the year 2020. Is this realistic?

JP: Considering the current state of antimicrobial development, this goal is lofty and may be unlikely. Most new antibiotics in development are not novel, but rather are more diverse derivatives of current antibiotics since they do not have a new mechanistic target. While these derivatives can lower the cost of current treatment, they are not considered novel development.

Currently, the two major antibiotics that work to fight Acinetobacter baumannii are ampicillin-sulbactam and imipenen. This microbe, by innate nature, is resistant to many antibiotics. However, it is becoming increasingly resistant to ampicillin-sulbactam and imipenen. The susceptibility of this organism to the two antibiotics decreased from 89 percent to 40 percent and 99 percent to 42 percent, respectively. Currently, there are not any new drugs to combat this organism, only leaving older medications as treatment options, which have an increased number of side effects. For example, colistin can be used, but causes nephrotoxicity in 40 percent of the patients. Therefore, many deleterious outcomes can occur due to the inability to utilize the first line therapy. Also, as resistance develops, the length of hospital stay and mortality rates increase, which highlights the importance of ASPs.

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Assessment Questions—Antimicrobial Stewardship Programs

1. Which is NOT a reason for concern dealing with the spread of antimicrobial resistance?

A. Decrease in research and development of antimicrobial agents by major pharmaceutical agents
B. Administration of the correct dose
C. Over-prescribing antibiotics
D. Inappropriate and/or prolonged use of broad-spectrum antimicrobial coverage

2. All of the following are benefits of successful ASPs EXCEPT:

A. Decrease in overall health care costs
B. Ability for institutions to decrease the number of staff health care professionals
C. Improved patient quality of care
D. Decrease length of hospital stay

3. The primary goal of an ASP is to:

A. Decrease overall health care costs
B. Increase the quality of patient care
C. Decrease the number of antimicrobial agents needed to be stocked in the pharmacy
D. Increase the need for improved laboratory resources and machinery

4. ASPs encourage all of the following EXCEPT:

A. Transfer of parenteral treatment to oral treatment
B. Off-cycle antibiotic prescribing
C. Streamlining or de-escalating antibiotic therapy immediately when appropriate
D. More than one of the above

5**. Which term correctly describes an event when broad-spectrum antibiotics are quickly and haphazardly administered if a patient does not improve health after the initial therapy?**

A. Antibiotic cycling
B. Spiraling empiricism
C. Stat treatment
D. Multi-drug resistant medication therapy

6. Common participants involved in the operation of a successful ASP include all of the following EXCEPT:

A. Information technology staff
B. Infectious disease physician
C. Clinical pharmacist
D. Physical therapist

7. Common strategies that are present in successful ASPs include all of the following EXCEPT:

A. Prescription approval
B. Educational resources for the involved health care professionals
C. Post-prescription review
D. Exclusive use of national guidelines

8. A strategy for incorporating an ASP that includes formulary restriction and preauthorization for the use of restricted antimicrobial agents is known as:

A. Front-end approach
B. Back-end approach
C. “Stat” approach
D. Guideline approach

9. This strategy for incorporating an ASP, also known as the prospective audit, utilizes interventions and feedback by an infectious disease clinical pharmacist to make suggestions to the prescriber:

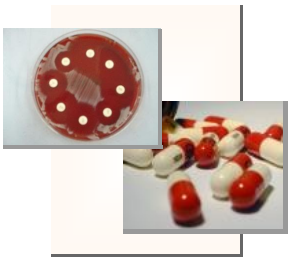
A. Front-end approach
B. Back-end approach
C. Computerized physician order entry
D. Formulary restriction/preauthorization

10. Common barriers facing the implementation of an efficacious ASP include all of the following EXCEPT:

A. Inadequate or absent diagnostic facilities
B. Communication among health care facilities and health care professionals
C. Poor data collection
D. Insufficient number of infectious disease physicians and pharmacists

To receive continuing education credit for this program, you must answer the above questions and fill out the evaluation form. Please visit www.onu.edu/pharmacy to enter the required information. Please allow two to three weeks for electronic distribution of your continuing education certificate, which will be sent to your valid email address in PDF format.

Ohio Northern University is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This program is eligible for credit until 02/28/15.



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Ohio Northern University Continuing Education Registration & Evaluation Form
Raabe College of Pharmacy Continuing Education Evaluation Form

Program Title: **Antimicrobial Stewardship Programs**
UAN: 0048-0000-12-009-H04-P CEUs: 0.1

All information must be printed CLEARLY to ensure accurate record keeping for attendance and the awarding of continuing education credit. Certificates will be distributed as a PDF document to a valid email address.

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City:	**State:**	**Zip:**	
Phone:	**E-mail:**		
Pharmacy License #:	**State:**	**ONU Alumni?**	**Y N**

Program Content:	**Strongly Disagree**				**Strongly Agree**
The program objectives were clear.	**1**	**2**	**3**	**4**	**5**
The program met the stated goals and objectives:					
Identify ways in which Antimicrobial Stewardship Programs (ASPs) are utilized to decrease microbial resistance.	**1**	**2**	**3**	**4**	**5**
Comprehend the multiple and interconnected roles of various health care professionals associated with ASPs.	**1**	**2**	**3**	**4**	**5**
Recognize the significant decrease in current research and development of antimicrobial agents by major pharmaceutical companies, and its impact on the need to properly utilize available antibiotics.	**1**	**2**	**3**	**4**	**5**
List strategies that can be established to create and run an effective institutional ASP.	**1**	**2**	**3**	**4**	**5**
Examine how the quality of patient health has been improved as a result of successful implementation of ASPs in a variety of health care settings.	**1**	**2**	**3**	**4**	**5**
The program met your educational needs.	**1**	**2**	**3**	**4**	**5**
Content of the program was interesting.	**1**	**2**	**3**	**4**	**5**
Material presented was relevant to my practice.	**1**	**2**	**3**	**4**	**5**

Comment/Suggestions for future programs:

_____

_____

Thank you!

Answers to Assessment Questions—Please Circle Your Answer

1. A B C D	**4. A B C D**	**7. A B C D**	**10. A B C D**
2. A B C D	**5. A B C D**	**8. A B C D**	
3. A B C D	**6. A B C D**	**9. A B C D**	

Any questions/comments regarding this continuing education program can be directed to Lynn Bedford, Advanced Administrative Assistant for the Office of Continuing Education (email: l-bedford@onu.edu, phone 419-772-1871).

Ohio Northern University is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This program is eligible for credit until 02/28/15.

Understanding Drug Shortages as a Pharmacist

Heather Helsel, fourth-year pharmacy student from Mentor, Ohio; Thomas Otroba, fourth-year pharmacy student from Bethel Park, Pa.; Juliana Zschoche, fourth-year pharmacy student from Rochester, N.Y.; **Elizabeth Dodds-Ashley**, PharmD, MHS, associate director of pharmacy, University of Rochester Medical Center-Strong Memorial Hospital

Pharmacists have the opportunity to develop strategies in order to circumvent drug shortages ensuring appropriate patient outcomes.

Introduction

A drug shortage is an inadequate supply of medication that negatively affects how a pharmacy dispenses, compounds or clinically uses a drug, as defined by the American Journal of Health-System Pharmacy. Drug shortages in the U.S. health care system are more prevalent now than ever, and their impact is very substantial. In 2010, there were 178 reported drug shortages, up from 61 in 2005 according the Federal Drug Administration (FDA) Center for Drug Evaluation and Research (CDER).[1] Our health care system is designed to rely on the availability of safe, effective and cost-efficient medications. When a medication is unavailable, there are significant consequences not only in the quality of care offered to patients but also in the economic viability of such services. Understanding the causes, challenges and impacts of drug shortages can help pharmacists effectively manage this problem. Pharmacists have the opportunity to develop strategies in order to circumvent drug shortages ensuring appropriate patient outcomes. In order for a pharmacist to effectively manage drug shortages, the pharmacist must first understand the causes as well as the impact on patient care, economical effects and enhanced professional responsibilities of this prevalent problem.

Why do Drug Shortages Exist?

