Reports on Surveillance of Antimicrobial Resistance in Individual Countries

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In preparation for the meeting of the World Health Organization Working Group on Monitoring and Management of Bacterial Resistance to Antimicrobial Agents, representatives of 10 countries were asked to provide brief reports on the status of surveillance in their countries. Some gave extensive information on the methods used to test susceptibility of nosocomial pathogens to a variety of antibiotics; some described in detail the network of reference laboratories available to hospitals and individual clinicians for monitoring, identifying, and testing infectious agents; others chose to describe how their countries deal with the resistance of the most frequently isolated pathogen to a commonly used drug. The following summary of these reports shows the broad range of problems encountered and solutions undertaken by these 10 countries in dealing with the increasingly alarming problem of bacterial resistance to antimicrobial agents.

Algeria

The Service of Medical Bacteriology, Antibiotherapy, and Nosocomial Infections at the Institut Pasteur d'Alger in Algiers is an antibiotic-resistance reference center for the country. Among its activities are the laboratory identification of resistant isolates submitted from hospitals and private laboratories; the provision of specialized laboratory teams to assist hospitals during outbreaks of nosocomial infection and to serve as diagnostic and therapeutic consultants during epidemics; the transmission of information on antibiotic resistance as well as recommendations for action to the Ministry of Health; the compilation of booklets containing current information on bacterial antibiotic resistance; and the publication of regular reports informing clinicians about new antibiotics.

Once an isolate has been identified as resistant, it is sent to the antibiotherapy and genetics laboratory, where its resistance is confirmed and genetic studies are undertaken. A molecular microbiology laboratory has recently been equipped; although the costliness of reagents and enzymes remains problematic, work has begun on DNA extraction and plasmid content analysis. The various β-lactamases are also being studied.

The principal pathogenic bacterial species that have been found to be resistant in Algeria are Vibrio cholerae El Tor, Neisseria gonorrhoeae, Streptococcus species, Salmonella species (including Salmonella typhi), Shigella species, and Staphylococcus aureus. Although most strains of V. cholerae El Tor isolated between 1989 and 1992 were susceptible to antibiotics, all those isolated from an epidemic that followed flooding in the northeastern community of Sétif in September 1994 were resistant to streptomycin, chloramphenicol, tetracyclines, sulfonamides, trimethoprim, and the furans. These strains were susceptible to ampicillin and erythromycin.

All 10 antibiotic-resistant strains of N. gonorrhoeae isolated between 1991 and 1994 (three of them acquired abroad) were resistant to penicillin. One strain was also resistant to tetracycline, and one showed multiple-drug resistance.

Forty streptococcal strains with high-level resistance to aminoglycosides were identified in 1993. In addition, four strains of Streptococcus pneumoniae have exhibited intermediate resistance to penicillin since 1992.

The Salmonella isolates shown to be resistant to multiple antibiotics include both recently appearing “minor” species, such as Salmonella mbandaka and Salmonella kedougou, and S. typhi, but rates of resistance in S. typhi remain low.

The resistance of S. aureus to the aminoglycosides and the lincomycins increased in the early 1900s. However, all strains of S. aureus tested were susceptible to quinolones and vancomycin.

Like Salmonella isolates, those of Shigella species have displayed several patterns of multiple-antibiotic resistance since the mid-1970s. Trimethoprim resistance remains very rare, and quinolone resistance has not yet been documented.

People's Republic of China

In 1993 a total of 6,286 isolates from Shanghai hospitals were tested for antimicrobial resistance; the indicator organisms and antimicrobial agents recommended by the World Health Organization (WHO) were used in this study. A number of species were also tested for the production of β-lactamase.

Of the isolates evaluated, ~84% were gram-negative and 16% were gram-positive. Rates of production of β-lactamase were high among isolates of a number of species, including...
Pseudomonas species (100%), S. aureus (95%), Klebsiella pneumoniae (95%), Enterobacter species (90%), Acinetobacter species (90%), Escherichia coli (88%), Serratia species (87%), Shigella flexneri (84%), and coagulase-negative staphylococci (83%). An increase over past figures for resistance to quinolones was noted, particularly among E. coli and among Enterobacter, Staphylococcus, and Citrobacter species.

