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REVIEW ARTICLE

Combating antimicrobial resistance: Antimicrobial stewardship program in Taiwan

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Multi-drug-resistant organisms are increasingly recognized as a global public health issue. Healthcare-associated infection and antimicrobial resistance are also current challenges to the treatment of infectious diseases in Taiwan. Government health policies and the health care systems play a crucial role in determining the efficacy of interventions to contain antimicrobial resistance. National commitment to understand and address the problem is prerequisite. We analyzed and reviewed the antibiotic resistance related policies in Taiwan, USA, WHO and draft antimicrobial stewardship program to control effectively antibiotic resistance

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Healthcare-associated infection (HAI);
Multi-drug-resistant organisms(MDROs)

and spreading in Taiwan. Antimicrobial stewardship program in Taiwan includes establishment of national inter-sectoral antimicrobial stewardship task force, implementing antimicrobial-resistance management strategies, surveillance of HAI and antimicrobial resistance, conducting hospital infection control, enforcement of appropriate regulations and audit of antimicrobial use through hospital accreditation, inspection and national health insurance payment system. No action today, no cure tomorrow. Taiwan CDC would take a multifaceted, evidence-based approach and make every effort to combat antimicrobial resistance with stakeholders to limit the spread of multi-drug resistant strains and to reduce the generation of antibiotic resistant bacteria in Taiwan.

Introduction

Multi-drug-resistant organisms (MDROs) are increasingly being recognized as a global public health issue.[1,2] The World Health Organization (WHO) chose antimicrobial resistance as its theme for World Health Day, April 7, 2011.[3] WHO strongly recommends that governments implement antibiotic stewardship programs for the containment of antimicrobial resistance.[4]

Healthcare-associated infection and antimicrobial resistance in Taiwan

Healthcare-associated infection (HAI) and antimicrobial resistance are current challenges to the treatment of infectious diseases in Taiwan.[5–11] Taiwan nosocomial infection surveillance system (TNIS),[12] a nationwide surveillance study on the incidence and prevalence of HAI and antimicrobial resistance in Taiwan during 2003–2010,[13] reported that the HAI incidence rates (number of HAIs/number of patient-days × 1000%) in the intensive care units (ICUs) of medical centers and regional hospitals has decreased significantly from 12.8% to 8.2% ($P = 0.002$) (Fig. 1A). HAI incidence rates in medical centers and regional hospitals decreased significantly from 4.1% to 2.7% ($P = 0.003$) (Fig. 1B). The proportion of site-specific HAIs in ICUs and regional hospitals are shown in Fig. 2A and Fig. 2B, respectively. In 2010, blood stream infections topped the list in the ICUs of medical centers, followed by urinary tract infections and pneumonia. Urinary tract infections topped the list in the ICUs of regional hospitals, followed by bloodstream infections and pneumonia in 2010. The proportion of blood stream infections increased significantly in the ICUs of medical centers ($p < 0.0001$) and regional hospitals ($p = 0.0039$) during 2003–2010. The common pathogens associated with HAIs in these ICUs are shown in Table 1A and B. In 2010, the top three pathogens in the ICUs were *Candida* species, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa* in medical centers; *A baumannii*, *Candida* species, and *Klebsiella pneumoniae* were the most common in regional hospitals. In the ICUs of medical centers and regional hospitals in 2010, the proportion of methicillin resistance in *Staphylococcus aureus* (MRSA) isolates was 76.6%, vancomycin resistance in enterococcal isolates (VRE) was 20.2%, imipenem or meropenem resistance in *A baumannii* isolates (carbapenem-resistant *A baumannii*; CRAB) was 70.1%, imipenem or meropenem resistance in *P aeruginosa* isolates (carbapenem-resistant *P aeruginosa*; CRPA) was 19.0%, carbapenem resistance in *Enterobacteriaceae* isolates (CRE) was 5.0%, carbapenem resistance in *E coli* isolates (CREC) was 2.2%, and carbapenem resistance in *K pneumoniae* isolates (CRKP) was 8.7%.

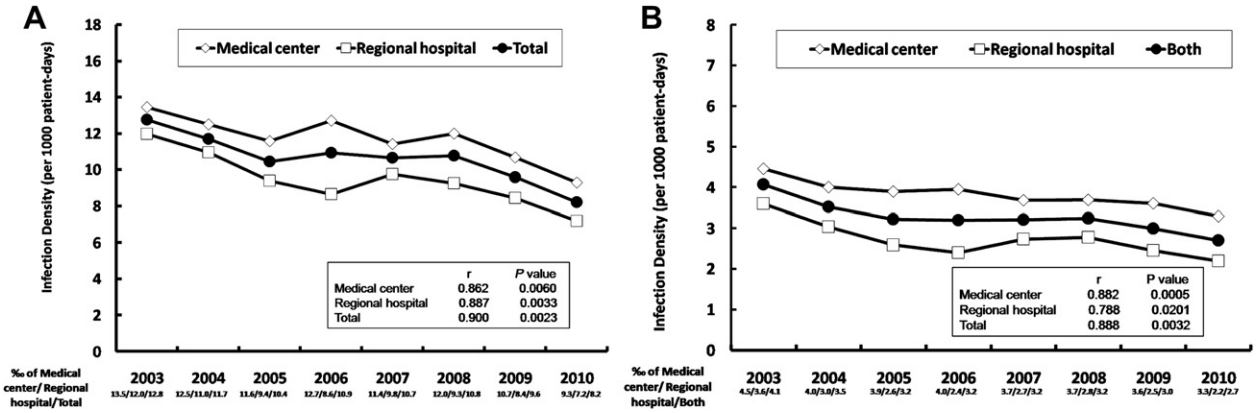

Figure 1. (A) Annual trends in the rates of healthcare-associated infection in the intensive care units of medical centers and regional hospitals in Taiwan. (B) Annual trends in the rates of healthcare-associated infection in medical centers and regional hospitals in Taiwan. Data from the Taiwan Nosocomial Infection Surveillance System, 2003–2010.