Due to the innate complexity of pharmaceutical supply chains, often it is very difficult to pinpoint a reason for a drug shortage. There are many factors that go into the production and distribution of a drug, and a disturbance at any phase may result in a drug shortage. A drug shortage may be the result of insufficient raw materials and may take over a year for a manufacturer to locate a new source of material and obtain FDA approval.[2] More than 80 percent of raw materials are imported from overseas, which makes the process even more challenging. Besides problems with raw materials, a manufacturer may discontinue production of a drug strictly for financial reasons. For example, if a drug does not achieve a certain profit margin, a pharmaceutical manufacturer may elect to stop its production. As a result, other manufacturers are left responsible to meet the demand of the product. Due to antitrust laws, a manufacturer is not permitted to notify competitors before discontinuing a product. The manufacturer does, however, have the ability to notify the FDA if they choose. The FDA will then post information to the public. Informing the FDA is not required unless the company is the sole manufacturer of a life-saving drug. In short, the FDA has no authority to require a manufacturer to make a product. Also, FDA regulation is a major cause of drug shortages. A manufacturer must meet good manufacturing practice (GMP) regulations. If a manufacturer fails to meet these regulations, the FDA will provide the manufacturer with a list of problems and potential corrective actions that need to be taken. Upon subsequent inspections from the FDA, if the manufacturer did not correct the problems, the FDA may take enforcement action. This could lead to the shutdown of manufacturing sites. Furthermore, manufacturers may choose to voluntarily recall a product due to production issues thus leading to temporary shortages. Although preservation of the availability of a drug is always attempted, sometimes it is just not possible.[2]

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How are Drug Shortages Handled?

Both manufacturers and health care systems have a large role in drug shortages and availability. For example, manufacturers commonly employ a just-in-time inventory management style due to the lack of available resources. As a result, when a drug shortage arises, manufacturers are unable to meet the increased demand. Similarly, many hospitals also employ the just-in-time inventory management style. However, an institution aims to maximize profits by reducing the cost of inventory. During a drug shortage, the small amount of inventory on hand will result in the unavailability of a medication to patients.[1]

For example, in March 2011, the FDA issued a bulletin regarding the drug shortage of calcium gluconate. Due to the calcium chloride shortage resulting from American Regent, Inc. ceasing its production seven months prior, an increased demand of the therapeutic alternative, calcium gluconate arose. Furthering the gluconate shortage, two other companies were also experiencing manufacturing delays with this product. As a result, other manufacturers of calcium gluconate such as APP Pharmaceuticals, LLC and Luitpold Pharmaceuticals, Inc., experienced an overwhelming demand for this drug starting in June 2011. At the time this article was written, calcium gluconate products were either on backorder, currently being allocated, and/or had been discontinued according to the FDA drug shortage list.[3] As of now, supplies are being released in limited quantities as they become available. There are many efforts being made to conserve this limited supply. First and foremost, health care practitioners began restricting the use of calcium within their institutions to the most critically ill patients and those who were experiencing severe symptoms of hypocalcemia.

There have been several recent examples where supplies of individual medications have been exhausted and health systems were forced to look at alternatives. Several approaches are often employed in concert to be sure that safe and effective care is not compromised. This usually includes convening content experts to determine criteria for using limited remaining drug supplies and identifying any alternatives that might be feasible. At the same time, unnecessary use of the medication is prevented through a variety of mechanisms that include use of electronic health information systems, provider education and direct pharmacist intervention. In the most extreme cases, hospital leadership is involved to determine if elective or other non-urgent procedures or admissions need

to be delayed if sufficient drug supplies are not available to meet the needs of target patient populations.

What Factors are Impacted?

The most significant impact of a drug shortage is compromised patient care. The Institution for Safe Medication Practices (ISMP) conducted a study in 2010 looking at the consequences of drug shortages on patient safety. Of the 1,800 practitioners that responded, 35 percent reported that their facility experienced a near miss that could have resulted in patient harm due to a drug shortage. Additionally, 25 percent reported that the error actually reached the patient and 20 percent testified that the error resulted in an adverse event.[4] With such a high incidence of medication errors related to drug shortages, it is important to understand how shortages compromise patient safety in such a substantial fashion. One of the most common ways to deal with a drug shortage is for a physician to prescribe an alternative medication. Many times the physician may not be very familiar with the alternative option. As a result, contraindications and dosing regimens may not be fully understood. Also, some alternative medications may not be as effective as the first-line therapy. Furthermore, therapeutic alternatives may not exist for certain drugs. All of these challenges compromise the care and safety of the patient.

In addition to having a negative impact on patients, the increased labor brought about by drug shortages cannot be ignored. A survey was conducted that included 353 directors of pharmacy from across the nation. It was found that pharmacist and pharmacy technicians spend a considerable amount of time (pharmacist: 9 hours/week, pharmacy technician: 8 hours/week) managing drug shortages as compared to other health care professionals (physicians: 0.5 hours/week, nurses: 0 hours/week).[5] This statistic is considerably higher than in 2004 when pharmacists spent 3 hr/wk managing drug shortages. This increased burden results in pharmacists having less time for other high value tasks such as medication therapy management, direct patient care, and enhanced drug delivery. Another very large contributor to increased labor is the extensive use of automation systems in most institutions. Frequently automation systems such as electronic physician ordering, barcode technology, and inventory systems are used in conjunction with one another. Although the increasing use of automation is beneficial within the realm of normal operations, the presence of a drug shortage can cause significant problems. The integration of a new drug and/or protocol into an automated system requires an extensive amount of human resources.[6] In contrast, a hospital with a more manual ordering system may present with other challenges such as notifying prescribers of a drug shortage at the time of prescribing.

Not only do drug shortages have a significant impact on patient care and safety, but they have a substantial impact economically as well. As mentioned, one of the most prevalent ways to deal with a drug shortage is through the use of alternative medications. Typically if an institution is able to purchase an alternative generic, it is attained at an increased cost due to off-contract pricing. A recent study estimated that the purchase of more expensive generics and therapeutic alternatives is at least $200 million annually. When this considerable cost is combined with the $216 million associated with increased labor cost[5], the extensive economic impact of drug shortages becomes very clear.

The Role of the FDA

As discussed, drug shortages are more prevalent and severe in today's society. Not only do they compromise patient safety, but they increase the workload of the pharmacy staff and have a substantial economic impact. Due to the severity of these consequences, the FDA works to minimize the effects of drug shortages. When a product that is considered a medical necessity becomes unavailable, the FDA follows a series of steps within the CDER to help resolve the situation. A medical necessity, as defined by American Society of Health-System Pharmacists (ASHP), is a medication that "is used to treat or prevent a serious disease…or condition, and there is no other available source of that product…[or] an adequate substitute."[1] Cost and inconvenience to the manufacturer and/or patient does not qualify the substance as a medical necessity. Therefore, if a drug is considered a medical necessity, the FDA will work with pharmaceutical manufacturers to help acquire additional raw material, technology, or machinery needed to produce the medication. Although the FDA cannot require companies to increase production, it can expedite the review of manufacturing practices.[7] This could include extending the product's expiration date, licensing distributors or using materials from different sources. More specifically, if a medication is available but is not identical to the needed product, the FDA can conduct a health hazard evaluation to determine the drug's risk profile.[8] Based on these findings, the drug may be used in some protocols. In severe drug shortage cases, the FDA has the authority to temporarily allow the import of non-FDA approved therapy equivalents.[9] Throughout these practices, however, maintaining patient safety is of upmost importance. The federal government is taking steps to regulate drug shortages as evidenced by the Executive Order on Reducing Prescription Drug Shortages, which was ordered by President Barack Obama on October 31, 2011.[10]

From communication advantages to determining therapeutic alternatives, utilization of pharmacist knowledge is vital when faced with a drug shortage.

Along with collaborating with manufacturers, the FDA also provides continuous updates to the community about the shortage. In 1999, the FDA created the Drug Shortage Program (DSP) as part of the CDER. One of the components of this program is to act as a

liaison between health care professional organizations and manufacturing companies.[7] Working closely with pharmaceutical distributors allows the FDA to provide accurate and timely information to patient groups. Therefore, if a manufacturer decides to discontinue a product and eventually cause a shortage, the FDA can notify important stakeholders and prepare accordingly. As a result, health care professionals are able to identify other treatments for their patients. However, there are additional considerations when utilizing alternative medications. Higher risk profiles, sub-therapeutic results and adverse events are only a couple of examples. Nonetheless, the FDA's open communication allows health care organizations adequate time to prepare for a drug shortage.

ASHP Guidelines

American Society of Health-System Pharmacists (ASHP) developed guidelines for health care professionals, specifically pharmacists, to use when faced with a drug shortage.[11] These guidelines are divided into a process that has three main phases: the assessment phase, the preparation phase and the contingency phase. It is important to note that pharmacists have a vital role in each of these phases.

