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Review Article

GET SMART IN HEALTHCARE TO PRESERVE THE POWER OF ANTIMICROBIALS : ANTIMICROBIAL STEWARDSHIP

***Rajeshwar Reddy Kasarla[1], Sidhya Choudhary[2], Aishwarya Verma[3], Ritesh Sharma[4], Laxmi Pathak[5]**

[1]Department of Microbiology, Universal College of Medical Sciences, Bhairahawa, Nepal, [2]Senior Resident, SMS Medical College, Jaipur, Rajasthan, India, [3]Intern Doctor, Universal College of Medical Sciences, Bhairahawa, Nepal, [4]MBBS Final Years Universal College of Medical, Sciences, Bhairawa, Nepal, [5]Department of Anesthesiology & Critical Care Medicine, Universal College of Medical Sciences, Bhairahawa, Nepal

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ABSTRACT

Antimicrobial resistance is one of the alarming health hazard to mankind. Unnecessary antibiotic usage leads to drug resistance, predisposes to opportunistic infections in immunodeficient and unnecessary economical loss to patient. This manuscript compiles & describes how crucial is Antimicrobial stewardship programs recommendations, strategies and implementation. Awareness and execution of institutional stewardship programs leads to better patient management, halt development of drug resistance and spread of resistant strains. This review is undertaken with an aim to discuss the development of an effective antimicrobial stewardship program and the key components and operating principles, and execution of these programs at healthcare facilities.

KEYWORDS: Antibiotic stewardship, Drug resistance, Hospital antibiogram.

Corresponding Author
Rajeshwar Reddy Kasarla
Email: reddysir4861@gmail.com
ORCID: https://orcid,org/0000-0001-5422-2328

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INTRODUCTION

Ever since the advent of penicillin, antimicrobial agents have played a pivotal role in modern medical practices, substantially enhancing worldwide well-being. However, decades of excessive, improper, and misguided utilization of antimicrobials, both within medical facilities and the general population have led to an alarming escalation in the occurrence of resistant bacteria.[1] This misuse occurs at an increasing rate, disregarding appropriate timing and necessity in both human and animal contexts. The indiscriminate application of antibiotics in veterinary care and animal feed has further contributed to the emergence of drug-resistant strains, a concern exacerbated by the potential transfer of these strains to human populations.[2] The inclusion of antibiotics in animal feed can lead to accelerated growth in animals; however, this practice is linked to an elevated prevalence of drug-resistant strains among farm workers. Because of overuse, misuse and abuse of antimicrobials indiscriminately led to selective pressure on bacterial strains, so that bacteria have developed new genes e.g. methicillin resistant staphylococci, vancomycin resistant enterococci; or there is a movement of old genes into new bacterial hosts e.g. penicillin resistant gonococci; or mutations of old genes resulting in more potent resistance e.g. beta-lactamase mediated resistance to advanced cephalosporins in *E.coli*, *Klebsiella*, and other Gram negative bacilli. Some strains of *Pseudomonas aeruginosa* and carbapenem-resistant enterobacteriaceae are resistant to almost all antibiotics. Thus, infectious organisms adapt to the antimicrobials designed to kill them, making the drugs ineffective and antimicrobial therapy extremely challenging.[3-5]
Most of the causative organisms of nosocomial infections have developed antimicrobial resistance. ICUs have become epicenters of antimicrobial resistance in hospitalized patients due to heavy use of antibiotics, presence of invasive devices, prolonged length of hospital stay, immune suppression, malnutrition, and cross-infection etc. The result is that today most antibiotics have lost their effectiveness against common bacterial infections. The emergence of antimicrobial resistance as a silent pandemic with a major public health concern combined with the downturn in the development of new antimicrobial agents in the pharmaceutical industry poses unanticipated challenges in the effective management of infection. Therefore, existing antimicrobials must be used more responsibly and managed carefully to extend their life span while being made available to the patients who truly need them. This issue serves as the fundamental basis for the concept of antimicrobial stewardship.[6-8]
The 30% rule described way back in 2007 portrayed that 30% inpatients at any given time to receive antibiotics, around 30% of antibiotics are prescribed incorrectly in community settings, up to 30% of surgical prophylaxis instances are deemed inappropriate, and approximately 30% of hospital pharmacy expenses can be attributed to antimicrobial usage. An antimicrobial stewardship program has the potential to result in a reduction of 10-30% in antimicrobial expenses.[9,10]

