

New Jersey Pharmacists Association | est. 1870

Update on Antibiotic Stewardship


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Bio

- Antimicrobial Stewardship Clinical Pharmacist at Monmouth Medical Center in Long Branch, NJ.
- Received Pharm.D. degree at Rutgers College of Pharmacy.
- Currently serves as an adjunct professor at Ernest Mario School of Pharmacy at Rutgers.

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Conflict of Interest

- I have no disclosures.

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Update on Antimicrobial Stewardship

Objectives: Pharmacists

- Describe the prevalence of antimicrobial resistance.
- Discuss the consequences of inappropriate antimicrobial prescribing.
- Describe the principles and objectives of an antimicrobial stewardship program.
- Discuss key strategies for developing an institutional program to enhance antimicrobial stewardship.
- Explain the pharmacist's role in antimicrobial stewardship programs.

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Update on Antimicrobial Stewardship

Objectives: Pharmacy Technicians

- Discuss the consequences of inappropriate antimicrobial prescribing.
- List the objectives of an antimicrobial stewardship program.
- Identify antimicrobial stewardship activities in an institutional setting.

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"The development of new antibiotics without having mechanisms to ensure their appropriate use is much like supplying your alcoholic patients with a finer brandy."

-Dennis Maki, 1998

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Introduction

- The management of healthcare-associated infections (HAI) has become an urgent healthcare priority.
- HAI account for an estimated 2 million infections, 90,000 deaths, and \$4.5 billion in excess healthcare costs annually.
- An increasing percentage of these infections are attributed to antimicrobial-resistant pathogens.

Am J Infect Control 2005;33:217-26
N Engl J Med 2010;362:1804-13

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Introduction

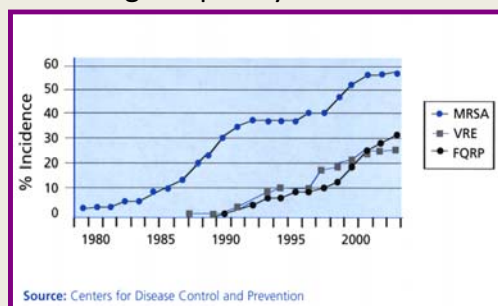
- Resistant gram-positive organisms continue to be important causes of HAI.
 - Methicillin-sensitive *S. aureus* (MRSA)
 - Vancomycin-resistant *Enterococcus* (VRE)
- The emergence of resistant gram-negative pathogens is perhaps of even greater concern.
 - Extended-spectrum β -lactamases (ESBL) producing pathogens
 - Multidrug-resistant *Acinetobacter* organisms
 - *Klebsiella pneumoniae* carbapenemases (KPC)

N Engl J Med 2010;362:1804-13

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Increasing Frequency of Resistance



MRSA = methicillin-resistant *Staphylococcus aureus*; VRE = Vancomycin-resistant enterococci
 FQRP = Fluoroquinolone-resistant *Pseudomonas aeruginosa*



The “Superbugs” Aren’t Waiting!



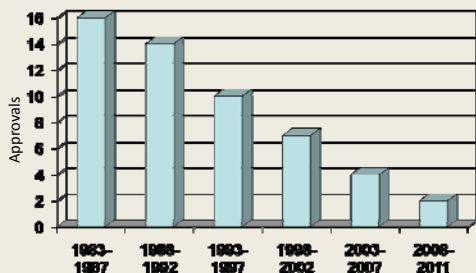
Infectious Diseases Society of America (IDSA) Press Release, 9/2004.

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- The pipeline of new antibiotics is drying up.
- Industry is losing interest in the antibiotic market because these drugs are simply not as profitable.
- From discovery to FDA approval can be 10 years or more.
- No new class of antibiotics targeting resistant Gram-negative organisms.

Declining New Antibacterial Drug Approvals, U.S.



Spellberg et al. *Clin Infect Dis* 2004.