Throughout the first phase (assessment phase) the duration of the shortage must be determined. Depending on the length of the shortage, institutions may respond differently to the situation. For example, a lack of raw material may cause multiple manufacturers to be unable to produce a drug. As a result, pharmacy and therapeutic committees must find a therapeutic alternative. Before beginning the preparation phase, it is also important for institutions to determine the amount of medication on hand. Based on the quantity and usage history, a measurement of how long a shortage can be endured can be determined.[11]

In order to maintain optimal patient care, the second phase (preparation phase) is vital for pharmacists to utilize in the management of drug shortages. This phase involves preparing for a shortage before its effects are actually seen. For instance, a medication substitution must be considered. Since pharmacists are the drug experts, they have a crucial role in selecting the most ideal alternative. Though a pharmacist should lead this selection, collaborating with doctors, nurses and residents is crucial. While determining drug alternatives, patient safety must also not be forgotten. Therefore, pharmacists are responsible for implementing plans for medical professionals so that patient safety is not compromised. Finally, during the preparation phase, other supply sources of the drug must be researched. If located, availability, contract agreements and payment terms should be discussed. It is crucial for pharmacists not to stockpile a medication. This could lead to a misidentified drug shortage and reduce patient care.[11]

The last and third phase (contingency phase) encompasses therapies that are nontraditional. These medications do not have any therapeutic alternatives nor can they be prepared by a traditional manufacturer. When this happens, institutions should work closely with the FDA. Pharmacists can counsel patients and their families if a delay or compromise in care will occur. Additionally, communicating with the media and other health care organizations can raise awareness of the shortage. As a result, nontraditional companies that produce the drug may be discovered or manufacturers may be motivated to formulate the medication. Throughout the three phases outlined by ASHP, pharmacists have an integral role. From communication advantages to determining therapeutic alternatives, utilization of pharmacist knowledge is vital when faced with a drug shortage.[11]

Conclusion

Understanding the contributing factors and consequences of drug shortages is critical for a pharmacist to provide optimal patient care. This is especially important in today's society due to the fact that drug shortages have reached an all time high. Though the causes of shortages are complex, some contributing factors are lack of resources and manufacturing regulations. One of the major implications of drug shortages is increased labor for the pharmacy staff. As a result, both patient care and health system economics are compromised. Fortunately, the FDA has a major role in preventing, regulating and promoting awareness of drug shortages. Despite the FDA's efforts, the ultimate responsibility of managing drug shortages falls upon the pharmacist. By applying the phase model created by ASHP, a pharmacist can effectively manage this prevalent problem.

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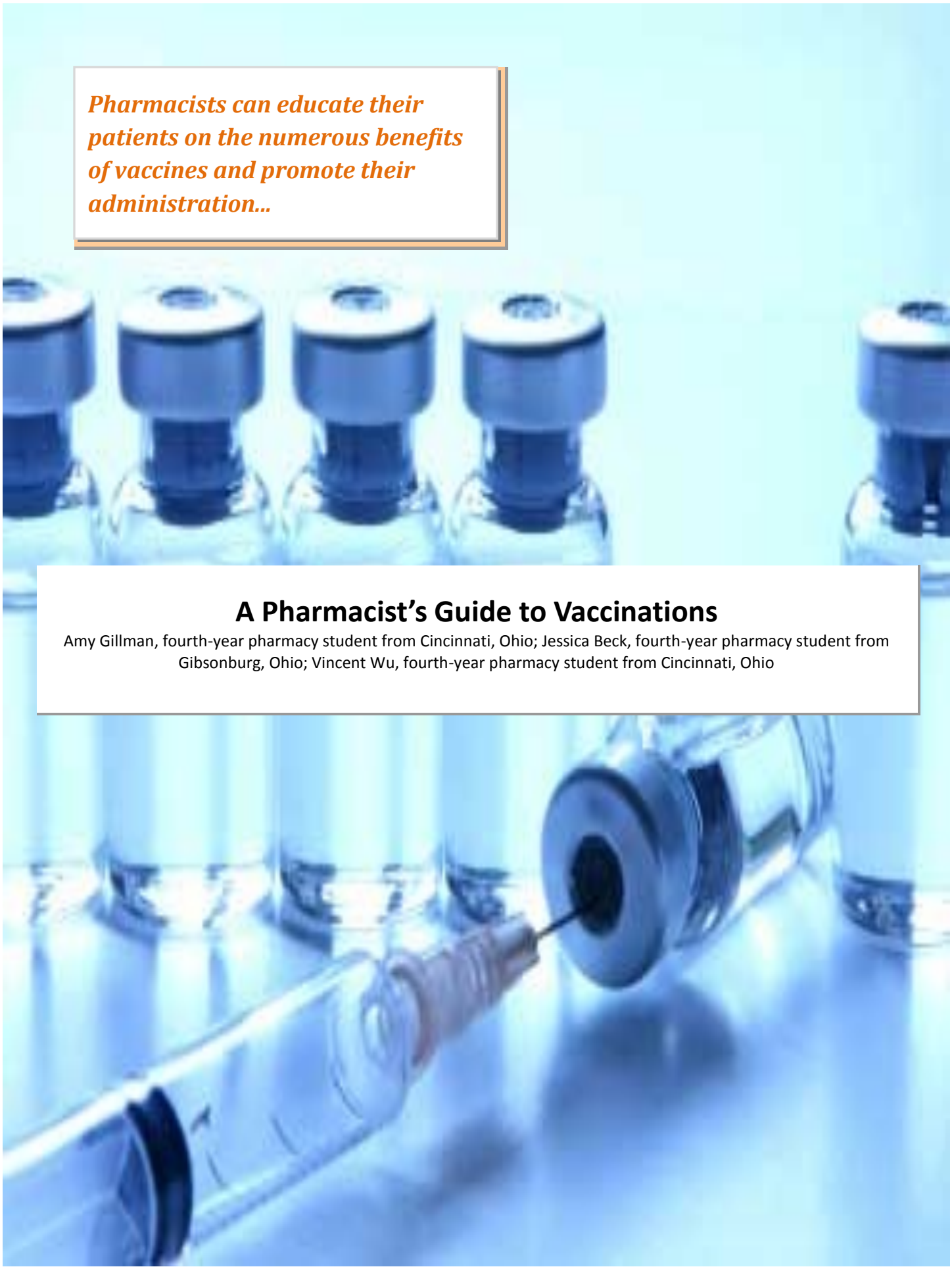

A Pharmacist's Guide to Vaccinations

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Introduction

Pharmacists play a crucial role in maximizing public health by being an accessible resource for patients of all populations. Pharmacists can educate their patients on the numerous benefits of vaccines and promote their administration, especially within high-risk populations. Most pharmacies today offer clinic hours where patients can receive their annual influenza vaccine; many also offer additional options such as the shingles vaccine. With vaccinations becoming an easy trip to the local pharmacy, one major barrier for immunizations has been eliminated, further opening the door toward maximum disease prevention. Every year, hospitals are ridden with patients suffering from preventable diseases and, while it seems unfathomable in our present-day society, people still die from diseases like influenza every winter. It is the pharmacists' role to educate on the simplicity and necessity of basic vaccinations. The vaccinations discussed in this article are a vital element in preventing disease states that can include a range of symptoms and complications which can vary from the inconvenience of keeping one away from their daily responsibilities for a short period of time to a potential precursor to cancer. There are five vaccinations in particular which target common transmittable disease states: human papillomavirus (HPV); diphtheria, tetanus, and pertussis; hepatitis B; herpes zoster virus (shingles); and influenza. The objective of this article is to provide pharmacists with the necessary information to properly educate, advise, and encourage their patients about common vaccinations that could have a significant effect on positively altering their long-term health and quality of life.