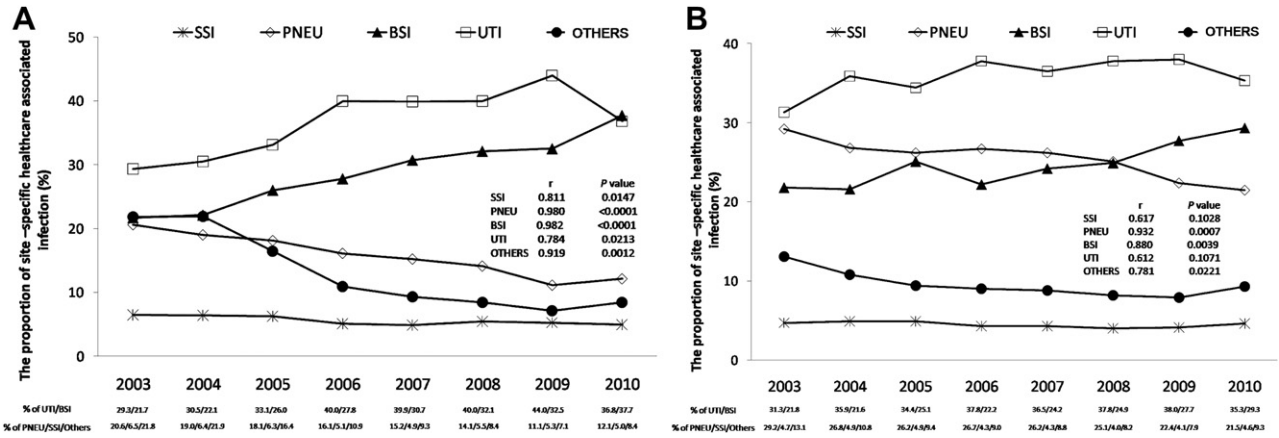

Figure 2. (A) Proportion of site-specific healthcare-associated infections in the intensive care units of medical centers in Taiwan. (B) The proportion of site-specific healthcare-associated infections in the intensive care units of regional hospitals in Taiwan. Data from the Taiwan Nosocomial Infection Surveillance System, 2003—2010. SSI, surgical site infection; PNEU, pneumonia; BSI, blood stream infection; UTI, urinary tract infection.

Impact of antimicrobial stewardship programs

Antimicrobial stewardship programs (ASPs) have the potential to reduce antimicrobial resistance, healthcare costs, and drug-related adverse events by improving clinical outcomes.[14—16] During 1988—2001, New York Hospital Queens has taken a series of management steps to address antimicrobial resistance, including monitoring ceftazidime and imipenem resistance in Gram-negative bacteria, providing infectious disease consultation and health education, and limiting the use of cephalosporins and cephamycins. This resulted in an 80% reduction in the use of cephalosporin-cephamycin, 44% reduction in *Klebsiella* species isolates resistant to ceftazidime, and 87% reduction in a surgical ICU.[17] Drew et al reported a reduction in the use of antibiotics at Chandler Medical Center in Kentucky after performing a prospective audit with intervention and feedback.[18] They also reported a 30% reduction in the cost of antimicrobials. Furthermore, formulary restriction and the preauthorization of prescriptions have significantly reduced the use of antibiotics and medical costs at Chandler Medical Center since 1991, reduced the use of ceftazidime, cefotaxime, and ceftriaxone by 80% in 2002, and also decreased the resistant rates of several important pathogens, including multidrug-resistant *P aeruginosa* and MRSA.

ASP in Taiwan

Based on the abovementioned studies, ASPs are considered to have significant and supporting scientific evidence. Taiwan's ASP, in reference to the Infectious Diseases Society of America (IDSA), Society for Healthcare Epidemiology of America (SHEA) guidelines (a hospital pharmacy guide), and WHO's global strategy for the containment of antimicrobial resistance to ASPs,[3,4,19,20] has adopted scientific approaches and emphasizes the impact of resistance to antimicrobial agents. These approaches include the appropriate selection of dosage, route of administration, and duration of antimicrobial therapy. The objectives of ASP in Taiwan are to strengthen the monitoring and surveillance systems used to prevent the spread of antimicrobial-resistant bacteria, maximize favorable outcomes, and minimize antimicrobial resistance after antibiotic use. Regarding patient safety concerns, Taiwan's ASP combines hospital infection control measures, such as hand hygiene and care bundles, that might control the emergence and spread of antimicrobial resistance. Taiwan's ASP operates as follows (Table 2).

Establishment of national inter-sectoral antimicrobial stewardship task force[3,4]

The implementation of a government's health policy and healthcare system is a key element to determining the efficiency of interventions. Also, national commitment and problem-solving skills are thought to be essential. To reduce antimicrobial-resistant bacteria and lower the occurrence of healthcare-associated infections, the Centers for Disease Control, R.O.C (Taiwan CDC) has put a lot of effort into making the containment of drug resistance a national priority. As a result, the national inter-sectoral antimicrobial stewardship task force was established that included physicians, infection control professionals, clinical microbiologists, information system specialists, nurses, clinical pharmacists, healthcare professionals, veterinarians, agriculturalists, pharmaceutical manufacturers, government representatives, media representatives, consumers, and other stakeholders. The aims of the task force were to increase the recognition of antimicrobial resistance, to reduce the inappropriate spread of antimicrobial-resistant bacteria, to establish a well-organized data-collection process, to facilitate the implementation of interventions such as education and surveillance, to develop indicators to assess the impact of drug-resistance policies, to reduce unnecessary medical costs, and to improve the quality of the medical services provided.