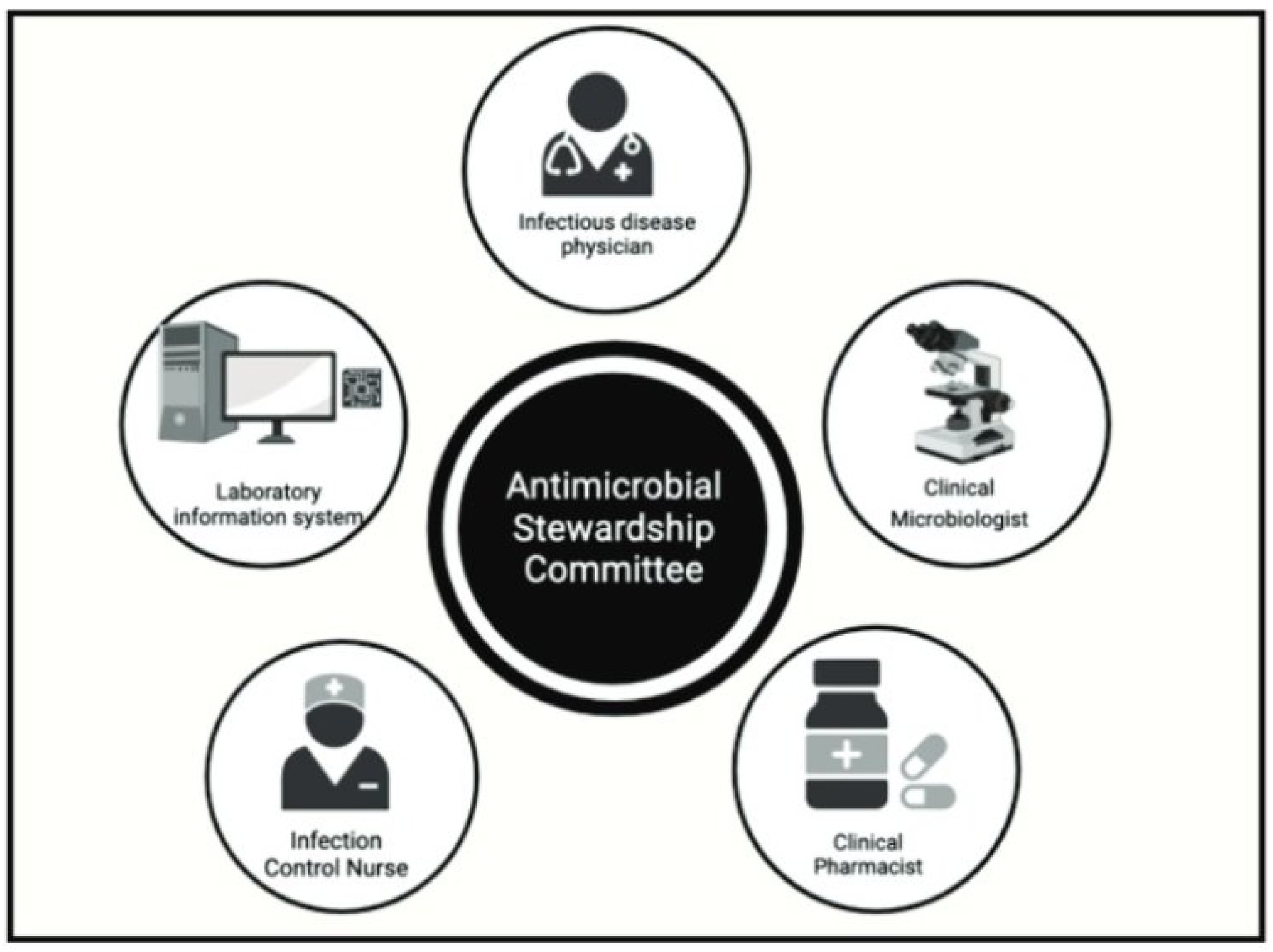
ANTIMICROBIAL STEWARDSHIP PROGRAM (AMSP)

Antimicrobial stewardship is characterized as the optimal choice, dosing, and duration of antimicrobial therapy that achieves the most favorable clinical results for infection treatment or prevention, while causing minimal harm to the patient and minimizing the potential for future resistance development.[11-14]
The objective of an antimicrobial stewardship program (AMSP) is to collaborate with healthcare professionals in order to ensure that each patient is administered the most suitable antimicrobial agent, adhering to accurate dosing and duration. Evidence-based guidelines should be used for diagnosing infections and initiating antibiotics. The **5 "D"s** of optimal antimicrobial therapy: right **D**rug (e.g. most narrow spectrum), right **D**ose (e.g. adjusted to patient renal function), right **D**rug-route, for the right **D**uration (e.g. shortest to successfully treat infection) timely **D**e-escalation to pathogen-directed therapy (e.g. Narrow spectrum based on culture and sensitivity test results).[13,14]
The primary goal is to optimize safe and appropriate use of antimicrobials to improve clinical outcomes and minimize adverse effects of antimicrobials, such as toxicity, selection of

pathogenic bacteria (e.g. *Clostridium difficile*), and emerging resistance. The secondary goal is to reduce health care costs without compromising quality of patient care, and to reduce the incidence of antimicrobial induced collateral damage**.** The ultimate goal of antimicrobial stewardship is to improve patient care and health care outcomes.[15,16] Antimicrobial stewardship programs (AMSP) also require ongoing education, training, encouragement, and evaluation of healthcare practitioners. Establishing effective antimicrobial stewardship involves inducing behavioral changes in individuals. Therefore, it is essential to provide sufficient motivational education to facilitate such transformation.[17-19]