Human Papillomavirus (HPV) Vaccine

The HPV vaccine is a recombinant subunit vaccine administered to prevent the subtypes of HPV that are known to commonly cause cervical cancer and genital warts.[1] There are currently two HPV vaccines available: Gardasil®, a quadrivalent vaccine containing viral types 6, 11, 16 and 18, and Cervarix®, a bivalent vaccine containing types 6 and 18. Both vaccines are given intramuscularly (IM) as a three-dose series; the second dose to be given one to two months after the first and the third dose to be given six months after the first dose.[2] Females age 9 to 26 years are recommended to receive either of the vaccines to protect against cervical cancer. Gardasil® has also been proven safe and effective for males age 9 to 26 years for the prevention of genital warts. The CDC recommends that males 22 through 26 years of age whose immune systems are weakened, who have sex with men, or who test positive for the human immunodeficiency virus (HIV), should receive this vaccination. The quadrivalent vaccine is also recommended for *all* boys at age 11 or 12 and catch-up vaccinations for males age 13 through 21 years.[3] Because sexually active patients are thought to benefit most from the vaccine, and a patient can be infected with HPV the first time they have sexual contact with a partner, it is important to get all three doses before being exposed to the virus to ensure protection.[1]

The HPV vaccine is contraindicated in patients who are allergic to yeast or any component of the vaccine and should not be given to a patient who is ill at the time a dose is planned. Neither formulation of the vaccine is recommended to be administered to pregnant women. Gardasil® can, however, be administered to nursing mothers.[2] Side effects of the vaccine include pain, redness and swelling at the injection site. Mild to moderate fever and headache have also been reported. While many private health plans are providing coverage for the HPV vaccine, the level of coverage can vary. Those patients who are uninsured or whose insurance does not pay for the vaccine may qualify for assistance programs such as Vaccines for Children (VFC) or patient assistance programs through the companies that supply the vaccines.[1]

Diphtheria, Tetanus and Pertussis Vaccines

The four combination vaccines associated with the prevention of diphtheria, tetanus and pertussis are DTaP, Tdap, DT and Td. DT and Td contain both the diphtheria toxoid and the tetanus toxoid, while DTaP and Tdap contain an additional dose of killed, acellular pertussis.[2] All four vaccines are administered IM, however there are different recommendations as to when they should be administered.[1]

DTaP and DT are given to children younger than 7 years of age. These children should receive five doses of DTaP: at ages 15 to 18 months, 2 years, 4 years, and 6 years, and any time between 4 and 6 years. DT should be used as a substitute for children who cannot tolerate the pertussis vaccine. DTaP and DT are contraindicated in anyone who is 7 years of age or older, is allergic to any component of the vaccine and has a moderate to severe illness on the day the vaccine is scheduled. Side effects of DTaP and DT include redness and swelling at the injection site, fever and seizures.[1]

Tdap and Td are given to adults and children 7 years of age and older. Td is given as a booster shot every 10 years to unvaccinated and previously vaccinated adults. Patients presenting with a major wound or exposure

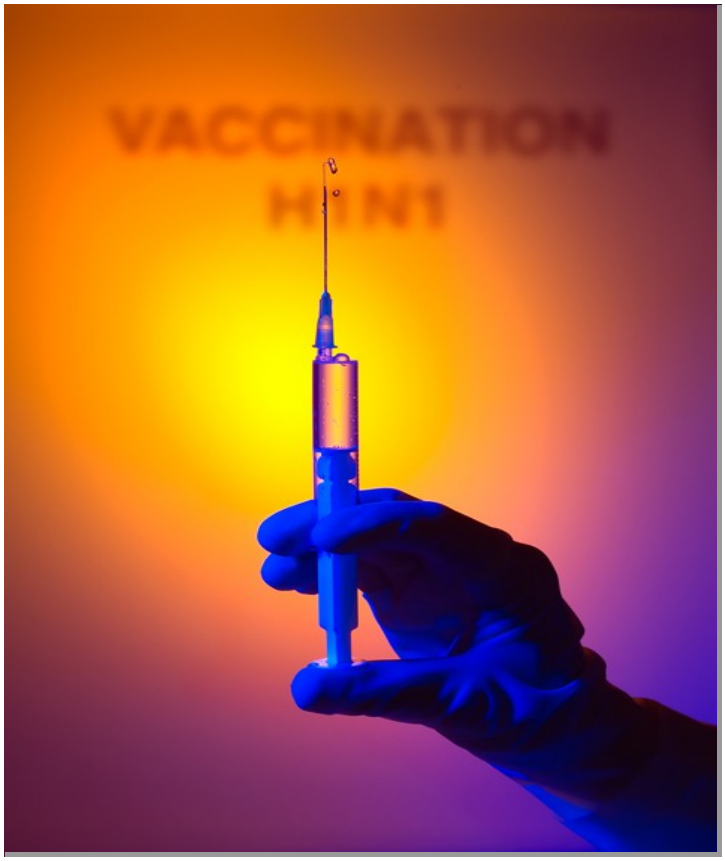
to tetanus more than five years after their last injection should also be revaccinated.[2] A single dose of Tdap should be given in place of Td booster in anyone 11 to 64 years of age, and in children 7 to 10 years old who are underimmunized or did not receive the full recommended series of DTaP before age 7 years. Adults 65 years of age and older should also receive one dose of Tdap if they are likely to come into contact with an infant younger than 12 months.[4] Tdap and Td are contraindicated in anyone with an allergy to any component of the vaccine and those individuals suffering from a moderate to severe illness on the day the vaccine is scheduled.[1] The Tdap vaccine is now recommended for women in the third or late second trimester (20th week or more) of their pregnancy.[3]

PharmaJet® is the newest technology in influenza vaccinations; it is a needle-free injection system that uses a spring-powered energy source to administer the vaccination without actually puncturing the skin.

Side effects of Tdap and Td include redness and swelling at the injection site, body aches and fever.[2] Most private health plans are providing coverage for all four of the diphtheria, tetanus and pertussis vaccines. Again, those patients who are uninsured may qualify for assistance programs such as VFC or discounted vaccines at their local health department.[1]

Hepatitis B Vaccine

The Hepatitis B vaccine is produced by yeast and contains a viral envelope protein, hepatitis B surface antigen (HBsAg). It is indicated for use in patients who are health care workers and those with chronic liver diseases as well as end-stage renal disease, MSM, patients with multiple sexual partners, or HIV-infected patients without immunity. Changes in the Centers for Disease Control and Prevention (CDC) guidelines for 2012 recommend that adults recently diagnosed with diabetes who are younger than 60 years old should receive the Hepatitis B vaccine as soon as possible.[3] However, it should be given to any adult who desires the vaccine. Post-vaccination serologic testing should be done on patients who are considered to be at high risk, such as health care workers. If the patient does not respond according to serum levels, the patient should be revaccinated.[2] The vaccine is given in three doses: at intervals of 0, 1, and 6 to 12 months.[1] If the series is not completed, it is not a requirement that it be restarted. However, it is recommended that the patient contact his/her medical provider about the situation.[5] The vaccine is administered IM and should be used with caution if the patient has yeast allergies.[2] The vaccine itself is safe to administer to pregnant women and has had almost no adverse effects reported in over 100 million administrations. Booster shots are not recommended for healthy patients but can be used in hemodialysis patients or patients with a weakened immune system. This vaccine may also be taken in conjunction with other vaccines.[5]

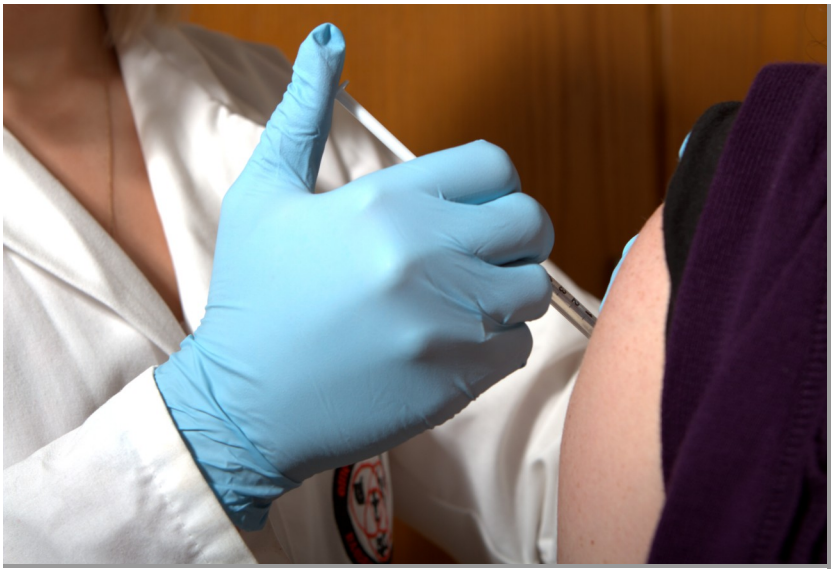


Influenza Vaccine

There are two forms of the vaccination available to target this unpredictable and highly contagious respiratory illness. Infection with influenza is caused by one of thousands of strains of this virus that infects the nose, throat and lungs. Each year, the U.S. Food and Drug Administration (FDA) selects which viruses to target for that particular year according to the recommendations from the World Health Organization (WHO). The 2011-2012 vaccination for the Northern Hemisphere targets these three viruses: an A/California/7/2009 (H1N1)-like virus, an A/Perth/16/2009 (H3N2)-like virus, and a B/Brisbane/60/2008-like virus (Influenza B).[1]