Antimicrobial-resistance management strategies

The core management strategies against antimicrobial resistance include the development of an effective health

Table 1 Distribution and rank order of selected pathogens associated with healthcare-associated infections in the (A) intensive care units of medical centers and (B) regional hospitals in Taiwan. Data from the Taiwan Nosocomial Infection Surveillance System, 2003—2010

Pathogens	2003		2004		2005		2006		2007		2008		2009		2010	
	Rank	No.	Rank	No.	Rank	No.	Rank	No.	Rank	No.	Rank	No.	Rank	No.	Rank	No.
A																
Pseudomonas aeruginosa	2	841	1	725	1	657	1	633	3	903	3	1017	3	914	3	753
Acinetobacter baumannii	3	776	3	625	2	535	3	499	2	944	2	1,148	2	1021	2	843
Candida species	8	255	8	236	7	237	5	475	1	1021	1	1529	1	1586	1	1128
C. albicans		200		188		192		339		678		1,024		989		701
Other *Candida* spp. or NOS[a]		55		48		45		137		343		505		597		427
Escherichia coli	4	569	4	512	3	526	2	550	4	819	4	898	4	884	4	656
Staphylococcus aureus	1	855	2	656	4	521	6	468	6	685	5	849	7	561	7	469
Klebsiella pneumoniae	5	439	5	468	5	448	4	479	5	696	6	747	5	698	5	537
Enterobacter species	6	348	6	316	6	242	9	221	8	411	8	529	8	498	8	379
E cloacae		273		254		187		177		335		419		402		292
Other *Enterobacter* spp. or NOS[a]		75		62		55		44		76		110		96		87
Yeast-like	10	181	9	200	9	158	7	253	7	564	7	647	6	669	6	505
Coagulase-negative staphylococci	7	271	7	270	8	225	8	250	9	360	9	512	9	364	9	348
Stenotrophomonas maltophilia	9	195	10	159	10	155	10	123	10	182	10	236	10	215	10	227
Other		1284		1249		1008		1110		1742		2373		2450		1999
Total		6014		5416		4712		5062		8327		10,485		9860		7844
B																
Pseudomonas aeruginosa	1	810	1	822	1	725	1	570	1	811	2	832	4	702	4	757
Acinetobacter baumannii	3	627	2	675	3	575	4	467	2	760	1	838	1	821	1	1,003
Escherichia coli	4	547	4	622	2	581	3	486	5	673	4	758	3	729	5	741
Klebsiella pneumoniae	5	522	5	618	4	559	2	501	4	683	5	735	5	700	3	793
Staphylococcus aureus	2	721	3	660	5	515	5	407	6	554	6	579	6	521	6	504
Candida species	11	116	10	139	9	129	6	214	3	697	3.	816	2	770	2	933
C albicans		82		115		96		175		531		600		547		648
Other *Candida* spp. or NOS[a]		34		24		33		39		166		216		223		285
Enterobacter species	6	285	6	255	6	260	7	181	7	273	7	308	7	298	8	297
E cloacae		187		183		191		132		198		235		227		220
Other *Enterobacter* spp. or NOS[a]		98		72		69		49		75		73		71		77
Coagulase-negative staphylococci	7	228	7	214	7	205	8	143	8	271	8	297	8	275	7	354
Proteus species	8	149	8	152	8	149	9	120	12	150	10	185	11	149	10	168
Proteus mirabilis		143		143		140		115		138		170		139		156
Other *Proteus* spp. or NOS[a]		6		9		9		5		12		15		10		12
Yeast-like	12	54	12	68	12	79	10	119	9	267	9	256	9	246	9	230
Other		1173		1183		1086		859		1417		1470		1426		1649
Total		5232		5408		4863		4067		6556		7074		6637		7429

[a] NOS, not otherwise specified.

information system, prospective audits of the intervention systems used, feedback, formulary restriction, preauthorization, and the development of a computer management system. An effective health information system can result in reduced antimicrobial resistance. Taiwan CDC encourages hospitals to establish an effective health information system for prospective audits of direct intervention and feedback to the prescriber. An effective health information system includes the mechanisms and functions of surveillance, can investigate the use of antibiotics, perform internal audits, evaluate antimicrobial agents, deal with inappropriate orders, and suggest alternative therapies. The prescribing physicians will be contacted if their orders are evaluated as inappropriate. Feedback might be provided as a verbal or

written notice.[18–20] The results of surveillance should be immediately reported back to clinicians so they can revise drug use. Formulary restriction, preauthorization, and computer management system requirements involve the development of a thorough computer management system, restricting the use of some particular antimicrobial agents to specific indications, periods of therapy, disease severity, physician services, prescribers, or patient populations. The features of this restriction depend on certain factors, such as institutional antimicrobial resistance and patient safety issues related to the antimicrobial agents in question.[15,19,21,22] The prospective audit with intervention and feedback, as well as the formulary restrictions and preauthorizations given to certain prescriptions by infection control physicians and clinical pharmacists with infectious disease training, can reduce inappropriate antibiotic use and additional medical costs by implementing antibiotic-management programs.[20] In order to urge hospitals to develop and implement strategies that address antibiotic control, Taiwan CDC has implemented a "core management strategy of antibiotic resistance" through audit mechanisms of hospital accreditation,[23] infection control inspection,[24] and the national health insurance payment system.[25] In relation to the standard criteria of hospital accreditation and hospital infection control inspections, standard criteria related to antibiotic management are shown in Table 3.

Supplemental antimicrobial-resistance management strategies

Supplemental strategies can play a crucial role in ASPs.[20,26] In order to lower the incidence of HAIs and prevent the spread of antimicrobial resistance within medical institutions, the following actions were listed as supplemental antimicrobial-resistance strategies by Taiwan CDC. These include preservice and in-service education programs that present related knowledge regarding the spread of multidrug-resistant microorganisms and the multidisciplinary development of evidence-based practice guidelines[27,28] and clinical pathways,[26,29] computerized physician-order entry, antimicrobial order forms,[30] real-time information systems, computerized decision-support systems, the streamlining or de-emphasis of empirical antimicrobial therapy based on culture

Table 2 Antimicrobial stewardship program in Taiwan

1. Establish a national inter-sectoral antimicrobial stewardship task force

2. Antimicrobial-resistance management strategies
- 2.1. Core antimicrobial-resistance management strategies
  - 2.1.1. Effective health information system, prospective audit with intervention and feedback
  - 2.1.2. Formulary restriction, preauthorization and computer management system
- 2.2. Supplemental antimicrobial-resistance management strategies
  - 2.2.1. Education, guidelines and clinical pathways
  - 2.2.2. Computer physician-order entry and antimicrobial order forms
  - 2.2.3. Streamlining or de-emphasis of empirical antimicrobial therapy
  - 2.2.4. Computer decision-support system and optimization of antibiotics
  - 2.2.5. Pharmacokinetic and pharmacodynamic characteristics of the drugs