It is necessary to establish a diverse **antimicrobial stewardship (AMS) committee** that is accountable for formulating, executing, and overseeing the adherence to the hospital's antimicrobial policy. AMS committee is led by a physician leader and other members include clinical microbiologist, clinical pharmacist, and nursing staff (Fig 1). Effective cooperation among the antimicrobial stewardship team, hospital infection control, pharmacy, and therapeutics committees is crucial.[20-23]

Figure 1: The ideal antimicrobial stewardship committee[23]



Each healthcare facility should develop its unique **hospital antimicrobial policy**, encompassing specific guidelines for selecting antimicrobials and determining their appropriate dosages based on different systems or syndromes. This policy creation process involves the antimicrobial stewardship (AMS) committee engaging in discussions with all clinicians, aiming to reach a collective agreement. It's imperative that this policy aligns with established national and international antimicrobial guidelines, as well as the local antibiogram pattern that reflects the resistance profile of local pathogens. **Hospital antibiogram** is an overall profile of antimicrobial susceptibility testing results of a specific microorganism to a battery of antimicrobial agents. The antibiogram serves as a valuable tool for clinicians when they need to make informed choices regarding the initial empirical antimicrobial treatment while waiting for culture and susceptibility results. Moreover, it proves to be beneficial for identifying and observing shifts in the prevalence of antimicrobial resistance within the hospital environment. Beyond this, the antibiogram facilitates the comparison of susceptibility rates across different medical institutions and assists in monitoring the evolution of resistance patterns. This broader application contributes significantly to the national antimicrobial resistance (AMR) surveillance database, enhancing our collective understanding of resistance trends on a larger scale.[24-26]

When **implementing an antimicrobial stewardship program**, there are two primary strategic approaches available: a) **front-end strategies**, specifically formulary restriction, and back-end strategies, involving **prospective audit and feedback**. The front-end strategy entails categorizing antimicrobial agents into different levels of restriction—restricted, semi-restricted, and non-restricted—with specific indications for their usage. This categorization is combined with an approval system overseen by the Antimicrobial Stewardship (AMS) committee. Initially, this approach appears appealing due to its potential for immediate impact and alignment with the ideal vision of achieving effective antimicrobial stewardship. However, it's important to acknowledge that the practical implementation of formulary restrictions presents significant challenges and complexities. On the other hand, **b) back-end strategies** involve the process of prospective audit and feedback. Despite being more difficult to execute, this strategy holds a reputation for being the most effective method for implementing Antimicrobial Stewardship Programs (AMSP). Prospective audit of antimicrobial use involves systematically reviewing prescriptions in real-time, followed by direct interaction and feedback to the prescriber. This approach, while demanding in terms of resources and efforts, has been proven to yield tangible results, particularly in terms of reducing inappropriate utilization of antimicrobials. This strategy's inherent benefit lies in its ability to provide personalized guidance to clinicians, ultimately contributing to improved antimicrobial prescribing practices.[27-31]

CORE ELEMENTS OF ANTIMICROBIAL STEWARDSHIP PROGRAM

CDC proposed and advised the implementation of the seven core elements of hospital antibiotic stewardship program to measure and improve how antibiotics are prescribed by clinicians and used by patients. Improving antibiotic use will ensure these life-saving medications are effective and available when we need them (Table 1).[32,33]

Table 1: Core elements of hospital antimicrobial stewardship program[32,33]

Committed Leadership	Allocate the required personnel, financial, and technological resources.
Accountability	Designate a leader or co-leaders, potentially a physician and pharmacist, to oversee program management and outcomes.
Pharmacy Expertise (previously "Drug Expertise")	Designate a pharmacist, preferably in a co-leadership role within the stewardship program, to play a key role in spearheading the efforts to enhance the utilization of antibiotics.
Action	Execute strategies, like prospective audit and feedback or preauthorization, to enhance the utilization of antibiotics.
Tracking	Supervise antibiotic prescription practices, evaluate the effects of interventions, and track significant outcomes such as C. difficile infections and patterns of resistance.
Reporting	Consistently provide updates to clinicians, staff nurses, pharmacists, and hospital leadership regarding details on antibiotic utilization and resistance.
Education	Offer educational sessions to inform clinicians, pharmacists, other healthcare workers, and patients about the potential side effects of antibiotics, the emergence of antibiotic resistance, and the best practices for prescription.