History of Medicine

- 2000 BC: Here, eat this root.
- 1000 AD: That root is bad.
Here, say this prayer.
- 1850 AD: That prayer is superstition.
Here, drink this potion.
- 1940 AD: That potion is snake oil.
Here, take this antibiotic.
- 2000 AD: That antibiotic doesn't work anymore.
Here, eat this root.

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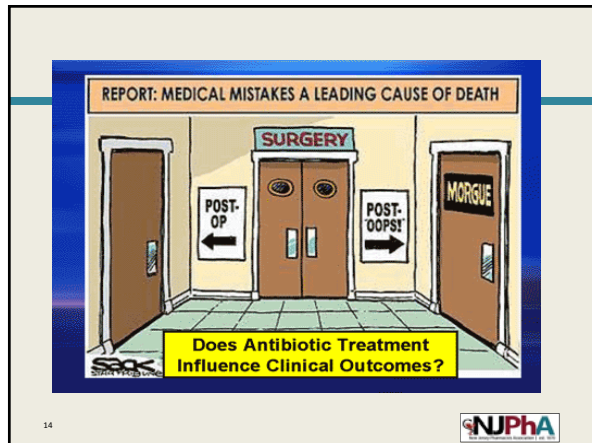
Factors Increasing Antimicrobial Resistance

- Increased severity of illness
- Severe immunosuppression
- Presence of invasive devices (for longer duration)
- Inadequate infection control practices
- Increased use of empiric, prophylactic antibiotics
- Higher antibiotic use per area, per unit of time

Patterson JE. *Chest* 2001;119:4265-4305

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Consequences of Inappropriate Use

- Inappropriate antibiotic use is associated with:
 - Increased morbidity and mortality
 - Increased length of stay (LOS)
 - Increased antimicrobial resistance
 - Increased adverse events
 - Increased cost

Hecker et al. *Arch Int Med* 2003;163:972-978.
Bartlett. *Clin Infect Dis* 2011;53 (S1): S4-S7.

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Inappropriate antibiotic use has been linked to which negative outcomes?

- a. Antimicrobial resistance
- b. Increased mortality
- c. Increased cost
- d. All of the above

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**ANTIMICROBIAL STEWARDSHIP
PROGRAM**

Information You Must Collect First...

- What are your institution's problem pathogens?
 - Speak to your hospital microbiologist and epidemiologist
- What do I do with the information?
 - Work proactively with the ID physicians and hospital administrative support to implement a plan that is best suitable for your institution
- What has been shown to work?
 - Antimicrobial stewardship programs

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Antimicrobial Stewardship

- Infectious Diseases Society of America (IDSA) Guidelines for Developing an Institutional Program (ASP) to Enhance Antimicrobial Stewardship
 - Based on a collaborative review and supported by
 - American Society of Health-System Pharmacists
 - Society of Infectious Diseases Pharmacists
 - American Academy of Pediatrics

Clin Infect Dis 2007;44:159-77.

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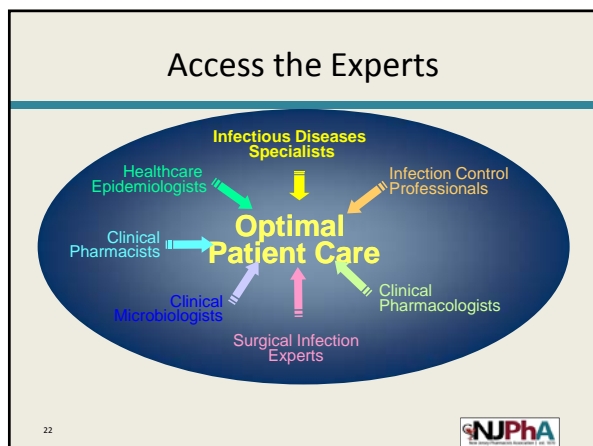
ASP

- Primary goal
 - To optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including
 - Emergence of resistance
 - Selection of pathogenic organisms, such as *C. difficile*
 - Toxicity
- A multidisciplinary, prospective, and interventional approach
- Types of stewardship programs
 - Concurrent review with feedback, or
 - Preauthorization requirements and formulary restriction

Clin Infect Dis 2007;44:159-77.