3. Surveillance of HAI and antimicrobial resistance
- 3.1. Taiwan CDC's infectious disease reporting system
- 3.2. Taiwan nosocomial infection surveillance system (TNIS)

4. Hospital infection control
- 4.1. Promote hand hygiene
  - 4.1.1. Hand hygiene demonstration centers (National Taiwan University Hospital, Kaohsiung Veterans General Hospital, and Tri-service General Hospital)
  - 4.1.2. Nationwide hand-hygiene certification and reward system
- 4.2. Promotion of care bundle: multimodal infection control measures and intervention
  - 4.2.1. Central line-associated blood stream infections (CLABSI)bundles
  - 4.2.2. Catheter-related urinary infections (CAUTI) bundles
  - 4.2.3. Ventilator-associated infections (VAP) bundles
  - 4.2.4. Surgical site infection (SSI) bundles
  - 4.2.5. Antibiotic care bundles

5. Regulation of pharmaceutical affairs and infection control
- 5.1. Pharmaceutical Affairs Act
- 5.2. Communicable Disease Control Act
- 5.3. Regulation of the implementation and inspection of infection control measures in medical institutions

6. Evaluation and audit mechanisms
- 6.1. Hospital accreditation system
- 6.2. Hospital inspection system
- 6.3. National health insurance payment system

Table 3 Standard criteria related to antibiotic management of hospital accreditation and hospital infection control inspections

1. Hospital should have antibiotic-resistance control measures.

1.1. Hospital should have effective antibiotics control through educational and administrative means:

1.1.1. Hospital should conduct a course on the "appropriate use of antibiotics" at least once every 6 months, and clinicians should attend the course at least once per year.

1.1.2. Hospitals should edit the control measures for antibiotic use so that physicians can search for the appropriate use of antibiotics at any time.

1.1.3. A monitoring mechanism should be set up for all types of antibiotic use in the hospital.

1.1.4. Implement reasonable usage of nonrestrictive antibiotics in the hospital. Hospital inspectors should review the medical records at random, the use of nonrestrictive antibiotics should be listed in the medical records, and none of the following circumstances should appear:

(1) Continuous use of first line of narrow-spectrum antibiotics with inappropriate reasons in patients with severe illness with multiorgan dysfunction or infection, transfer to the hospital after ineffective treatment at other hospitals, and circumstances such as hospital-acquired pneumonia or immune deficiency.

(2) Continued use of first-line narrow-spectrum antibiotics with irrational reasons after ineffective use of first-line narrow-spectrum antibiotics for 3 days.

(3) Not selecting the appropriate antibiotics based on the site of infection, such as intra-abdominal anaerobic bacteria.

(4) Use of ineffective treatment for community-acquired infection without rational reasons.

(5) Doses are given without considering the patient's weight and liver and kidney functions.

1.1.5. Reasonable use of restricted antibiotics. Hospital inspectors should review the medical records at random, and the use of restrictive antibiotics should be listed in the medical records without any of the following circumstances.

(1) Use of broad-spectrum antibiotics for irrational reasons when the clinical status is listed as mild or if there are no symptoms.

(2) Use three or more antibiotics at the same time for an irrational reason.

(3) The given drug types do not meet the national or international guidelines for antibiotics treatment.

(4) Doses are given without considering the patient's weight and liver and kidney functions.

1.1.6. Review all of the uses of restrictive antibiotics.

1.1.7. Correctly analyze and improve any mistakes by reviewing the involved mechanisms.

1.1.8. Hospitals should set up an information system for checking antibiotic use and implement a reminder mechanism that is activated when prescribing antibiotics.

1.1.9. Correctly execute and analyze the conditions that do not meet the regulated uses of antibiotics and to propose improvement measures.

1.1.10. Lower the inappropriate use of antibiotics.

2. Correct use of prophylactic antibiotics in hospitals.

Use of prophylactic antibiotics should be listed in the medical record, and hospital inspectors should review the medical records at random.

2.1. The first dose of the prophylactic antibiotic should be given within 1 hour before the surgical incision if the use of prophylactic antibiotic is required (e.g., for cesarean section, prophylactic antibiotics should be given immediately after umbilical ligation excision).

2.2. Drug selection should be consistent with the guidelines for antibiotic use in Taiwan.

2.3. The antibiotic dose should be consistent with the patient's weight.

2.4. Additional antibiotics should be given as necessary during a surgery (with consideration of the pharmacokinetics).

2.5. Discontinue the use of antibiotics after clean surgery. Antibiotics should be used for less than 24 hours after major surgery.

2.6. Set up monitoring and improve the mechanisms for the effective use of prophylactic antibiotics.

3. Reasonable antibiotics use in outpatients.

Hospital inspectors should review the medical records at random.

3.1. Use antibiotics only if it is required. Detailed explanations should be written on the medical record when using antibiotics.

3.2. Antibiotics cannot be used for treating the common cold.

3.3. Rational use of the types and dosages of antibiotics with consideration of the patient's weight and kidney functions.

3.4. Use antibiotics for a rational period of time. Detailed explanations should be written to explain any irregularities.

3.5. Monitoring and improve the mechanisms for the effective use of antibiotics in outpatients.

4. Effective management and reporting of multi-drug resistance bacteria in hospitals.

4.1. Based on the bacterial isolate and the type of ward, responsible infection control staff, clinicians, and nurses can control the isolates, especially antimicrobial-resistant bacteria such as CRAB, VRE, MRSA, and CRE. Analytical reports should include the isolated strain and antibiotic sensitivity.