Most strains of methicillin-resistant S. aureus were resistant to cephalosporins, amikacin, and quinolones, whereas most strains of methicillin-susceptible S. aureus were still susceptible to these drugs. All staphylococcal strains were highly susceptible to vancomycin; 5% of enterococcal strains were resistant to this agent. Among isolates of E. coli, rates of resistance not only to the quinolones but also to piperacillin and gentamicin increased markedly to >50%. Most Enterobacteriaceae were found to be susceptible to cefotaxime, the third-generation cephalosporin tested.

Czech Republic

Computer monitoring of antibiotic resistance in the Czech Republic dates back to 1974, when a surveillance study of isolates from inpatients at the Teaching Hospital in Prague was undertaken. Later, in the early 1980s, a systematic study of antibiotic resistance at 14 hospitals in the nation was begun under the sponsorship of the Ministry of Health. The methodology used in this study to monitor resistance was refined in 1989, and surveillance continues today.

Strains are selected, identified, and examined for susceptibility by standardized methods at public health laboratories. In some instances, the surveillance of time-limited samples (e.g., community isolates of S. pneumoniae and Haemophilus influenzae) is performed. In the first part of the year, an annual report on the preceding year's data is published and distributed free to all laboratories in the Czech Republic and to all other interested parties.

Studies are limited to the most relevant kinds of specimens, bacterial species, and wards. Isolates are collected from at least four types of specimens: blood, urine, pus, and sputum. The wards included are surgical, urologic, gynecologic, medical, pediatric, intensive care, and burn. In 1993 the 30,917 strains processed included mostly isolates of E. coli, K. pneumoniae, Enterobacter cloacae, Serratia marcescens, Proteus mirabilis, Providencia retgeri, Pseudomonas aeruginosa, Acinetobacter baumannii, H. influenzae, S. aureus, coagulase-negative staphylococci, S. pneumoniae, Streptococcus pyogenes, and enterococci. Levels and patterns of resistance vary with the hospital, but the highest rates of resistance are in burn units, surgery departments, and intensive care units.

In the future, areas of emphasis in the surveillance program will include patterns of multiple resistance and frequency distributions of MICs or zone diameters. Other goals include prospective studies of new drugs, participation in a global monitoring system, prediction of trends, and dissemination of all this information through all means available.

United Kingdom

Surveillance of key pathogens is carried out by individual reference laboratories in the Public Health Laboratory Service (PHLS). The Meningococcal Reference Unit has observed a trend in 11,000 isolates tested over the last decade for decreased penicillin susceptibility (without occurrence of resistance such as would demand a change of treatment policy), consistent levels of sulfonamide resistance (30%), but rare occurrence of rifampin resistance and no quinolone resistance. The Gonococcus Reference Unit correlates antibiotic resistance in referred isolates with their geographical origin. New cases of tuberculosis are notified to the National TB Reference Laboratory, which checks the test results in isolates showing primary resistance; such strains are still uncommon in the United Kingdom. The Anaerobe Reference Unit tests isolates submitted by 12 "sensitive" laboratories in a rolling program. Bacteroides species have shown consistent susceptibility to metronidazole and imipenem; Clostridium perfringens isolates have been generally susceptible to commonly prescribed antibiotics (except for tetracycline, 40% resistance).

The Antibiotic Reference Unit in the PHLS Laboratory of Hospital Infection monitors the levels and mechanisms of resistance in referred isolates, with currently a particular emphasis on methicillin-resistant S. aureus (MRSA), S. pneumoniae, S. pyogenes, and Enterococcus species. These data are supplemented by periodic (e.g., over a 2-week period) surveys of all isolates encountered by the PHLS network of 53 laboratories. In addition, clinical laboratories notify their susceptibility test results on isolates from patients with bacteremia and meningitis to provide a large and geographically representative data base for analysis. These data receive the validation that is essential for acceptance of such information from the results of the PHLS National External Quality Assurance Scheme (NEQAS), to which almost all laboratories in the United Kingdom subscribe (as well as many others in Europe). Typing data and antibiotic data are being merged in the data bases. The spread of specific epidemic clones of MRSA, vancomycin-resistant Enterococcus species, and gram-negative rods such as P. aeruginosa and Klebsiella species is well established, and surveillance is being enhanced by computerized analyses of molecular typing data and increased data exchange with referring hospitals.

Government committees have repeatedly recommended the continuing need to monitor antibiotic resistance in enteric pathogenic bacteria from humans and food animals and have recognized the usefulness of this information in policy formulation. To that end, the Laboratory of Enteric Pathogens provides a national reference facility to which public health laboratories, hospital laboratories, and veterinary and food manufacturers’ laboratories throughout England and Wales refer strains of en-
teric bacteria (except Campylobacter) for identification, detailed typing, and antibiogram testing (R-typing).