MONITORING THE COMPLIANCE TO ANTIMICROBIAL STEWARDSHIP PROGRAM

The assessment of compliance with Antimicrobial Stewardship Programs (AMSP) involves the examination of both process and outcome indicators, thereby providing a comprehensive evaluation of program effectiveness. The **process indicator**, often termed the policy adherence indicator, hinges on the application of prospective audit and feedback—a core element elucidated within the backward strategy. This entails conducting an antimicrobial stewardship audit, encompassing assessment of both prescription and administrative compliance.[27]

Antimicrobial usage outcome indicators are gauged through established indicators such as the **Defined daily dosage (DDD)** and **Days of therapy (DOT)**. DDD serves as a measure of the average daily maintenance dose for a drug's principal adult indication. Meanwhile, DOT reflects the cumulative number of days a patient is administered at least one dose of a specific antimicrobial drug. This metric is especially advantageous in estimating drug consumption within specific populations like patients with renal impairment and pediatric patients, making it preferable over DDDs.[34,35]

The evaluation of alterations in antimicrobial resistance patterns involves the conduct of **periodic antimicrobial resistance surveillance**—an outcome indicator dedicated to monitoring changes in resistance profiles. **Clinical** outcomes, serving as crucial indicators of program success, encompass metrics such as morbidity, represented by factors like length of hospital stay, and mortality, measured through infection-related deaths. Additionally, the **economic** implications of AMSP are assessed through financial outcome indicators, encompassing metrics like antimicrobial cost per patient per day, per year, or per admission.[27,34,35] This holistic array of indicators underscores the multifaceted impact and effectiveness of AMSP across clinical, epidemiological, and financial domains.[34,35]

RATIONAL USE OF ANTIMICROBIAL AGENTS

Antimicrobials must be administered at the correct dose (as per the age/body weight), and frequency and duration of therapy. The clinicians should prescribe antibiotics only when it is indicated (Figure 2). There are various conditions where antibiotics are not required.[36-38] e.g.

- In diarrhea, oral rehydration solution is the mainstay of treatment, not antibiotics. More so, the most common cause of diarrhea is of viral etiology.

- Upper respiratory tract infections such as common cold and sore throat, where the primary cause is viral infections, except when bacterial infections such as streptococcal sore throat or diphtheria are strongly suspected
- When an alternative diagnosis is suspected/confirmed such as dengue, chikungunya, malaria etc.

The judicious utilization of antimicrobials is predicated on several crucial principles that ensure their efficacy and mitigate the development of resistance. The appropriate administration of antimicrobials necessitates adherence to correct dosing parameters that align with factors like age and body weight, as well as the prescribed frequency and duration of therapy. It is imperative to recognize that there are numerous scenarios where the employment of antibiotics is unwarranted.[36-38] Few examples:

a) For instance, in cases of diarrhea, the cornerstone of treatment is oral rehydration solution, obviating the need for antibiotics. This is particularly pertinent given that viral etiologies constitute the predominant cause of diarrhea.

b) Furthermore, in upper respiratory tract infections such as the common cold and sore throat, the primary causative agents are viral pathogens. Antibiotics are only justifiable when bacterial infections like streptococcal sore throat or diphtheria are robustly suspected.

c) Another imperative consideration is refraining from antibiotic prescription when an alternative diagnosis is either suspected or confirmed—typified by conditions such as dengue, chikungunya, and malaria.

These delineations highlight the importance of clinicians' discretion in prescribing antibiotics, grounded in the principles of evidence-based medicine. Such clinical discretion not only ensures optimal patient care but also safeguards the efficacy of antibiotics and contributes to the broader effort in mitigating antimicrobial resistance.

Based on antimicrobial susceptibility (AST) report, the **empirical therapy** should be modified subsequently towards **targeted or pathogen-directed therapy.** The modifications may be of two types: **Escalation approach** is chosen if local antimicrobial resistance pattern is unlikely and/or the patient is clinically stable. The empirical therapy is started with a narrow spectrum antibiotics (e.g. ceftriaxone for *E.coli*). If antimicrobial susceptibility test report shows resistance, then can be escalated to a higher rank antibiotic subsequently (e.g. meropenem for *E.coli*). **De-escalation approach** is chosen if local antimicrobial resistance pattern is expected to be high and/or the patient is critically ill. Empirical therapy is started with broad spectrum antibiotics (e.g. meropenem for *E.coli*). If antimicrobial susceptibility test report shows susceptible, can be de-escalated to a narrow spectrum antibiotic subsequently (e.g. ceftriaxone for *E.coli*).[38,39]

The modification of **empirical therapy** based on the results of antimicrobial susceptibility testing (AST) is a pivotal step in achieving **targeted or pathogen-directed therapy**. This adaptation process comprises two distinct approaches, each chosen based on specific clinical and resistance considerations. The first strategy is the **escalation approach**, which is employed when the local antimicrobial resistance pattern is anticipated to be low, or when the patient's clinical condition remains stable. In such cases, the initial empirical therapy commences with a narrow-spectrum antibiotic, such as ceftriaxone for *E. coli*. However, if the antimicrobial susceptibility test report reveals resistance, the therapy can subsequently be escalated to a higher-ranked antibiotic, like meropenem for *E. coli.*[38,39]