4.2. Reports on antibiotic susceptibility of clinically isolated strains should be edited annually. The latest statistical reports should be distributed to every physician or announced through the internet in order to allow physicians to check these reports at any time.
4.3. Consideration of patient privacy, mark and proper isolation should effectively be done for those with specific antimicrobial resistant infection or colonization.
4.4. Statistical reports regarding bacterial isolates of HAI should be performed at least every 6 months. These should be distributed to physicians and related staff or be made public through the internet.
4.5. Strains, isolates, and analytical reports on inpatients should be provided to healthcare staff as reference.
4.6. Multidrug resistant-related data should be reported to Taiwan CDC per their policy.
4.7. Set up relative mechanisms and make sure each physician understands related information.
4.8. Analyze the trends in antimicrobial resistance and antibiotic use every 6 months.
4.9. Based on the report, related policies should be implemented to improve the control of VRE, MRSA, CRAB, CRE, and others.

results, the elimination of redundant combination therapies,[31,32] optimization of antimicrobial dosing based on individual patient characteristics, causative organism, site of infection, pharmacokinetic and pharmacodynamic characteristics of the drug, and a systemic plan for parenteral to oral conversion of antimicrobials.[33,34] Besides, these were incorporated into the standard criteria of hospital accreditation, hospital infection control inspection, as well as audits of national health insurance payments. The aim is to supervise and urge hospitals to establish appropriate mechanism for antibiotic use with effective implementation.

Surveillance of HAI and antimicrobial resistance

The surveillance of antimicrobial resistance is fundamental to the effective implementation of any strategy for the containment of antimicrobial resistance because it is the means by which physicians can monitor the efficacy of various interventions. Taiwan CDC established TNIS to monitor HAI and antimicrobial resistance. Taiwan CDC adopted voluntary participation, in reference to the HAI surveillance mechanism of Europe[35] and USA.[36] This surveillance mechanism has been extended to all levels of hospitals since the ICUs of medical centers began to report their findings at the end of 2001. In order to understand the trends of multidrug-resistant strains, Taiwan CDC undertook the monitoring of HAI and antimicrobial resistance. The current TNIS has enrolled more than 300 hospitals, of which more than 70 hospitals report cases through an information exchange center.[12] This surveillance system, which utilizes standard tables for data analysis, can report back to individual hospitals their own analysis tables on HAI, antimicrobial resistance, the distribution of pathogens, and antibiotic resistance. In order to analyze, interpret, and apply the HAI and antimicrobial resistance data, the HAI and antimicrobial-resistance data-analysis task force under Taiwan's Healthcare Infection Control Practices Advisory Committee (Fig. 3) was set up and the results of the analysis were distributed to hospitals for reference and other documents, journals, and reference channels were provided. The feedback mechanisms of the regular data analysis provide self-monitoring within the hospitals and reference to hospitals at the same level. The committee will also continue to review and improve the surveillance reporting system in order to improve data validation, accuracy, and completeness, which should help both the government and the hospitals effectively use the national surveillance data.

Control of hospital infections

Poor compliance with infection control measures in any setting can greatly increase the spread of drug-resistant bacteria, especially during outbreaks. Collaboration between the ASP and hospital infection control programs is essential.[4,22,37] The combination of effective antimicrobial stewardship with a comprehensive infection control program has been shown to limit the emergence and transmission of antimicrobial-resistant bacteria.[38] The following actions were listed as the main strategies for infection control by Taiwan CDC: to promote hand hygiene in healthcare facilities[39] and communities; to conduct a project entitled "care bundle to lower HAIs"; to establish guidelines[40] for infection control measures and contact precautions[40]; to strengthen aseptic practices, sterilization, and disinfection[41]; to promote environmentally friendly hygiene and waste management procedures; and to facilitate environmental designs for appropriate infection control practices.[42] Among those strategies, continuing to promote hand hygiene in healthcare facilities and communities and conducting a project entitled "care bundle to lower the HAIs" are two of the top priorities of Taiwan CDC. These initiatives are described below.

Promotion of hand hygiene

Ensuring good hand hygiene is key to preventing the spread of infections and bringing disease outbreaks under control.[43,44] In order to effectively prevent HAIs, a theme promoting hand hygiene was planned based on the "Clean Care is Safer Care" initiative of Patient Safety Alliance (WHO).[45] Three medical centers (National Taiwan University Hospital, Kaohsiung Veterans General Hospital, and Tri-service General Hospital) were chosen as hand-hygiene demonstration centers by Taiwan CDC. The goal is to achieve hospital-wide participation, including involvement at the management level and patient participation. At the same time, the culture of patient safety was formed through the creation of a nationwide hand-hygiene certification and reward system that might increase the