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Antimicrobial Stewardship: Key Elements

- Education
- Guidelines and clinical pathways (national and localized)
- Antimicrobial order forms, computerized physician order entry (CPOE) templates
- Streamlining or de-escalation of empirical antimicrobial therapy
 - Based on culture and sensitivity results
 - Elimination of redundant combination therapy

Clin Infect Dis 2007;44:159-77
Mayo Clin Proc;2011;86:1113-23

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Antimicrobial Stewardship: Key Elements

- Dose optimization
 - Based on individual patient characteristics
 - Causative organism
 - Site of infection
 - PK/PD characteristic of the drug
- Parenteral to oral conversion
 - Agents with enhanced oral bioavailability
 - i.e. Quinolones, linezolid, metronidazole, fluconazole
 - Facilitates early hospital discharge

Clin Infect Dis 2007;44:159-77
Mayo Clin Proc;2011;86:1113-23

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The Pharmacist's Role

- Promote multi-disciplinary collaboration
- Work with ID physicians and P&T to develop and implement localized antibiotic guidelines
- Recommend appropriate antimicrobial therapy and dose optimization
- Provide therapeutic drug monitoring
- De-escalation of antimicrobial therapy

Mayo Clin Proc;2011;86:1113-23

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Antimicrobial Utilization Strategies to Reduce Resistance

- “Fool them” strategy
 - Best exemplified by antimicrobial cycling or “crop rotation”
 - Based on the concept that alternating antibiotics periodically will help decrease selective pressure favoring the growth of resistant bacteria
 - No compelling data to support antimicrobial cycling as an effective strategy for preventing or reducing resistance

Clin Infect Dis 2008;46:491-6.

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Antimicrobial Utilization Strategies to Reduce Resistance

- “Blast them” strategy
 - Using more than 1 antimicrobial agent to prevent the emergence of resistance.
 - Derived from early observation that multiple antibiotics were effective at preventing the emergence of resistance in *M. tuberculosis*.
 - However, application of this strategy to most routine bacteria may be problematic. Evidence suggests that more antibiotics will likely lead to more resistance.
 - No convincing data has validated this strategy for HAI.

Clin Infect Dis 2008;46:491-6.

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Antimicrobial Utilization Strategies to Reduce Resistance

- “Stop irritating them” strategy
 - Reduce the use of antibiotics to the bare minimum necessary to safely treat patients with serious infections → reduce selective pressure → reduce the prevalence of resistance
 - Seems to be the most reasonable strategy to minimize resistance

Clin Infect Dis 2008;46:491-6.

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What is the goal of ASP?

- a. Optimize clinical outcomes while minimizing unintended consequences of antibiotic use
- b. Make pharmacists fight off Superbugs
- c. All of the above
- d. None of the above

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The Target Points

- Before initiating therapy
 - Treat only those patients who are truly infected
- During therapy
 - Avoiding the use of combination agents when a single antibiotic is sufficient
- At the completion of therapy
 - Treat only for as long as is required to cure the infection

Clin Infect Dis 2007;44:159-77.

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Optimizing Pharmacokinetic (PK) and Pharmacodynamic (PD) Principles

- Time-dependent agents
 - Time above the minimum inhibitory concentration (MIC) is the key predictor of outcome.
 - β -lactam antibiotics, vancomycin
- Concentration-dependent agents
 - Maximum serum concentration (C_{max})/MIC ratio is the key predictor of outcome.
 - Aminoglycosides, fluoroquinolones

Ann Pharmacother 2004;38:S14-S18.