Alternatively, the **de-escalation approach** is opted for when a high local antimicrobial resistance pattern is expected, or when the patient's clinical status is critically compromised. Here, the empirical therapy begins with a broader spectrum antibiotic, such as meropenem for *E. coli*. In the event that the antimicrobial susceptibility test report indicates susceptibility, the therapy can be de-escalated to a narrower spectrum antibiotic, such as ceftriaxone for *E. coli*.[38,39]

Prescribing antimicrobials based on their efficacy at the site of infection is a pivotal tenet of responsible and targeted therapy. In this regard, a comprehensive assessment of antimicrobial activity at specific infection sites becomes paramount. The careful selection of antimicrobials hinges on their demonstrated activity within the affected region. Consequently, there are certain antimicrobials that, due to their specific characteristics, should be excluded from treatment considerations.[38,40]

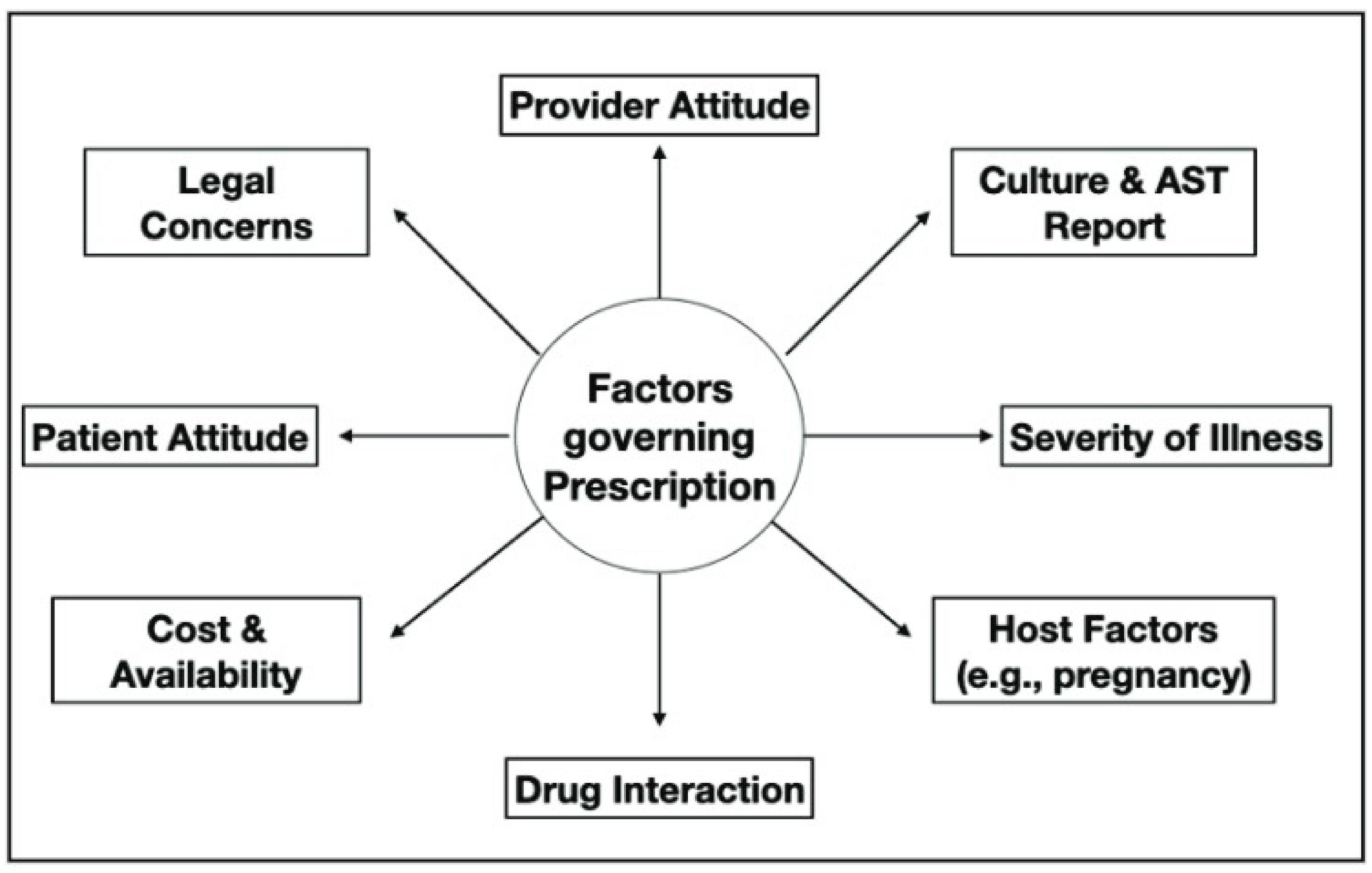
a) One such example pertains to daptomycin, which, due to its susceptibility to inactivation by pulmonary surfactants, lacks activity at respiratory sites, such as the lungs. Therefore, its utility for treating infections within these regions is limited.