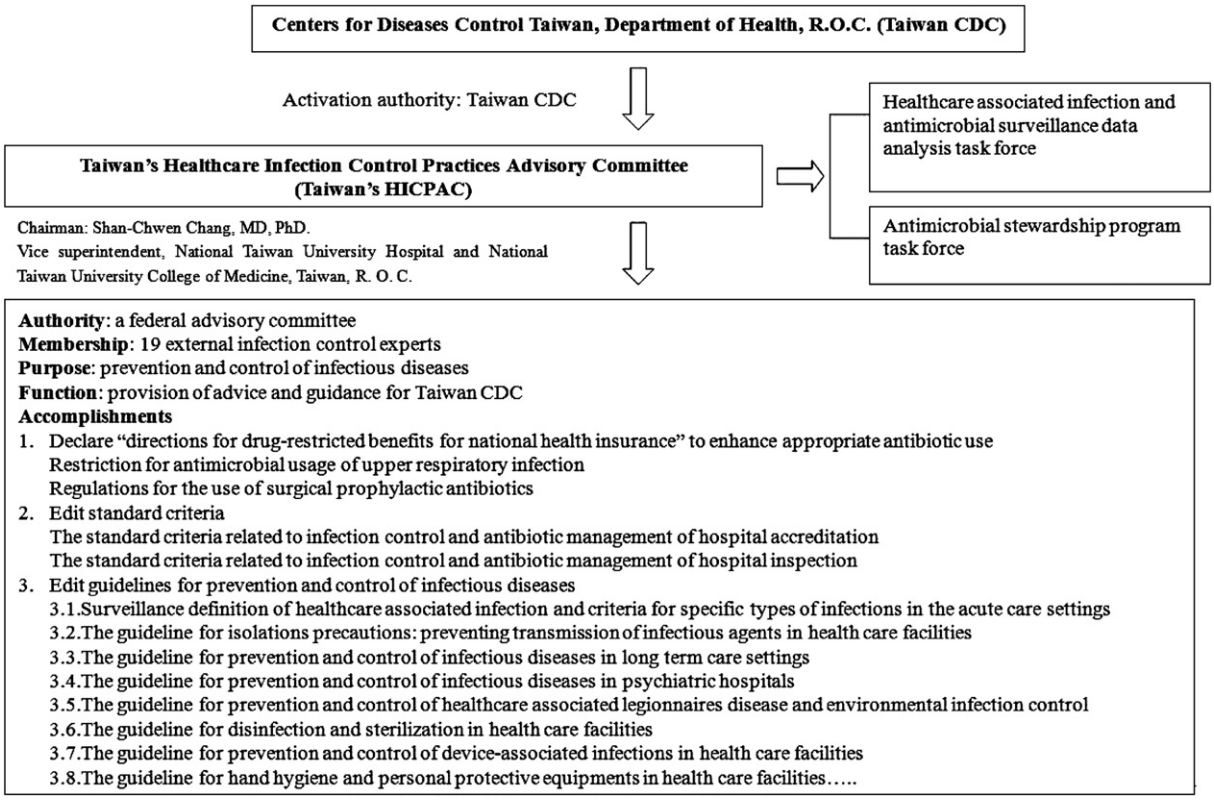

Figure 3. Taiwan's Healthcare Infection Control Practices Advisory Committee.

accessibility of hand-hygiene equipment and hand-hygiene recognition by healthcare workers. Furthermore, continuous hospital quality improvements and effective implementation of hand hygiene can be encouraged through assessment, performance indicators, and audit mechanisms of both the hospital accreditation process and hospital infection inspections.

Promotion of care bundle: multimodal infection control measures and interventions

HAIs are the leading causes of death in the USA, accounting for an estimated 1.7 million infections, 99,000 associated deaths, and an estimated $28–33 billion in additional healthcare costs in 2002. Four categories of infections, including surgical site infections (SSI), central line-associated bloodstream infections (CLABSI), ventilator-associated pneumonia (VAP), and catheter-associated urinary tract infections (CAUTI), account for approximately three quarters of HAIs that present in the acute care hospital setting. Currently, CAUTI comprise the highest percentage (34%) of HAIs, followed by SSI (17%), CLABSI (14%), and VAP (13%) in the USA.[46–49] Many of these HAIs can be prevented through increased awareness and implementation of recommended infection control practices. A "care bundle" is a group of interventions related to a disease process that, when executed together, results in better outcomes than when implemented individually. The individual bundle elements are built upon evidence-based practices.[46–52] In recent years, large-scale regional and statewide projects, such as the Pittsburgh Regional Healthcare Initiative and the Michigan Keystone Project, have demonstrated roughly 70% reductions in CLABSI rates in ICUs by increasing adherence to the recommended care bundle for the insertion of central lines.[47,50] Taiwan CDC promotes a care bundle that includes CLABSI bundles,[53] CAUTI bundles,[54] VAP bundles,[55] SSI bundles[56], and antibiotic care bundles for lowering multidrug resistant bacteria infections, such as MRSA, VRE, and CRAB.

Pharmaceutical affairs and infection control regulations

The Pharmaceutical Affairs Act was amended in 2005 by the Taiwan Food and Drug and Administration (TFDA),[57] and this act clearly attempts to regulate the sale, supply, and dispensing of prescriptions in order to ensure that antimicrobials meet the international standards of quality, safety and efficacy. The Communicable Disease Control Act, which was amended in January 2004, clearly states that medical institutions should prevent the occurrence of HAI.[57,58] In November 2004, the "regulation for communicable disease control and vaccination measures in health/medical institutions" was promulgated. In January 2008, the title was amended as the "implementation and inspection of infection control measures for medical institutions," and the amended document clearly indicates that medical institutions should implement infection control measures and standard items for inspection by competent authority.

Audit mechanism of hospital accreditation, inspection, and national health insurance payment system

The existence of appropriate legislation regarding antimicrobial agents and infection control cannot improve the quality of infection control and use of antibiotics unless enforced. To reduce HAIs and antimicrobial resistance, the standard criteria for hospital infection control inspection have been published by the central health authority every year since 2005, and a local health officer is responsible for the inspection of hospitals within each area. Improvements have been made to the hospital infection control program since 2008; infection control experts were allocated to assist local health officers and evaluate the infection control practices. This program involves the integration of standard criteria for hospital infection control inspection and hospital infection control accreditation and the establishment of a fair audit mechanism. The latter includes the results of hospital infection control inspections into hospital infection control accreditation and national health insurance payment system as references. In 2011, there were a total of 10 items and 31 secondary items listed in the standards for infection control inspection.

HAIs and antimicrobial resistance are two of the most preventable leading causes of mortality. These infections also add a significant economic burden to the healthcare system. Taiwan CDC is responsible for supervising medical institutions and establishing a robust and organized infection control framework. Potential measurements include, for example, the application of healthcare information technology to antimicrobial stewardship, establishment of infection control committees and dedicated units, and the allocation of physicians and nurses to address infection control, antibiotic regulations, and the promotion of these practices.

Taiwan CDC, in conjunction with infectious diseases physicians, infectious control experts, and other multidisciplinary experts, conducts antimicrobial stewardship and infection control programs through the audit mechanisms of hospital accreditation, hospital inspection, and the national health insurance payment system to reduce, prevent, and eventually eliminate most of the significant burden to our national health system. The Taiwanese government also encourages drug development programs to foster the innovation, research, and development of new tools that work to reduce the financial incentives that encourage the irrational use of medicine, i.e., "No action today, no cure tomorrow." Taiwan CDC makes every effort to combat antimicrobial resistance by targeting consumers, prescribers, dispensers, veterinarians, managers of hospitals and diagnostic laboratories, patients and visitors to healthcare facilities, as well as national governments, the pharmaceutical industry, professional societies, and international agencies.[3,4]