What many Americans think of as the traditional "flu shot" is a trivalent inactivated vaccine (TIV) and can be one of three subcategories: a regular IM flu shot indicated for all ages over 6 months (Fluzone®), a high dose IM shot indicated for patients over 65 years (Fluzone® High-Dose)[1] [higher dose is not preferred[2]] and an intradermal shot indicated for patients ages 18 to 64 (Fluzone®-Intradermal).[1] These vaccinations are acceptable for administration to pregnant women and result in minimal side effects, with the most common being irritation at the injection site, a low-grade fever and/or muscle aches (generally lasting 1 to 2 days).[2]

The other available form is a live attenuated influenza vaccine (LAIV) administered via the intranasal route (Flumist®). This is indicated for non-pregnant, healthy adults 49 years and younger and can cause some minor adverse reactions, most commonly nasal congestion, headache and/or cough.[2] This form is an excellent alternative for patients who are uncomfortable with needles. While no studies specifically focusing on influenza have been done for an adult population, one large study of children age 15 to 85 months concluded a 92 percent decrease in chance of influenza infection versus placebo with the LAIV vaccine.[1]



Following administration of either vaccine, it takes approximately two weeks for the proper antibodies to develop and infer protection from the influenza virus.[1] Neither vaccination is recommended for patients with a history of Guillain-Barré Syndrome.[1] While in the past, patients with chicken egg allergies have refrained from receiving the vaccine, the CDC's Advisory Committee on Immunization Practices (ACIP) has made a recommendation based upon several thorough studies stating that people who have experienced hypersensitivity reactions which manifested as only hives following egg consumption can receive TIV intramuscularly as long as it is administered by a health care professional familiar with the manifestations of egg allergies who can observe the patient for 30 minutes post-administration.[1]

PharmaJet® is the newest technology in influenza vaccinations; it is a needle-free injection system that uses a spring-powered energy source to administer the vaccination without actually puncturing the skin.[6] However, the FDA released a statement on October 26, 2011, clarifying that inactivated influenza vaccines labeled for IM injection are only labeled for administration using a sterile needle and syringe.[7] Their statement explained that the necessary safety and effectiveness information has not been submitted to the FDA and therefore there is no definitive information to support approval of this injection system. Currently, Measles, Mumps, Rubella (MMR) is the only vaccination approved and specifically labeled for administration via a jet injector.[7]

The ACIP recommends a yearly flu vaccination for everyone six months of age and older, but especially for seniors over 65, pregnant women, and those with health conditions like diabetes, asthma or heart disease.[3] These groups are at high risk for serious flu-related complications. Children ages 6 months through 8 years are recommended to receive two doses of the flu vaccine four or more weeks apart (unless they received the vaccination last season).[1] The first dose will "prime" the immune system and the second dose 28 days or more later will provide the true immune protection.[1]

Zostavax®

Zostavax® is a live attenuated virus vaccine administered as a one-time subcutaneous dose for use in adults over the age of 60. It is not recommended for use in immunocompromised, gelatin sensitive or pregnant patients. The main goal of Zostavax® is to prevent shingles, a disease that is more likely to be seen in older patients who have lost their immune system efficiency. The vaccine has been tested in about 20,000 people aged 60 years old and older. The most common side effects that were observed were redness, soreness, swelling or itching localized at the injection site and headache.[2] Patients should space this vaccine at least four weeks apart from the pneumococcal vaccination to ensure they receive the maximum efficacy from both vaccinations.[8] Any patients using acyclovir, famciclovir, or valacyclovir should cease taking their medication for at least 24 hours before getting Zostavax®.[2] While the usage of the vaccine is recommended for those above 60, it is FDA approved for use in those over 50 if deemed medically needed. The vaccine itself is not covered by Medicare Part B. Private insurances and Medicaid may cover the vaccine.[8] Currently there are no programs available to help patients purchase Zostavax® in the event of no coverage.

Vaccine	Indications	Route	Frequency	Contraindications	Adverse Reactions
HPV	Males and females aged 9-26 years (Gardasil®) Females aged 9-26 years (Cervarix®)	IM	3 doses; 0, 1-2, and 6 months	Allergy to yeast or vaccine component, pregnancy	Injection site pain, redness, swelling fever, headache
Diphtheria, Tetanus, Pertussis					
• DTaP and DT	Children < 7 years	IM	5 doses; 15-18 months, 2, 4, 4-6, 6 years	≥ 7 years, allergy to vaccine component, illness	Injection site redness, swelling fever, seizure
• Tdap	Adults and children ≥ 7 years, < 65 years	IM	Once in place of Td booster	Allergy to vaccine component, illness	Injection site redness, swelling fever, body aches
• Td	Adults and children ≥ 7 years	IM	Booster every 10 years	Allergy to vaccine component, illness	Injection site redness, swelling fever, body aches
Hepatitis B	Health care workers, chronic liver disease, end-stage renal disease, MSM, multiple sexual partners, or HIV-infected without immunity	IM	3 doses; 0, 1, and 6-12 months	Yeast allergy	Injection site swelling, warmth, soreness, nodule formation
Influenza					
• Trivalent Inactivated (TIV)	Adults and children > 6 months	IM	Once at the beginning of every flu season	Allergy to vaccine component, history of Guillain-Barré Syndrome, severe egg allergy	Injection site irritation, low grade fever, body aches (lasting 1-2 days)
• Live Attenuated (LAIV)	Children > 2 years, non-pregnant and healthy adults < 49 years	Intra-nasal	Once at the beginning of every flu season	Allergy to vaccine component, pregnancy, history of Guillain-Barré Syndrome, egg allergy	Nasal congestion, headache, cough
Zostavax®	Adults > 60 years	SC	Once	Immunocompro-mised, gelatin allergy, pregnancy	Injection site soreness, swelling, itching, headache

Pneumococcal Vaccine

The U.S. Food and Drug Administration (FDA) recently approved of Prevnar 13, a pneumococcal vaccine, for use in adults age 50 years and older. Although CDC recommends that those age 65 and older and those age 19 through 64 with certain health conditions get another pneumococcal vaccine called Pneumovax, CDC has not issued any formal recommendation concerning Prevnar 13.[3]

Additionally, Prevnar 13 is approved for use in children 6 weeks through 5 years of age (prior to the sixth birthday) for active immunization. Prevnar 13 is also indicated for the prevention of otitis media caused by streptococcus pneumoniae serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F. No otitis media efficacy data are available for serotypes 1, 3, 5, 6A, 7F, and 19A.[9]

Pharmacy is a dynamic profession, continuously adapting to meet the needs of our present day society.

Conclusion

Pharmacy is a dynamic profession continuously adapting to meet the needs of our present day society. By utilizing the convenience and accessibility of pharmacists, more patients in more populations can be immunized and protected from preventable disease states. It is crucial to educate all patients on the long term health benefits of a simple vaccination and how it can improve their quality of life. HPV, DTaP, hepatitis B, herpes zoster and influenza vaccines are a great foundation to maximizing public health, and expanding one's knowledge to other vaccinations can only Improve the care for patients overall.

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Phase IV Clinical Trials: Postmarketing Surveillance of Prescription Drugs

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Information provided in post-marketing surveillance and pharmacovigilance is often the impetus for further investigations, including controlled clinical trials and formal epidemiologic studies.

Introduction

When a newly developed drug is approved by a regulatory body for initial licensure, researchers have already conducted extensive testing and evaluation of adverse events and risks associated with the medication. However, due to constraints involving the patient population of the testing group, it is possible that additional or rare side effects have yet to be seen. For this reason, drugs are subject to phase IV trials after approval for patient use. Phase IV clinical trials, which include postmarketing surveillance, are observational studies performed on U.S. Food and Drug Administration (FDA)-approved drugs primarily to identify adverse reactions not manifested during phases I, II, and III of the drug development process. Also assessed is drug effectiveness in real world therapeutic use, which may be markedly dissimilar to restricted clinical trials.[1] Because clinical trials may not have the statistical power to reveal these rare occurrences nor the temporal scope to detect long-latent events, it is imperative that drug manufacturers, health care professionals, and consumers themselves submit reports of adverse events. Adverse drug reaction (ADR) reports may be submitted via the FDA's MedWatch program, designed for spontaneous and voluntary reporting of serious adverse drug reactions (Table 1).