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Maintaining the appropriateness of existing antibiotics

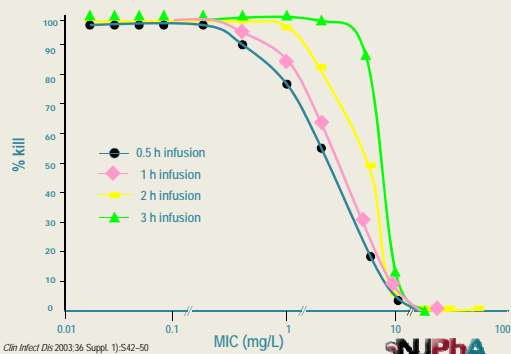
- Duration of therapy
 - a shorter course of treatment can be as clinically effective as a longer course, i.e. 8 days vs. 15 days for VAP
- Alternative dosage regimens
 - i.e. high-dose (2 g) infusion of meropenem over 3 hours to overcome pathogens with high MIC
 - high peak concentrations
 - continuous infusion

Chastre et al. JAMA 2003;290:2588–2598;
Drusano et al. ICAAC 2004;Abstract A-15:3

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Longer infusion of meropenem: *P.aeruginosa*



Drusano. Clin Infect Dis 2003;36 Suppl. 1):S42-50



Shorter Courses of Antibiotic Treatment

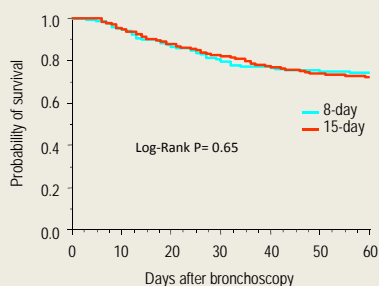
- Prolonged administration of antibiotics in ICU patients has been shown to be an important risk factor for emergence of colonization and infection with antibiotic-resistant bacteria.
- Several studies now show that 7-8 days of antibiotic treatment is acceptable for most patients with ventilator-associated pneumonia (VAP).

Crit Care Med 2001;29:1109-1115
Chest 2004;125:1791-1799

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Cumulative survival estimates according to duration of antimicrobial treatment



Chastre et al. *JAMA* 2003



Surgical Care Improvement Project (SCIP)

- Guidelines are intended to provide practitioners with standardized approach to rational, safe, and effective use of antimicrobial agents for the prevention of surgical-site infections
- Pharmacist's role
 - Decide what antimicrobials will be included for each surgery type
 - Work with anesthesia and surgery

AJHP 2013;70:195-283

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SCIP Process Measures

- Pre-operative dose-timing
 - 60 mins before surgical incision
- Selection and dosing
 - Recommendations for selection of antibiotics for specific surgical procedures
- Duration of prophylactic antibiotic therapy
 - Single dose or less than 24 hours

AJHP 2013;70:195-283

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Computer Surveillance and Decision Support

- CPOE and clinical decision support enhances antimicrobial decisions through the incorporation of:
 - Patient-specific microbiology data
 - Renal and hepatic function
 - Drug interactions
 - Antibiotic expenditures
- Computer-based surveillance facilitates tracking of:
 - Antimicrobial resistance patterns
 - Identification of HAI infections and adverse drug events

Clin Infect Dis 2007;44:159-77.

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Which strategies can be used to limit emergence of resistance?

- Develop localized antibiotic use guidelines
- Antibiotic de-escalation
- Provide education to key prescribers
- All of the above

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Monitoring of Process and Outcome Measures

- Process measure
 - Did the intervention result in the desired change in antimicrobial use?
- Outcome measures
 - Did the process implemented reduce or prevent resistance or other unintended consequences of antimicrobial use?

Clin Infect Dis 2007;44:159-77.

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Outcome Measures

- Antimicrobial use data can be standardized using
 - Defined daily dose (DDD)
 - Calculated as the total number of grams of an antibiotic used divided by the number of grams in an average adult dose
 - The World Health Organization (WHO) publishes DDD values for nearly all antibiotics
 - By using DDD, hospitals may compare their antibiotic use with that of similar hospitals

http://www.whocc.no/ddd/definition_and_general_considera/

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SUCCESSFUL ANTIMICROBIAL STEWARDSHIP PROGRAMS

Successful Stewardship Programs

- Prospective audit with intervention and feedback
 - Study conducted in a large teaching hospital
 - House staff were randomized to receive either no intervention or one-on-one education by a clinical specialist
 - Intervention prompted by an order for either levofloxacin or ceftazidime
 - Educational intervention emphasized microbiological data, local resistance patterns, and clinical literature

Arch Intern Med 2001;161:1897-1902.