b) Moreover, oral antibiotics, along with first and second generation cephalosporins, tetracyclines, macrolides, quinolones, and clindamycin, exhibit inadequate activity within the cerebrospinal fluid (CSF). Consequently, they should be avoided for infections that involve the CSF, given their suboptimal efficacy in this context.

c) A further consideration arises in the context of urinary tract infections, where the efficacy of certain antibiotics becomes questionable. Specifically, antibiotics like chloramphenicol, macrolides, and clindamycin may not achieve sufficient concentrations within the urinary tract, thereby rendering them less effective for treatment purposes.

These nuanced considerations underscore the importance of tailoring antimicrobial therapy to align with the specific site of infection. Moreover, the prescription of antibiotics should be meticulously governed by their clinical indications and various other factors, as illustrated in Figure 2.[41] By adhering to this principle, healthcare practitioners can optimize treatment outcomes, mitigate the risk of resistance, and uphold the principles of evidence-based medicine.

Figure 2: The art of prescribing antimicrobials[41]



Optimization of antimicrobial dosing based on individual patient characteristics, causative organism, site of infection, and pharmacokinetic and pharmacodynamic characteristics of the drug is an important part of antimicrobial stewardship. The assessment of antimicrobial susceptibility encompasses two primary methodologies: disk diffusion and MIC-based (Minimum Inhibitory Concentration) methods. Of these, the MIC-based approach is recognized for its heightened precision and dependability. This method provides a comprehensive understanding of the minimum concentration of an antimicrobial required to inhibit the growth of a specific microorganism.[29]

In select scenarios, the choice of antibiotic treatment is guided by the MIC values. A prominent instance is the case of vancomycin administration for *Staphylococcus aureus* infections. In such cases, it is imperative to exercise caution and refrain from utilizing vancomycin when the MIC surpasses 1 μg/mL. This parameter serves as a critical threshold that informs clinicians about the potential ineffectiveness of vancomycin against the specific *Staphylococcus aureus* strain. This evidence-based approach ensures that antimicrobial therapies are appropriately tailored to maximize their therapeutic impact and minimize the risk of treatment failure.[34,38]

The effectiveness of treatment is not solely determined by the in vitro susceptibility result (MIC), but is also contingent upon the in vivo activity. This in vivo performance, in turn, hinges on the intricate interplay of pharmacokinetic and pharmacodynamic (PK/PD) parameters specific to the antimicrobial agent. Consequently, the need for therapeutic drug monitoring becomes evident as it provides insight into how the drug behaves within the living organism. This monitoring process holds particular significance for antibiotics like vancomycin, amikacin, and colistin, where understanding the dynamic interaction between drug, organism, and host is essential for optimizing treatment outcomes.[39,40]

A structured strategy for transitioning from parenteral to oral administration of antimicrobials, especially those with high bioavailability, can result in shortened hospital stays and reduced healthcare expenses, provided the patient's condition permits such a transition. It is essential to discontinue the antimicrobial treatment at the appropriate juncture, a decision that can be guided by clinical improvement, negative culture results, or the utilization of biomarkers like procalcitonin (PCT) or C-reactive protein (CRP) to predict bacterial infections. The clinical microbiology laboratory assumes a pivotal role within the antimicrobial stewardship program, contributing significantly to its effective implementation.[42,43]

The primary and most influential risk factor for contracting a Clostridium difficile infection is exposure to antibiotics. It is imperative to identify antibiotics that are particularly associated with a increased risk of *Clostridium difficile* infection, such as cephalosporins, clindamycin, ampicillin, fluoroquinolones, and amoxicillin. Efforts should be made to curtail the use of these antibiotics, and close monitoring of patients for the emergence of gastrointestinal symptoms is essential.[44,45]

CONCLUSION

The Antimicrobial Stewardship Program (AMSP) is structured with the aim of advancing, enhancing, overseeing, and assessing the prudent utilization of antimicrobial agents. This overarching objective is geared towards safeguarding their efficacy for the future while concurrently upholding and safeguarding public health interests. The implementation of an antimicrobial stewardship program within a hospital setting will contribute to the assurance that hospitalized patients are administered the correct antibiotic, in the appropriate dosage, at the optimal timing, and for the correct duration of treatment.. As a result, there is reduced mortality, reduced overall antimicrobial resistance, and reduced risk of *Clostridium difficile* infections, shorter hospital stays, and cost savings. Therefore, antimicrobial stewardship must be an integral component of healthcare system.