Table 1. Reporting an adverse event to the FDA[9]

- Online reporting form
  - MedWatch: the FDA Safety Information and Adverse Event Reporting System
    - Go to www.fda.gov/Safety/MedWatch/default.htm
    - Under the "Resources for You" side menu, select "Report a Serious Medical Product Problem Online"
    - Proceed to fill out the MedWatch Online Voluntary Submission Form 3500, including as much pertinent information as possible
- Download a copy of the paper form and either fax it to 1-800-FDA-0178 or mail it using the postage-paid addressed form. (Send only one page plus any continuation pages-do not send instruction pages.)
- Call FDA at 1-800-FDA-1088 to report by telephone

"Pharmacovigilance," or the process of broadening known information about a drug by way of detection, analysis, and prevention of these events, is an evolving science with novel techniques in development.[2, 3] Information provided in postmarketing surveillance and pharmacovigilance is often the impetus for further investigations, including controlled clinical trials and formal epidemiologic studies.[4]

Therapeutic Modifications: What Role does Postmarketing Surveillance Play?

The majority of postmarketing requirements mandated by the FDA are categorized into one of four areas: general reporting requirements, current good manufacturing practices, phase IV clinical study commitments, and adverse drug event (AE) reporting requirements. In regard to the latter, New Drug Application (NDA) holders and "nonapplicants" (any manufacturer, packer, or distributor included on the pharmaceutical product's label) have ADR reporting responsibilities. [4]As per the FDA's Code of Federal Regulations, NDA holders must "promptly review all adverse drug experience information obtained or otherwise received by the applicant from any source, foreign or domestic, including information derived from commercial marketing experience, postmarketing clinical investigations, postmarketing epidemiological/surveillance studies, reports in the scientific literature, and unpublished scientific papers."[5]

Uncovering Simvastatin-associated Myopathy

As a direct result of these obligations, postmarketing surveillance has been an integral tool in the discovery of dangerous interactions between various drugs. For example, a significant interaction between Zocor® (simvastatin) and Lopid® (gemfibrozil) was uncovered during a 2010 double-blind, randomized crossover study that was conducted as a result of several case reports detailing myopathy in patients concurrently using simvastatin and gemfibrozil.[6] This study showed that plasma concentrations of active simvastatin were increased by concomitant gemfibrozil treatment. Prior to this study, no information was available regarding if or how gemfibrozil affected the pharmacokinetics of simvastatin. The area under the curve (AUC) of simvastatin acid was 185 percent larger with the coadministration of gemfibrozil than with placebo ($P<0.001$). Researchers concluded that because gemfibrozil significantly increased the concentration of simvastatin acid, the pharmacokinetics of the drugs impact the increased risk of myopathy.

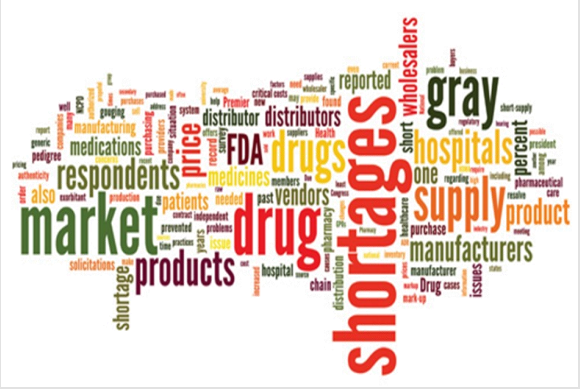
…the process for identifying serious drug interactions as well as altering dosage recommendations may demand copious amounts of time and additional studies.

On June 8, 2011, the FDA advised that simvastatin 80 mg should not be used as a starting dose of the medication.[7] This decision was based on a review of the seven-year Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH) trial. The results of SEARCH augmented the researchers' decision that simvastatin 80 mg was more likely to induce myopathy than simvastatin 20 mg. Additionally, FDA officials assessed postmarketing surveillance information contained in the agency's Adverse Event Reporting System (AERS) database which supported the conclusions of the SEARCH trial.

As evidenced by this example of postmarketing surveillance, the process for identifying serious drug interactions, as well as altering dosage recommendations, may demand copious amounts of time and additional studies. Case reports and subsequent trials which indicated that simvastatin bore an increased risk of myopathy when used in combination with certain drugs were published in the late 1990s into 2000. More than a decade later, in 2011, the FDA made a recommendation to limit the use of simvastatin 80 mg due to the significant risk of myopathy. The appropriate utilization of postmarketing surveillance has allowed health care professionals and patients to be cognizant of potentially detrimental interactions and side effects of simvastatin and many other medications when taken under specific therapeutic conditions.

Pharmacists' Unique Experience and Perspective

To gain insight into further practical application of ADR monitoring and assessment, we interviewed two pharmacists working in the postmarketing surveillance sector. The interviews were conducted independently of one another and later intercalated in the format below. For over 12 years, Kathleen Rand, PharmD, has worked in pharmacovigilance and safety surveillance and is currently product manager and senior scientist of global safety surveillance and analysis at Procter and Gamble. Christina Cognata Smith, PharmD, MBA, has held medical leadership positions at Johnson and Johnson and Bristol-Myers Squibb; she is currently executive director of medical affairs at Medicis Pharmaceutical Corporation.



Q: By whom are the majority of ADRs reported? After received, how is the supplied information processed?

KR: ADRs may be reported by anyone—health care professionals, physicians, nurses, the person who experienced the event, or his or her family or friend. Because the reporter may not necessarily have a medical background, it can be very challenging to obtain a medically meaningful report. To obtain additional information, a medical release may be requested to obtain medical records if necessary. The report is entered into our safety database after an initial screening. Depending on the seriousness of the report, it may be expedited to the FDA.

CCS: ADRs are reported by non-health care professionals and health care professionals. As an employee within the industry, when I become aware of an ADR for one of my company's drug products, I am required to gather the appropriate information and report the event to the Pharmacovigilance Department immediately. The case is reviewed by drug safety experts in the Pharmacovigilance Department and additional information is gathered, as necessary, for case and trend analysis. In my company, the Pharmacovigilance Department oversees all drug safety reports and is responsible for ensuring that the company reports adverse events to the FDA as required by federal regulations.

Q: How has postmarketing surveillance developed throughout your career?

KR: Postmarketing surveillance has evolved over the past 12 years with increasing use of technology in the reporting process; it is certainly more "real time." Additionally, surveillance is more rigorous and is focused on detecting and preventing safety issues. The postmarketing surveillance team is comprised of members with varied backgrounds: physicians, pharmacists, nurses, epidemiologists, statisticians, and data entry personnel.

CCS: The FDA is evolving how postmarketing surveillance reports are collected and used in an effort to better inform patients and health care providers about the safe and appropriate use of medicines. Because many spontaneous ADR reports do not result in a definitive conclusion about a drug's safety, postmarketing surveillance frequently serves as a foundation for further investigation via epidemiologic or clinical research to determine a drug's relationship to an ADR. Advances in information technology, such as the electronic medical record, are providing additional information and resources to support postmarketing surveillance programs and facilitating a shift to include more active surveillance methodologies.

Q: In what ways can a pharmacist practicing clinically contribute to accurate postmarketing data?

KR: The FDA's MedWatch reports are an important tool. A pharmacist can also call the manufacturer and provide as much information about the event as possible. Despite the time constraints, a pharmacist can provide high quality data.

CCS: Pharmacists are an important part of the postmarketing surveillance process due to their expertise in pharmacology and patient care role. Pharmacists in all health care settings not only play a key role in collecting and reporting complete and accurate information when presented with an ADR, but can also play a key role in patient counseling as it relates to the ADR.

Possibilities for Future Advancement: the Sentinel Initiative

With spontaneous and voluntary reporting as the current basis for documenting ADRs, under-reporting and a dearth of complete information denote challenges in developing an accurate assessment of such occurrences. To transition to the implementation of a signal-based active surveillance program, the purpose of which is to "ascertain completely the number of adverse events" associated with a medical product, the FDA has created the Sentinel Initiative.[8] Launched in 2008, the Sentinel Initiative is a system designed to build and implement a national electronic system for monitoring the safety of FDA-approved drugs and other medical products. In this system, electronic data regarding drug safety is collected from a number of participating data partners. These health information sources consist of academic medical centers, health care practices, health insurance companies, and regulatory industry, including Weill Cornell Medical College, Cincinnati Children's Hospital Medical Center, Humana, and Kaiser Permanente Center for Effectiveness and Safety Research. The collaboration features a distributed system in which data are not consolidated, but rather remain in their secure local environments. This system seeks to enhance the passive collection of voluntarily reported information by monitoring these databases in order to proactively discover potential adverse events.