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Successful Stewardship Programs

- Study results
 - 37% decrease in days of unnecessary antibiotics for the intervention services compared to controls ($p < 0.001$)
 - Reduction of new antibiotic initiation
 - Length of stay, ICU transfers, readmission rates, and in-hospital death rates similar in both groups

Arch Intern Med 2001;161:1897-1902.

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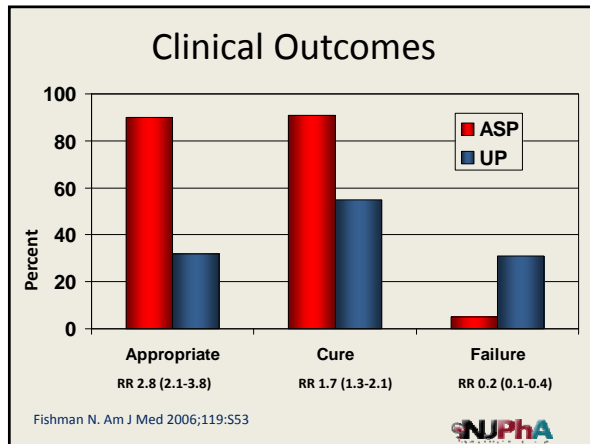
Successful Stewardship Programs

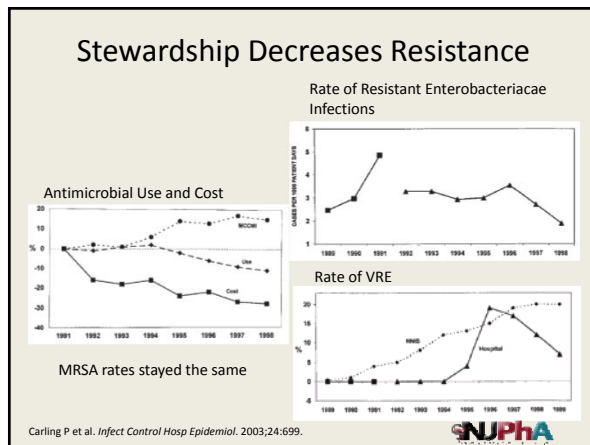
- Intervention
 - Prospective evaluation of the impact of a multidisciplinary antibiotic management program to minimize the inappropriate use of third-generation cephalosporins
- Results
 - 22% decrease in the use of parenteral broad-spectrum antibiotics ($p < 0.0001$)
 - Decrease in nosocomial infections caused by *C. difficile* ($p = 0.002$) and resistant *Enterobacteriaceae* ($p = 0.02$)

Infect Control Hosp Epidemiol 2003;24:699-706.

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Successful Stewardship Programs

- ASP conducted at a large teaching institution for 7 years
- ASP goal
 - Reduce 10-20% of antibiotic costs (savings of \$600,000 to \$1,200,000 over a 3-year period)
- Results
 - 45% decrease in antibiotic utilization costs
 - Reduction of about \$3 million in the first 3 years, primarily due to a decrease in antifungal therapy use

Standiford. Infect Control Hosp Epidemiol 2012;33:338-345

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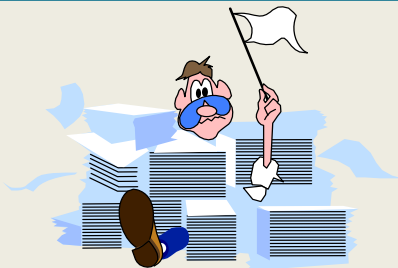
A Time of Challenge and Opportunity

- The high prevalence of antimicrobial resistance is associated with increased morbidity and mortality.
- However, this challenge creates tremendous opportunities for infectious diseases specialists and infection control experts.
- Successful strategies include proactive interventions, such as antibiotic stewardship programs, and optimal infection control measures.