Salmonella. In 1993 about 31,000 strains from human infections were serotyped and, if applicable, subjected to phage typing and molecular typing; their resistances to a wide range of antimicrobials were determined. Of 194 isolates of S. typhi examined, 25% were resistant to chloramphenicol, in contrast to 0.9% in 1988. Most chloramphenicol-resistant strains were also resistant to ampicillin and trimethoprim (i.e., they were multiresistant strains). Most of the multiresistant strains were found in travelers returning from the Indian subcontinent, particularly Pakistan and India. Multidrug resistance may be related to the poorly controlled use of antibiotics in developing countries. Because multidrug resistance included resistance to ampicillin and trimethoprim, ciprofloxacin is now the recommended drug for treating patients with typhoid in the United Kingdom, except for young children.

Among nontyphoidal salmonellae, multiple resistance (to four or more antimicrobials) is most prevalent in Salmonella typhimurium (39%) and Salmonella virchow (14%) and least prevalent in Salmonella enteritidis (0.4%). In S. typhimurium, multidrug resistance is seen in a wide range of phage types, but definitive phage type (DT) 104 now dominates. Because the three phage types of S. typhimurium in which multidrug resistance has been most frequently identified are those most common in cattle, the overuse and often unnecessary use of antimicrobials in bovine animal husbandry are considered important factors. In contrast, in S. virchow multidrug resistance is most common in a number of phage types associated with poultry. A further concern regarding this serotype is the increasing incidence of resistance to ciprofloxacin, possibly related to the use of fluoroquinolones in poultry; fluoroquinolones were licensed for veterinary use in the United Kingdom in 1993.

Shigella. From 1989 to 1991, just over 2,300 strains of Shigella dysenteriae, S. flexneri, and Shigella boydii were isolated from patients in England and Wales, most of whom had recently traveled in another country. Ninety-seven percent of strains were drug resistant (84% were multidrug-resistant), most commonly to tetracyclines (75%), chloramphenicol (63%), trimethoprim (58%), and ampicillin (52%). Resistance to nalidixic acid was 0.1% among all strains, but it was 2.0% among S. dysenteriae isolates.

Escherichia coli O157. Between 1991 and 1993, only 11%–19% of strains of this important pathogen were resistant to any agent, and multiple resistance was very rare.

Future Concerns

The primary concerns in the United Kingdom are the occurrence of chloramphenicol resistance, which is often associated with resistance to ampicillin and trimethoprim, in S. typhi; the continuing high incidence of multidrug resistance in S. typhimurium, which is probably related to the overuse of antibiotics in bovine husbandry; and the appearance of ciprofloxacin resistance in S. virchow. Multiple resistance of Shigella species in infections acquired abroad—in particular, resistance to 4-quinolone drugs, especially in S. dysenteriae type 1 (Shiga's bacillus)—is also a concern. The latter is probably due to the increasing use of 4-quinolones in Southeast Asia and Africa.

Finland

There has been a resurgence of infections due to group A streptococci (GAS) in recent years in Finland, as there has been throughout the world. Fortunately, GAS have remained susceptible to penicillin, but they have acquired resistance to the second choice, erythromycin, which is widely used for treatment of patients allergic to penicillin. Although erythromycin resistance in GAS is uncommon in most parts of the world, resistance increased from 5% in 1988 to 13% in 1990 and 16% in 1992, and it remained on that level in 1994. At the end of 1991, recommendations were made to avoid use of erythromycin for patients with streptococcal pharyngitis and skin infections.

However, during the same time, while erythromycin resistance increased among throat isolates from 11% in 1990 to 17% in 1992 and 18% in 1994, it decreased among pus isolates, from 19% in 1990 to 14% in 1992 and 6% in 1994. The reason for these trends is not known. Many serotypes are represented among the erythromycin-resistant GAS in Finland, and the possible correlation of this increase/decrease pattern to variations in serotypes remains to be studied. In the meantime, an analysis of the development of resistance in relation to local erythromycin consumption is under way.

Since erythromycin resistance persists among GAS isolates in Finland and the emergence of erythromycin-resistant strains may occur rapidly, frequent susceptibility testing remains a necessity in Finland as in other countries.