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REFERENCES

1. Awad Al-Omari, Abbas Al Mutair, Saad Alhumaid. et al. Antimicrobial resistance and infection control. 2020; 9:95.
2. Lloyd DH, Page SW. Antimicrobial Stewardship in Veterinary Medicine. Microbiol Spectr. 2018 May;6(3).
3. Prestinaci F, Pezzotti P, Pantosti A: Antimicrobial resistance: a global multifaceted phenomenon. Pathog Glob Health. 2015;109(7):309-18.
4. Tanvir Mahtab Uddina, Arka Jyoti Chakrabortya, Ameer Khusro, BM Redwan Matin Zidana, Saikat Mitraa, Talha Bin Emran, et al. Antibiotic resistance in microbes: History, mechanisms, therapeutic strategies and future prospects. Journal of Infection and Public Health. 2021;14:1750-1766.
5. Aslam B, Khurshid M, Arshad MI, Muzammil S, Rasool M, et al. Antibiotic Resistance: One Health One World Outlook. Front. Cell. Infect. Microbiol. 2021;11:771510.
6. Rice LB: Antimicrobial stewardship and antimicrobial resistance. Med Clin North Am. 2018, 102:805-818.
7. Md Anwarul Azim Majumder, Sayeeda Rahman, Damian Cohall, Ambadasu Bharatha, Keerti Singh, Mainul Haque, Marquita Gittens-St Hilaire. Antimicrobial Stewardship: Fighting Antimicrobial Resistance and Protecting Global Public Health. Infection and Drug Resistance. 2020;13:4713–4738.
8. Bertollo LG, Lutkemeyer DS, Levin AS. Are antimicrobial stewardship programs effective strategies for preventing antibiotic resistance? A systematic review. Am J Infect Control. 2018;46 (7):824–836.
9. Dyar OJ, Huttner B, Schouten J, Pulcini C. What is antimicrobial stewardship? Clin Microbiol Infect. 2017;23(11):793–8.
10. Sahra S, Jahangir A, De Chavez V. Antimicrobial Stewardship: A Review for Internal Medicine Physicians. Cureus. 2021;13(4): e14385.
11. Anderson DJ, Watson S, Moehring RW, Komarow L, Finnemeyer M, Arias RM, et al. Feasibility of Core Antimicrobial Stewardship Interventions in Community Hospitals. JAMA Network Open. 2019;2(8):e199369-e.
12. Buckel WR, Veillette JJ, Vento TJ, Stenehjem E. Antimicrobial stewardship in community hospitals. Med Clin North Am. 2018;102(5):913–928.
13. Hegewisch-Taylor J, Dreser-Mansilla A, Romero-Mónico J, Levy-Hara G. Antimicrobial stewardship in hospitals in Latin America and the Caribbean: a scoping review. Rev Panam Salud Publica. 2020;44:e68.
14. Alghamdi S, Shebl NA, Aslanpour Z, Shibl A, Berrou I. Hospital adoption of antimicrobial stewardship programmes in gulf cooperation council countries: a review of existing evidence. J Glob Antimicrob Resist. 2018;15:196–209.
15. Nathwani D, Varghese D, Stephens J, Ansari W, Martin S, Charbonneau C. Value of hospital antimicrobial stewardship programs [ASPs]: a