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References

1. Boucher HW, Talbot GH, Bradley JS, Edwards JE, Gilbert D, Rice LB, et al. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. *Clin Infect Dis* 2009;**48**:1—12.
2. Kumarasamy KK, Toleman MA, Walsh TR, Bagaria J, Butt F, Balakrishnan R, et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. *Lancet Infect Dis* 2010;**10**: 597—602.
3. World Health Organization (WHO). *Antimicrobial resistance and its global spread*. Available from: http://www.who.int/world-health-day/en/index.html; 2011.
4. World Health Organization (WHO). WHO global strategy for containment of antimicrobial resistance. Available from: http://www.who.int/csr/resources/publications/drugresist/en/EGlobal_Strat.pdf; 2010.
5. Hwang KP, Tang YF, Shen YH. Activity of ertapenem, ciprofloxacin, ceftriaxone, piperacillin-tazobactam, and ampicillin-sulbactam against 12 common clinical isolates of community-acquired bacteremia. *J Microbiol Immunol Infect* 2009;**42**: 433—8.
6. Lee CM, Yeh SC, Lim HK, Liu CP, Tseng HK. High prevalence rate of multidrug resistance among nosocomial pathogens in the respiratory care center of a tertiary hospital. *J Microbiol Immunol Infect* 2009;**42**:401—4.
7. Chen WY, Jang TN, Huang CH, Hsueh PR. In vitro susceptibilities of aerobic and facultative anaerobic gram-negative bacilli isolated from patients with intra-abdominal infections at a medical center in Taiwan: results of the Study for Monitoring Antimicrobial Resistance Trends (SMART) 2002-2006. *J Microbiol Immunol Infect* 2009;**42**:317—23.
8. Liu CY, Liao CH, Chen YC, Chang SC. Changing epidemiology of nosocomial bloodstream infections in 11 teaching hospitals in Taiwan between 1993 and 2006. *J Microbiol Immunol Infect* 2010;**43**:416—29.
9. Lee CY, Chen PY, Huang FL, Lin CF. Microbiologic spectrum and susceptibility pattern of clinical isolates from the pediatric intensive care unit in a single medical center - 6 years' experience. *J Microbiol Immunol Infect* 2009;**42**:160—5.
10. Chen PL, Ko WC. A continuous challenge from Gram-negative bacteria: more carbapenemases. *J Microbiol Immunol Infect* 2010;**43**:351—3.
11. Tseng SH, Lee CM, Lin TY, Chang SC, Chang FY. Emergence and spread of multi-drug resistant organisms: think globally and act locally. *J Microbiol Immunol Infect* 2011;**44**:157—65.
12. Taiwan Centers for Disease Control. *Nosocomial infection control*. Available from: http://www.cdc.gov.tw/ct.asp?xItem=7789&ctNode=928&mp=5; 2009.
13. Taiwan Centers for Disease Control. *Surveillance of noscomial infection*. Available from: http://www.cdc.gov.tw/ct.asp?xItem=32212&ctNode=1711&mp=1; 2009.
14. Ansari F, Gray K, Nathwani D, Phillips G, Ogston S, Ramsay C, et al. Outcomes of an intervention to improve hospital