Hungary

In the mid-1970s the Hungarian National Institute of Hygiene established a surveillance system simultaneously with the elaboration of an efficient laboratory quality control system. The laboratories of the public health network have provided data on the susceptibility of pathogenic bacteria to a great variety of antibiotics since 1974. The surveillance system follows the emergence of and changes in resistance, oversees the standardization of resistance tests, and surveys the introduction of new testing methods.

Laboratories of the public health centers of 19 countries and the Central Hospital for Infectious Diseases process 100% of
fetal specimens and 60% of all other clinical specimens in Hungary. These laboratories meet high standards of microbiological practice, working under strict proficiency control in close contact with the National Institute of Hygiene. They work with a uniform reporting system assisted by a nearly uniform computer program. The remaining 40% of clinical specimens are processed by hospital laboratories in closer contact with physicians but in poorer facilities with less-well-trained personnel and no obligation with regard to data processing and reporting. Efforts are being made to involve these hospital laboratories in the surveillance system.

Resistance data are based on disk-diffusion test results. Interpretive zone standards are determined by comparison of inhibition zones with zones of reference strains with MICs identical to the National Committee for Clinical Laboratory Standards susceptibility breakpoint.

According to the latest survey (1993), resistance was much more common in Hungary than elsewhere in Central and Western Europe, the United States, and Japan. There is an extremely high incidence of infections that are caused by penicillin-resistant pneumococci. New therapeutic challenges include ampicillin-resistant *H. influenzae*; multiresistant *Acinetobacter*, *Enterobacter*, and *Serratia* strains in nosocomial infections; and *Enterococcus* species that are resistant to ampicillin and highly resistant to gentamicin.

**Resistance in Gram-Negative Bacteria**

The widespread use of ampicillin in the 1970s and 1980s may account for the high prevalence of resistance to this drug in gram-negative bacteria. Resistance to amoxicillin/clavulanate in several species is 50% lower than that to ampicillin. *E. coli* is the only species that has retained >90% susceptibility to the second- and third-generation cephalosporins.

A significant increase in resistance to gentamicin became evident in 1983, and all of 60 multidrug-resistant strains of *Proteus* species exhibited β-lactamase production. The gradual selection of *Shigella sonnei* resistant to co-trimoxazole resulted in a 91% resistance rate in 1992. Imipenem remains an effective agent against most of the multidrug-resistant bacteria, including *Acinetobacter* species.

**Resistance in Gram-Positive Bacteria**

The resistance profile of gram-positive isolates has also changed in recent years. A 1990 survey found resistance to ampicillin, gentamicin, or both in 29.1%. Only 35% of isolates were susceptible to erythromycin, while only 1% of isolates were resistant to vancomycin. No β-lactamase-producing *Enterococcus* has been isolated yet. Oxacillin has been available only in hospitals and consequently has had limited usage and low resistance rates. Yet, in 1993, 31.5% of coagulase-negative staphylococci were resistant to oxacillin.

Resistance of *S. pneumoniae* to penicillin began as early as 1975, peaked at 50% resistance in 1989, and declined moderately and stabilized from 1990 to 1993. Isolates from pediatric inpatients with respiratory infections and acute otitis media showed 59.4% and 68.6% resistance to penicillin, respectively, in 1993–1994. However, only 1 in 10 or 12 isolates of *S. pneumoniae* from other sites, is resistant.

Isolates of *E. coli* from inpatients and outpatients had comparable rates of drug resistance. The difference was remarkable, however, for wound isolates and for isolates of staphylococci, *P. aeruginosa*, and *Klebsiella*, *Serratia*, *Enterobacter*, and *Acinetobacter* species from intensive care units, surgical wards, and urological units. Gentamicin resistance among gram-positive isolates rose from 1977 to 1983, remained high till 1989, and since then has decreased. There has been no remarkable change in resistance to cephalosporins.

**Future Concerns**

With a population of 10 million and a consumption of nearly 100 million defined daily doses in 1990, each person could have undergone a 10-day course of antibiotic treatment. Yet, the high rate of resistance in *S. pneumoniae* and some gram-negative bacteria is hard to explain. The frequent and injudicious application of antibiotics and the unsatisfactory hygienic conditions in hospitals probably play a role in the selection of resistant bacteria.

What measures are to be taken to change these practices? Three courses of action are recommended for Hungary: (1) provision of more information for clinicians on the principles and practical aspects of antibiotic therapy; (2) introduction of the “consultant microbiologist” system; and (3) accessibility of microbiological investigations to general practitioners in an effort to rationalize the implementation of antibiotic policy. On a global scale, this would mean mandatory standardization of the assessment of resistance by uniform guidelines and breakpoints; imposition of controls on devices, facilities, and reagent kits on the market; and control of protocols of trials launched by pharmaceutical companies. The question of whose responsibilities these activities are remains open.