…the Sentinel Initiative provides a representative picture of the range of patients using a drug, biologic, vaccine, or medical product while still allowing clinicians to focus on a particular data set of interest.

Through the Mini Sentinel pilot program, a systematic format is being tested for large-scale applications. The process starts with the FDA submitting a safety inquiry based on its analysis of the database to a Coordinating Center. The Coordinating Center will send the question to data partners, who will assess the safety signal in their own databases. Following this evaluation, the data partners' responses will consist of only summaries of results in an effort to protect patient privacy. The Coordinating Center then aggregates the submitted results and relays the information to the FDA, which then disseminates the findings to the health care community. In this way, the Sentinel Initiative provides a representative picture of the range of patients using a drug, biologic, vaccine, or medical product while still allowing clinicians to focus on a particular data set of interest. Since the data is collected directly, it can be evaluated as being as credible as possible in the practical setting. In an August 2011 report to Congress, the Department of Health and Human Services and the FDA announced that safety data from 25 million patients had been conglomerated, with that number expected to increase to 100 million by July 2012. Although encouraging progress has been achieved, technological, financial and security challenges, especially in regard to protection of patient privacy, mandate extensive collaboration and further study to determine the most effective and accurate novel postmarketing surveillance methodology. Following total implementation of the Sentinel Initiative, the field of pharmacovigilance will continue to enhance drug development and the methods by which adverse drug events are reported and evaluated.

Conclusion

Postmarketing surveillance plays an integral role in the evidence-based approach to drug development and therapy. With technological advancements that allow for greater facility of reporting, as well as analysis-driven databases, postmarketing surveillance is an important tool for meeting the ever increasing standards for optimal patient care. Pharmacists, as medication experts, will continue to foster innovative approaches to the challenges presented by pharmacovigilance.

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New Federal Ban on Bath Salts: Attempts to Contain a Growing Epidemic

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Bath salts are the dangerous new trend in designer drugs that have erupted in the United States within the last year.

Introduction

Within the last year, there has been an alarming increase in emergency department (ED) visits due to a new trend in illicit drug use. On January 22, 2011, ABC News reported that a Mississippi man was admitted to the emergency room after mutilating his face and stomach.[1] In September 2011, a woman from Minnesota sought emergency medical treatment for her 32-year-old son who claimed he was shooting towards the people who were "messing" with his car; when the woman went to investigate, she found only a dark empty street.[2] In Virginia, a paranoid, delusional man admitted himself to the hospital due to an elevated heart rate and tissue damage in his nose and mouth.[3] What did all of these ED admissions have in common? The aforementioned individuals all required hospital admission following the consumption of bath salts. Experts suggest that EDs are experiencing an unparalleled influx due to illicit use of bath salts.[4]

Although bath salts are a new fad in the United States, they have already wreaked havoc in other parts of the world.

Bath salts are the dangerous new trend in designer drugs that have erupted in the United States within the last year. Many are calling bath salts the "new" PCP (phencyclidine), a popular hallucinogen from the 1970s.[5] Law enforcement is taking action to control the situation through the development of new legislation and an emergency ban of bath salts and their lead compounds.

History

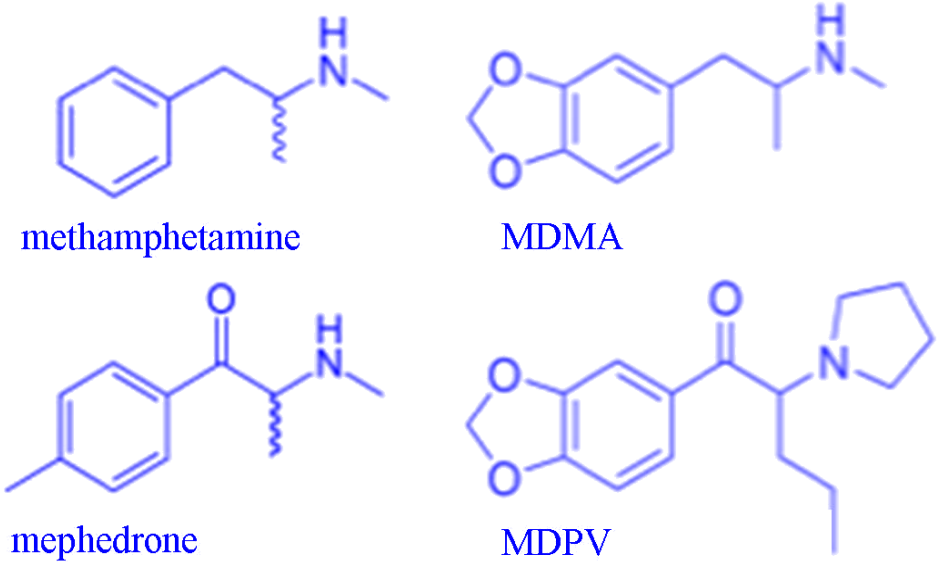
Although bath salts are a new fad in the United States, they have already wreaked havoc in other parts of the world. Bath salts, which have been available in Europe since 2007, were first sold primarily over the Internet and shipped from businesses based out of China and bordering countries in Southeast Asia to the United Kingdom (UK).[6] As their popularity grew, these substances became more readily available to the public through retail outlets, known as headshops, and street drug dealers. Many individuals within the population experienced similar effects as those which have been more recently witnessed within the United States. When the UK realized the harm these drugs were causing, legislation was enacted, beginning in April 2010, declaring the chemicals illegal substances. By that time, bath salts had spread to 28 European and neighboring countries, which were also then forced to pass legislation outlawing the substances.

The chemical compounds found in bath salts, some of which were once used as therapeutic agents, are now being used recreationally. Originally designed and used for the treatment of chronic fatigue in the 1960s, 3,4-methylenedioxypyrovalerone (MDPV) is one of the constituents commonly found in bath salts. Pharmaceutical manufacturer, Boehringer Ingelheim, filed a patent application for MDPV in 1969. Because of dependency issues, its use was largely discontinued within the medical community and seemed to be largely forgotten until it was seized by customs officials in Germany in 2007, reportedly shipped from China.[7] In 2008, the first seizure of the compound in the United States was reported. Since that time, bath salts have become an increasing problem in the United States. In 2010, the American Association of Poison Control Centers (AAPCC) reported 303 calls regarding bath salt exposures. Furthermore, as of July 31, 2011, the AAPCC has received 4,137 calls regarding bath salts toxicity.[8]

Compounds of Concern

The most commonly reported substances found in bath salts are 3,4-methylenedioxypyrovalerone (MDPV), mephedrone, and methylone. These individual chemicals or combinations thereof are the psychoactive components found within a variety of street products. Bath salts are a part of the synthetic cathionone drug class, which include chemicals structurally similar to natural cathinones extracted from the Eastern African *khat* plant.[9] These stimulants have produced many side effects similar to those caused by cocaine, amphetamine, and ecstasy.[7] The chemistry of these cathinone analogs bears a striking similarity to that of methamphetamine and ecstasy (MDMA), which can be seen in the chemical structures (Figure 1).[7]

Figure 1. Structural comparison of methamphetamine, MDMA, Mephedrone and MDPV[13]



There is limited information on the mechanism of action for these substances. Studies in mice have shown that these compounds may be potent inhibitors of the natural neurotransmitter membrane transporter complexes that are responsible for neuronal reuptake of dopamine and norepinephrine, causing increased levels of these neurohormones in the blood. There are also conflicting beliefs concerning the inhibition of serotonin transporters; some studies affirm that these transporters are indeed inhibited, while others do not.[6,10] In one study, the elimination of mephedrone was evaluated. After mice were orally administered a single 20 mg/kg dose of mephedrone, multiple mephedrone metabolites were measured in urine samples.[11] This study suggested that there are multiple pathways in which the drug is metabolized, and that mephedrone is excreted renally. As for the other common compounds, there is limited information available concerning their pharmacokinetic disposition and elimination. All in all, further studies need to be conducted in order to elucidate the pharmacokinetics and pharmacodynamics of these now illicit substances.