antibiotic prescribing: interrupted time series with segmented regression analysis. *J Antimicrob Chemother* 2003;**52**:842—8.
15. Carling P, Fung T, Killion A, Terrin N, Barza M. Favorable impact of a multidisciplinary antibiotic management program conducted during 7 years. *Infect Control Hosp Epidemiol* 2003;**24**: 699—706.
16. Ruttimann S, Keck B, Hartmeier C, Maetzel A, Bucher HC. Long-term antibiotic cost savings from a comprehensive intervention program in a medical department of a university-affiliated teaching hospital. *Clin Infect Dis* 2004;**38**:348—56.
17. Rahal JJ, Urban C, Segal-Maurer S. Nosocomial antibiotic resistance in multiple gram-negative species: experience at one hospital with squeezing the resistance balloon at multiple sites. *Clin Infect Dis* 2002;**34**:499—503.
18. Drew RH. Antimicrobial stewardship programs: how to start and steer a successful program. *J Manag Care Pharm* 2009;**15**: S18—23.
19. American Society of Health-System Pharmacists. *A hospital pharmacist's guide to antimicrobial stewardship programs*. Available from: http://onlinece.ashpadvantage.com/stewardship/stewardship-white-paper.pdf; 2011.
20. Dellit TH, Owens RC, McGowan Jr JE, Gerding DN, Weinstein RA, Burke JP, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007;**44**:159—77.
21. Lan CK, Hsueh PR, Wong WW, Fung CP, Lau YT, Yeung JY, et al. Association of antibiotic utilization measures and reduced incidence of infections with extended-spectrum beta-lactamase-producing organisms. *J Microbiol Immunol Infect* 2003; **36**:182—6.
22. MacDougall C, Polk RE. Antimicrobial stewardship programs in health care systems. *Clin Microbiol Rev* 2005;**18**:638—56.
23. Taiwan Centers for Disease Control. *Standard criteria of hospital accreditation*. Available from: http://www.doh.gov.tw/CHT2006/DM/DM2.aspx?now_fod_list_no=11240&class_no=472&level_no=2; 2011.
24. Taiwan Centers for Disease Control. *Standard criteria of hospital infection control inspection*. Available from: http://www.cdc.gov.tw/ct.asp?xItem=13464&ctNode=1891&mp=1; 2011.
25. Bureau of National Health Insurance. *Pay for performances*. Available from: http://www.nhi.gov.tw/english/webdata.asp?menu=11&menu_id=597&webdata_id=3188; 2011.
26. Marrie TJ, Lau CY, Wheeler SL, Wong CJ, Vandervoort MK, Feagan BG. A controlled trial of a critical pathway for treatment of community-acquired pneumonia. CAPITAL study investigators. Community-acquired pneumonia intervention trial assessing Levofloxacin. *JAMA* 2000;**283**:749—55.
27. Hsueh PR, Ko WC, Wu JJ, Lu JJ, Wang FD, Wu HY, et al. Consensus statement on the adherence to Clinical and Laboratory Standards Institute (CLSI) Antimicrobial Susceptibility Testing Guidelines (CLSI-2010 and CLSI-2010-update) for Enterobacteriaceae in clinical microbiology laboratories in Taiwan. *J Microbiol Immunol Infect* 2010;**43**:452—5.
28. Guidelines on antimicrobial therapy of pneumonia in adults in Taiwan, revised 2006. *J Microbiol Immunol Infect* 2007;**40**: 279—83.
29. Jan IS, Cheng SH, Hsu HC, Hsueh PR. Physicians' adherence to guidelines for empirical treatment of urinary tract infection in Taiwan. *J Microbiol Immunol Infect* 2007;**40**:532—6.
30. Echols RM, Kowalsky SF. The use of an antibiotic order form for antibiotic utilization review: influence on physicians' prescribing patterns. *J Infect Dis* 1984;**150**:803—7.
31. Glowacki RC, Schwartz DN, Itokazu GS, Wisniewski MF, Kieszkowski P, Weinstein RA. Antibiotic combinations with redundant antimicrobial spectra: clinical epidemiology and pilot intervention of computer-assisted surveillance. *Clin Infect Dis* 2003;**37**:59—64.
32. Soo Hoo GW, Wen YE, Nguyen TV, Goetz MB. Impact of clinical guidelines in the management of severe hospital-acquired pneumonia. *Chest* 2005;**128**:2778—87.
33. Dunbar LM, Wunderink RG, Habib MP, Smith LG, Tennenberg AM, Khashab MM, et al. High-dose, short-course levofloxacin for community-acquired pneumonia: a new treatment paradigm. *Clin Infect Dis* 2003;**37**:752—60.
34. Nicolau DP. Pharmacodynamic optimization of beta-lactams in the patient care setting. *Crit Care* 2008;**12**(Suppl. 4):S2.
35. EARS-net. Antimicrobial resistance surveillance in Europe 2009. Available from: http://www.ecdc.europa.eu/en/activities/surveillance/EARS-Net/Pages/index.aspx; 2009.
36. Hidron AI, Edwards JR, Patel J, Horan TC, Sievert DM, Pollock DA, et al. NHSN annual update: antimicrobial-resistant pathogens associated with healthcare-associated infections: annual summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006-2007. *Infect Control Hosp Epidemiol* 2008; **29**:996—1011.
37. Nicolle L. Infection control programmes to contain antimicrobial resistance, 2001 Organization WH WHO/CDS/CSR/DRS/2001.7.
38. Center for Disease Control. *Campaign to prevent antimicromial resistance in healthcare settings. Fact sheet: 12 steps to prevent antimicrobial resistance among hospitallized adults*. Available from: http://www.cdc.gov/drugresistance/healthcare/ha/12steps_HA.htm; 2010.
39. Boyce JM, Pittet D. Guideline for Hand Hygiene in Health-Care Settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/-SHEA/APIC/IDSA Hand Hygiene Task Force. Society for Healthcare Epidemiology of America/Association for Professionals in Infection Control/Infectious Diseases Society of America. *MMWR Recomm Rep* 2002;**51**:1—45. quiz CE1—4.
40. Siegel JD, Rhinehart E, Jackson M, Chiarello L. 2007 Guideline for isolation precautions: preventing transmission of infectious agents in health care settings. *Am J Infect Control* 2007;**35**: S65—164.
41. Rutala WA, Weber DJ. *HICPAC. Guideline for disinfection and sterilization in healthcare facilities, 2008*. Available from: http://www.cdc.gov/ncidod/dhqp/pdf/guidelines/Disinfection_Nov_2008.pdf; 2008.
42. Sehulster L, Chinn RY. Guidelines for environmental infection control in health-care facilities. Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). *MMWR Recomm Rep* 2003;**52**:1—42.
43. Boyce JM, Pittet D. Guideline for hand hygiene in health-care settings: recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. *Infect Control Hosp Epidemiol* 2002; **23**:S3—40.
44. Pittet D, Boyce JM. Hand hygiene and patient care: pursuing the Semmelweis legacy. *Lancet Infect Dis* 2001;**1**:9—20.
45. Pittet D, Allegranzi B, Storr J. The WHO clean care is safer care programme: field-testing to enhance sustainability and spread of hand hygiene improvements. *J Infect Public Health* 2008;**1**: 4—10.
46. CDC. Reduction in central line-associated bloodstream infections among patients in intensive care units—Pennsylvania, April 2001—March 2005. *MMWR* 2005;**54**:1013—6.
47. Pronovost P, Needham D, Berenholtz S, Sinopoli D, Chu H, Cosgrove S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med* 2006;**355**: 2725—32.
48. Department of Health and Human Services. *Action plan to prevent healthcare-associated infections*. Available from:

http://www.hhs.gov/news/press/2009pres/01/20090106a.html; 2009.
49. Agency for Healthcare Research and Qualit. *AHRQ projects to prevent healthcare-associated infections*. Available from: http://www.ahrq.gov/qual/haify10.pdf; 2010.
50. Michgen Health & Hospital Association. *MHA Keystone: Intensive Care Unit (ICU)*. Available from: http://www.mhakeystonecenter.org/icu_overview.htm; 2010.
51. Vital signs: central line-associated blood stream infections—United States, 2001, 2008, and 2009. *MMWR Morb Mortal Wkly Rep* 2011;**60**:243–8.
52. Render ML, Hasselbeck R, Freyberg RW, Hofer TP, Sales AE, Almenoff PL. Reduction of central line infections in Veterans Administration intensive care units: an observational cohort using a central infrastructure to support learning and improvement. *BMJ Qual Saf* 2011.
53. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis* 2011;**52**:e162–93.
54. Gould CV, Umscheid CA, Agarwal RK, Kuntz G, Pegues DA. Guideline for prevention of catheter-associated urinary tract infections 2009. *Infect Control Hosp Epidemiol* 2010;**31**:319–26.
55. Tablan OC, Anderson LJ, Besser R, Bridges C, Hajjeh R. Guidelines for preventing health-care–associated pneumonia, 2003: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. *MMWR Recomm Rep* 2004;**53**:1–36.
56. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol* 1999;**20**:250–78. quiz 79–80.
57. Taiwan FDA. *Pharmaceutical affairs act*. Available from: http://www.fda.gov.tw/files/people_laws/200507_Pharmaceutical%20Affairs%20Act.doc; 2005.
58. Taiwan CDC. *Communicable diseases and prevention*. Available from: http://www.cdc.gov.tw/lp.asp?ctNode=1807&CtUnit=991&BaseDSD=7&mp=1; 2010.