**India**

Foremost among the various factors that have hindered the monitoring of antimicrobial resistance in India is the lack of a national networking system and of uniformly sound techniques for generating accurate data on susceptibility patterns. Despite these limitations, both multicenter and institution-based projects on issues related to antimicrobial agents and resistance to them have regularly been undertaken.

A prominent center for such projects is the Christian Medical College and Hospital (CMCH) in Vellore, a 1,500-bed tertiary-care center encompassing both community- and hospital-based
practices. The most current information on antibiotic susceptibility profiles at this institution is provided to clinicians through the CMCH monthly newsletter. In addition, relevant information on the most commonly encountered pathogens in the community is compiled and disseminated to practitioners in the district through a health information system.

Data are generally sought for isolates from four categories of infection: (1) community-acquired infections, including invasive disease caused by *S. pneumoniae*, *H. influenzae*, *Neisseria meningitidis*, β-hemolytic *Streptococcus*, *S. typhi*, *V. cholerae*, and *Shigella* species; (2) acute serious hospital-acquired infections, including those due to methicillin-resistant *S. aureus* and *Klebsiella*, *Pseudomonas*, and *Enterococcus* species; (3) infections of undefined origin, caused by organisms such as *E. coli* and gram-negative anaerobic bacilli; and (4) infections in immunocompromised patients.

The studies conducted so far have made clear the necessity for systematic and judicious action to curb the evolution of antimicrobial resistance in India. Efforts are already being made to this end and include the advocacy of rational drug use, which is promoted through workshops for clinical staff members at all levels; continued active surveillance of resistance; quality control of resistance determinations; studies of newer mechanisms of resistance; formulation and implementation of clear hospital policies on antibiotic use under the direction of the infection control committee and the pharmacy and therapeutic committee; continued education of clinicians through the microbiology newsletter and the health information system; and periodic workshops at the national level aimed at increasing awareness and exchanging ideas in this field.

**Russia**

The Centre for Epidemiological Surveillance of Antimicrobial Resistance in Microorganisms was founded at the Central Russia Institute of Epidemiology in 1986 to monitor certain microorganisms whose etiologic significance differs in health facilities of various types and from one geographic area to another. The base institutions — hospitals specializing in burns, septic diseases, obstetrics, and surgery in cities across the former USSR (Moscow, Omsk, Vologda, Smolensk, Minsk, Samarkand, Vnujius, and Tbilisi) — provide information on hospital-acquired infections in the form of a “strain passport” for each isolate, indicating the patient’s name, sex, and age; diagnosis; material tested; taxonomic category of pathogen; quantity isolated; and drug resistance of the isolate. The center monitors the activities of the base institutions, conducts staff training, collects and analyzes data (using WHONET programs and WHO guidelines), conducts genetic research, maintains communications with the base institutions, and reports information to the WHO Center in Geneva.

**Resistant Strains**

Eighty-six percent of *Klebsiella* strains tested were multidrug-resistant: 90% of *K. pneumoniae* strains were resistant to rifampin and amoxicillin, 80% to carbencillin and chloramphenicol, 60% to tetracycline and cephalothin, and 35% to gentamicin. Not more than 7% of strains were resistant to amikacin and cefotaxime.

All strains of *P. aeruginosa* studied were multidrug-resistant, and 87% of them were simultaneously resistant to 5%–10% of drugs: >90% of strains were resistant to amoxicillin, cefazolin, cefotaxime, and ciprofloxacin, and >85% to rifampin and gentamicin. Fewer than 1% of strains studied were resistant to amikacin.

Likewise, all strains of *S. marcescens* were multidrug-resistant: >90% to β-lactam drugs, 80% to first- and second-generation cephalosporins, >75% to chloramphenicol and aminoglycosides, and 40% to cefotaxime, a third-generation cephalosporin. Not more than 10% were resistant to amikacin.

While 85% of *E. coli* isolates were resistant to ampicillin, 80% to tetracycline, 60% to chloramphenicol and cephalothin, and 35% to kanamycin, only 5% were resistant to amikacin and none were resistant to cefotaxime, polymyxin, and nalidixic acid.