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Questions?



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NJPHA OVERVIEW

NJPhA Mission

To advance the profession of pharmacy enabling our members to provide optimal care to those they serve.

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NJPhA Membership

Becoming an Active Member

- Founded in 1870 as a not-for-profit corporation to represent pharmacists in the State of New Jersey who practice in all areas of pharmacy.
- Get involved in ways that meet your specific goals:
 - Write for our **peer reviewed journal**
 - **Submit a poster** to our annual convention
 - Join one of our **Academies** (Consultant, Compounding, Disaster Management)
- Learn skills outside of the office that hasten your development:
 - Network and Make Connections
 - Be Recognized
 - Advance Your Expertise
 - Champion the Profession

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NJPhA Legislative Representation

- Organizational leadership and support has led to the development of many **legislative reforms** on a **state and federal** level. Some include:
 - 1965: NJPhA proposed limited quantity of children's aspirin
 - Saved lives, national recognition, President Johnson signed law, FDA action
 - 1969: First public anti-smoking campaign
 - 1970: First mandatory patient profile
 - 1975: Concern for senior citizens health prompted development of PAAD law in NJ
 - First in US, has helped millions, now has 200,000 beneficiaries
 - 1994: Pharmacists may be reimbursed as Diabetes Educators by NJ Reg. Insurance Plans
 - 1999: Insurance audits must be performed at a mutually agreeable time
 - 2000: Mandatory Mail Order is not permitted for NJ State Regulated Plans.
 - 2005: Modernization of the Practice of Pharmacy
 - 2009: Pharmacists immunize patients in New Jersey; 2013: bill was amended to lower the age for flu vaccine administration
 - 2013: Collaborative Practice between Physicians and Pharmacists
 - 2014: Separation between consultant and provider extended

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NJPhA Federal Advocacy

Strength in Numbers!

- NJPhA is an active member of APhA – American Pharmacists Association, NASPA – National Alliance of State Pharmacy Associations, NCPA - National Community Pharmacists Association and others. Our state leadership works in concert with these groups to promote grassroots federal advocacy on key issues
- NJPhA is supporting APhA's initiative to advocate for national **healthcare provider status** for pharmacists. This will allow pharmaCISTS, not just pharmaCIES, to bill and receive reimbursement for patient care related services

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NJPhA Regulation Representation

Influence Laws and Regulation to Impact Change

- NJ Board of Pharmacy
- NJ Board of Medical Examiners
- NJ Drug Utilization Review Board
- NJ Health Information Technology Committee
- National Organizations
 - NABP
 - APhA
 - CMS

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In Summary...

We are committed to...

- Presenting a unified voice for NJ pharmacists and pharmacy technicians.
- Providing a forum for exchange of innovative ideas to establish progressive health systems.
- Promoting the optimization of drug therapy for the patients our members serve.
- Anticipating future information and professional development needs.
- Strengthening relationships between practitioners, student pharmacist, pharmacy technicians, and other health professionals.

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Becoming an Active Member

Sign up at today's event – see the registration desk for details

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- The online evaluation code will be sent from the office tomorrow morning:
- This code will be active for one week from the date of the lecture.
 - Deadline: **November 12, 2014**
- **NOTE: your credits will be posted to CPE monitor within 45 days of program date**

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- It is critical that you have signed in to this live presentation (either in person or via the Join Me webinar) and that you have provided your correct NABP number; both your name and NABP number must be legible
- You are accountable to check your CE Monitor account for the credit for all CE programs including this one
- Everyone's credits are uploaded to the CE Monitor when all individuals have completed the post-lecture evaluation
- When a failure occurs during the upload to CE Monitor, the failure will not identify the individual with the issue; therefore, there is no way for the office to contact the individual with the error
- The credit for this program will appear at a maximum of 60 days after the program; please do not contact the office prior to this for "missing" credit

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