systematic review. Antimicrob Resist Infect Control. 2019;8:35.
16. Korea. Infect Chemother. 2021;53:617-59.
17. Goff DA, Rybak MJ. Global antimicrobial stewardship: challenges and successes from frontline stewards. Infect Dis Ther. 2015;4:1–3.
18. Majumder MAA, Singh K, Hilaire MG, Rahman S, Sa B, Haque M. Tackling antimicrobial resistance by promoting antimicrobial stewardship in medical and allied health professional curricula. Expert Rev Anti Infect Ther. 2020;1–14.
19. Gyssens IC. Role of education in antimicrobial stewardship. Med Clin North Am. 2018;102(5):855–871.
20. Kim J, Craft DW, Katzman M. Building an antimicrobial stewardship program: cooperative roles for pharmacists, infectious diseases specialists, and clinical microbiologists. Lab Med. 2015;46 (3):e65–e71.
21. Mas-Morey P, Valle M. A systematic review of inpatient antimicrobial stewardship programs involving clinical pharmacists in small-to-medium-sized hospitals. Eur J Hosp Pharm. 2018;25 (e1):e69–e73.
22. Heil EL, Kuti JL, Bearden DT, Gallagher JC. The Essential Role of Pharmacists in Antimicrobial Stewardship. Infection control and hospital epidemiology: The Official Journal of the Society of Hospital Epidemiologists of America. 2016 Jul;37(7):753-4. Kathy Tang, PharmD
23. Emily L. Heil, PharmD, BCPS-AQ ID, AAHIVP. Antimicrobial Stewardship: A Primer for Hospital Pharmacists. Pharmacy Times Health Systems Edition. March 2016; Volume 5, Issue 2.
24. Rai R, Bhat P. Hospital Antibiogram- A Tool for Safe Antimicrobial Therapy. J. Evolution Med. Dent. Sci. 2020;9(03):124-128.
25. National treatment guidelines for Antimicrobial Use in Infectious Diseases. National Centre for Disease Control, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India. Version 1.0. 2016:1-64. Accessed on 7th Aug, 2023: https://www.researchgate.net/ profile/Vikas-Manchanda/publication/298306442_National_Treatment_Guidelines_for_Antimicrobial_Use_in_Infectious_Diseases/links/576cc7bb08ae193ef3a9acda/National-Treatment-Guidelines-for-Antimicrobial-Use-in-Infectious-Diseases.pdf
26. Joshi, Sangeeta. Hospital antibiogram: A necessity. Indian Journal of Medical Microbiology. 2010;28:277-80.
27. Chung GW. Antimicrobial stewardship: a review of prospective audit and feedback systems and an objective evaluation of outcomes. Virulence. 2013;4:151–7.
28. Barlam TF, Cosgrove SE, Abbo LM, MacDougall C, Schuetz AN, Septimus EJ et al. Implementing an antibiotic stewardship program: guidelines by the IDSA/SHEA. Clin Infect Dis. 2016;62:e51–77.
29. Li DX, Cosgrove SE. Efficacy and implementation of strategies to address antimicrobial overuse and resistance. In: Pulcini C, Ergönül Ö, Can F, Beović B, editors. Antimicrobial stewardship. Amsterdam: Elsevier; 2017:13–28.
30. Akpan MR, Isemin NU, Udoh AE, Ashiru-Oredope D. Implementation of antimicrobial stewardship programs in African countries: a systematic literature review. J Glob Antimicrob Resist. 2020;22:317–324.
31. Singh S, Menon VP, Mohamed ZU, et al. Implementation and impact of an antimicrobial stewardship program at a tertiary care center in South India. Open Forum Infect Dis. 2018;6(4):ofy290.
32. Centers for Disease Control and Prevention. CDC, the core elements of hospital antibiotic stewardship programs; 2019. Available from: https://www.cdc.gov/antibiotic-use/core-elements/ hospital.html
33. Centers for Disease Control and Prevention (2020b). Implementation of antibiotic stewardship core elements at small and critical access hospitals. U.S. Department of Health and Human Services. https://www.cdc.gov/antibiotic-use/core-elements/small-critical.html
34. Kallen MC, Prins JM. A systematic review of quality indicators for appropriate antibiotic use in hospitalized adult patients. Infect Dis Rep. 2017;9:6821.
35. Timmons V, Townsend J, McKenzie R, Burdalski C, Adams-Sommer V. An evaluation of provider chosen antibiotic indications as a targeted antimicrobial stewardship intervention. American Journal of Infection Control. 2018 Oct;46(10):1174-9.
36. Momattin H, Al-Ali AY, Mohammed K, Al-Tawfiq JA. Benchmarking of antibiotic usage: an adjustment to reflect antibiotic stewardship program outcome in a hospital in Saudi Arabia. J Infect Public Health. 2018;11(3):310–3.
37. Murni IK, Duke T, Kinney S, Daley AJ, Soenarto Y. Reducing hospital-acquired infections and

improving the rational use of antibiotics in a developing country: an effectiveness study. Arch Dis Child. 2015;100(5):454–9.

38. Apurba S Sastry, Sandhya Bhat. Essentials of Medical Microbiology. Jaypee Brothers Medical Publishers. New Delhi, India. Third edition. 2021.
39. McLeod M, Ahmad R, Shebl NA, Micallef C, Sim F, Holmes A. A whole-health-economy approach to antimicrobial stewardship: analysis of current models and future direction. PLoS Med. 2019;16(3):e1002774.
40. Dyar O, Beović B, Pulcini C, Tacconelli E, Hulscher M, Cookson B et al. ESCMID generic competencies in antimicrobial prescribing and stewardship: towards a European consensus. Clin Microbiol Infect. 2019;25:13–19.
41. Fishman N. Antimicrobial stewardship. Am J Infect Control. 2006 June;34(5 Suppl 1):S55-63; discussion S64-73.
42. Doernberg SB, Abbo LM, Burdette SD, Fishman NO, Goodman EL, Kravitz GR, et al. Essential Resources and Strategies for Antibiotic Stewardship Programs in the Acute Care Setting. Clin Infect Dis. 2018 Sep 28;67(8):1168-74.
43. Morency-Potvin P, Schwartz DN, Weinstein RA. Antimicrobial stewardship: how the microbiology laboratory can right the ship. Clin Microbiol Rev. 2016;30(1):381–407.
44. Baur D, Gladstone BP, Burkert F, Carrara E, Foschi F, Döbele S, et al. Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and Clostridium difficile infection: a systematic review and meta-analysis. Lancet Infect Dis. 2017;17(9):990–1001.
45. Vadala R, Princess I. Antimicrobial stewardship program in critical care-need of the hour. Indian J Crit Care Med. 2020 Sep;24(9):847-854.