Methods of Abuse

There are a wide variety of ways in which bath salts can be abused. Bath salts can be administered orally, intravenously, intranasally, rectally or smoked.[12] These compounds are extremely potent; it only takes approximately 3 to 5 mg to start feeling the effects of the drugs, and doses from 5 to 20 mg are generally accepted to represent the doses used by individuals seeking a high from bath salts.[12] This average drug dosing varies depending on which compound is being used. For example, MDPV is a very lipophilic drug and only requires roughly 5 to 10 mg for the user to feel its effects, while mephedrone is not as lipophilic and therefore requires anywhere from 100 to 250 mg to induce a similar effect.[13] These variations in effective doses can cause a number of problems for abusers because of the potential for overdose. Some products sold commercially can contain as much as 500 mg of any one compound.[12] Due to the large amounts of powerfully psychoactive drugs in these products, it is no surprise that many people are being admitted to emergency departments nationwide with signs and symptoms of a toxic overdose.

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Product Distribution

Common street slang for bath salts include “Ivory Wave,” “Vanilla Sky,” “Purple Wave,” “Plant Food,” and “Meow Meow.” Bath salts have been purchased from local stores, over the Internet and from drug dealers. Currently, Internet sites from foreign countries are the main suppliers of these substances.[6] Due to the emergency ban on the products within the United States, drug dealers may soon become the more convenient mode of distribution for these products. Prior to the ban, commercially purchased bath salts were labeled “not for human consumption.”[14] Despite this warning, consumers would still ingest the products with the intention of experiencing the psychoactive effects of the drug. Inclusion of the warning enabled legal distribution of the products as “bath salts,” though they were never intentionally manufactured for such use. Furthermore, prices of the products are relatively inexpensive compared to other recreational drugs.[6,7] This made the substances far too affordable and available, thereby enabling consumers to repeatedly purchase the product and ingest larger quantities at one time.

Outcomes of Use

Bath salts have a wide variety of pharmacological effects once systemically administered (Table 1).[12,13] The “high” the individual experiences generally occurs quickly and lasts two to four hours.[13] Unfortunately there have been no clinical trials involving any of these compounds, so all information has come from user reports. Severe symptoms have been associated with higher doses and prolonged and/or extensive use.[6] There are many conflicting reports as to whether or not these compounds are addictive. Dargan et al. mention that mephedrone may not appear to cause physical dependence and/or withdraw upon discontinuence.[6] However, due to its similarity to amphetamines (Figure 1), it may be associated with psychological dependence.[6] Similarly, user reports suggest that there is some level of addiction associated with the use of bath salts. Because mephedrone was recently introduced to the United States, addiction potential cannot be determined until long term studies have been conducted.

Table 1: Bath Salt Side Effects [12,13]

Central Nervous System Effects	Cardiovascular Effects	Other
Seizures Panic attacks Euphoria Sexual Stimulation Heightened Mental Focus Increased Energy Anxiety Depression Paranoia Aggressive/Violent Behaviors Insomnia	Tachycardia Hypertension Arrhythmias Myocardial Infarction	Hyperthermia Anorexia Stroke Rhabdomyolysis Death

Treatment Options

A major concern in emergency departments nationwide is how best to treat patients who have overdosed on bath salts. These substances are so new to the United States that many physicians and health care providers do not know the most effective emergency measures to employ in treating patients who experience toxicity. Unfortunately, there are no antidotal medications that can be directly used to help these patients at this time, and symptomatic treatment is far from adequate in treating patients intoxicated with bath salts.[13] Intravenous benzodiazepine administration is recommended as first line treatment to control the patient's agitation, aggressive behavior, muscle tremors and spasms and panic attacks. In severe cases, restraints may be needed to prevent intoxicated patients from harming themselves or others.[12] Once the patients are calm, symptomatic treatment and supportive care such as fluid management, temperature control and, in severe cases, intubation may be necessary.[13] Seizures may also occur in these patients, and suggested treatments include benzodiazepines, barbiturates or propofol.[13] Further research is needed to reveal more effective treatment options for patients on bath salts.

Legislation

There have been dramatic increases in medical complications from the use of bath salts, which resulted in many individuals protesting for federal legislation to ban these compounds. Bath salts were originally sold in local stores and were legal because the labeling explicitly stated, "not for human consumption."[13] On September 7, 2011, the U.S. Drug Enforcement Administration (DEA) issued emergency C-I scheduling of mephedrone, MDPV and methylone. The U.S. government was able to enact this temporary ban under the Controlled Substances Act (CSA). All distribution, possession, and usage of these three compounds is therefore illegal for one year following the emergency scheduling while the United States Department of Health and Human Services (DHHS) and the FDA determine the eventual scheduling status of these compounds.[15] This is the first legislative action taken against bath salts at the federal level in the United States. Many municipalities and states have already taken independent legislative and regulatory actions in an attempt to control the illicit use of these compounds at a local level. Current legislation makes the possession, distribution and use of one or more of these bath salt compounds illegal in the following states: New Jersey, Alabama, Florida, Idaho, Iowa, Louisiana, Maine, Michigan, Mississippi, North Carolina, North Dakota, Pennsylvania, Ohio and Utah.[9] A total of 34 states currently have laws in place or are in the process of passing laws to make these compounds illegal.[15] During the temporary one-year ban, the FDA will study and evaluate these compounds and decide if a permanent controlled substance designation is appropriate.[15] Once the DEA and DHHS officials have considered additional research involving these compounds, further legislation may be warranted to protect the public.

On September 7, 2011, the United States Drug Enforcement Administration (DEA) issued emergency C-I scheduling of mephedrone, MDPV and methylone.

Conclusion

Illicit use of bath salts has become frighteningly prevalent within the United States. The popularity of these substances in foreign countries was noted some time before U.S. law enforcement agencies took action against these substances. Through the emergency room visits already seen throughout the United States, usage of bath salts has clearly resulted in substantial harmful effects. Currently, there is not a universally accepted emergency treatment protocol for these patients, but various reports have suggested that symptomatic management and supportive care are the best options to treat patients intoxicated with bath salts. In an attempt to contain the unfolding epidemic, the DEA has enacted an emergency ban on all bath salt products, pending further studies in order to determine what legal actions should be taken to help minimize public harm. Within these studies, investigational clinical trials, and treatment approaches, pharmacodynamics and pharmacokinetics will also need to be assessed and possible treatment options explored. Until that time, the federal ban and public warnings will hopefully help to curtail the threat of further morbidity and mortality caused by the illicit use of bath salts.

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continued from inside front cover

Short Pharmacy Facts

A Brief Look at Some Fun Facts from the Rich History of the Profession of Pharmacy

History of Vicks®

Every day, television and other media are flooded with information and advertisements for drugs. Recently one company has advertised with a different approach than most; sharing both its history as a company and the importance of a pharmacist to its development.

> Lunsford Richardson was a pharmacist in Greensboro, North Carolina, at the turn of the twentieth century. Richardson was born in 1855 and grew up in his father's drug store in Selma, North Carolina. Richardson graduated from Davidson College and decided to move the family business to Greensboro. Like many other druggists of the time, Richardson created medications for the treatment of minor ailments, such as the treatment of colds. Richardson's treatments became so popular that he decided to market his new discoveries under the name Vicks®, after his brother-in-law's name. Richardson has 21 patents under the name Vicks®, the most popular being the "Vicks® Croup and Pneumonia Salve." The salve, which is now known as Vicks® VapoRub® was used for the treatment of colds and included menthol as an ingredient. When the ointment is rubbed onto a person's chest, body heat vaporizes the menthol which releases soothing, medicated vapors for hours. Other Vicks® products at the time included Vicks® Liniment and Vicks® Chill Tonic. Due to the success of his Vicks® line of products, Richardson moved from retail to wholesale pharmaceuticals in 1898 and created the Lunsford Richardson Wholesale Drug Company. He marketed his 21 Vicks® products under the name of Vicks Family Remedies to the surrounding community, until 1905 when he founded a business dedicated specifically to these 21 products called the Vicks Family Remedies Company.

This company, originally started out of a small retail pharmacy, has been providing flu and cold relief for over 100 years. Richardson's salve, Vicks® VapoRub® is still a very popular product today and was the top-selling branded children's product in the cough/cold/flu/respiratory-treatment category based on category value sales as reported by the Nielsen Food, Drug, Mass Respiratory Market in 2010.[4,5]

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