Ninety-four percent of *S. aureus* strains were resistant to at least one antibiotic: >95% to penicillins, 38% to erythromycin, 35% to tetracycline, and 30% to chloramphenicol.

A special place among nosocomial pathogens belongs to methicillin-resistant *S. aureus* (MRSA), which is responsible for the epidemic spread of staphylococcal infections. Although MRSA represents only 14% of the *S. aureus* isolates studied, it is distinguished by its resistance to most clinically used antibiotics and its nonsusceptibility to phages in the international phage-typing kit, thus making treatment very difficult and impeding epidemiological analysis.

From 1986 through 1991, 48 nosocomial complications were caused by MRSA in the Minsk burn center. Use of antibiograms in phage typing, study of enterotoxigenicity, and examination of plasmid profiles showed that these complications were caused by four clone strains. Exogenous infection was ruled out, and therapy was tailored to the individual strains. No suppuration of burn wounds has been observed since 1992. It should be emphasized that exceptional use of antibiograms as markers is not effective when decoding outbreaks of nosocomial infections.

**Future Concerns**

Continued surveillance of resistance will provide a greater base of information, making it possible to assess the dynamics of regional differences in nosocomial infection, the resistance levels of leading pathogens, and the speed with which resistance develops to new drugs, all of which will inform antibiotic policies.
Sweden

While the Nordic countries have always had remarkably low antibiotic resistance rates, for reasons not fully elucidated, the increasing spread of antibiotic resistance in pathogenic bacteria is a cause of great concern to everyone involved in patient care and health service. Annual surveillance of antibiotic resistance is performed in Sweden under the auspices of the Swedish Reference Group on Antibiotics (SRGA) and organized by the Technical Subcommittee of the SRGA, the SRGA-M. The annual surveillance is targeted to critical combinations of antibiotics and bacterial species and to combinations for long-term monitoring.

All laboratories use the disk-diffusion method for susceptibility testing of clinical isolates, and interpretive MIC limits and species-specific zone diameter breakpoints are set by the SRGA on the basis of methodological studies by the SRGA-M. Although there is some variation in resistance rates from laboratory to laboratory, no conclusions can be drawn about geographical differences in resistance within the country.

Antibiotic Consumption

Drug consumption in Sweden is monitored by the National Corporation of Swedish Pharmacies, Apoteksbolaget, a commercial company running 865 pharmacies that is two-thirds owned by the government. Drug consumption amounts to 9.9% of the total health care costs in the country, and antinfective drugs make up 10.1% of the total drug costs. Sweden has only 3,200 licensed drugs, as compared with Switzerland, which has 25,000 drugs or drug combinations. In 1993 the mean for the whole country was 20.3 defined daily doses per 1,000 inhabitants/day. Regional differences in consumption were positively correlated with population density.

The problems facing many practitioners and specialists regarding choice of antibiotic and the possible emergence of resistance are reflected in ongoing discussions in the Journal of the Swedish Society of Medicine and in the individual societies of different specialties. The information available on health statistics, drug usage, and antibiotic resistance among bacteria provides the necessary background for these discussions.

Organization and Practical Aspects of Surveillance

SRGA members are elected by the following societies of the Swedish Society of Medicine: the Swedish Society of Medical Microbiology, the Swedish Society of Infectious Diseases, the Swedish Society of Pediatrics, and the Swedish Society of Clinical Pharmacology. The SRGA meets three to five times a year to decide MIC limits for new or established antibiotics, to set interpretive breakpoints for different groups of bacterial species, and to write the professional information about the drugs in question.

The SRGA-M meets four or five times a year to organize and collect methodological information on old and new antibiotics and their performance in susceptibility tests. It produces inhibition-zone-diameter values for clinical isolates and reference strains at five selected microbiology laboratories, MIC values for a certain number of clinical isolates, and histograms of zone-diameter values and MIC data.

These histograms are used with data from drug studies, clinical trials, and in vitro susceptibility tests to work out the interpretive zone-diameter breakpoints for the major groups of bacterial species: (1) Enterobacteriaceae and Acinetobacter species; (2) P. aeruginosa and other pseudomonads; (3) S. aureus and coagulase-negative staphylococci; (4) enterococci; (5) streptococci and pneumococci; (6) H. influenzae; (7) Listeria monocytogenes; and (8) Corynebacterium jeikeium and Corynebacterium urealyticum. The SRGA-M gives courses on methodological aspects of disk-diffusion testing and new technical developments for clinicians, laboratory technicians, and drug company representatives.

The SRGA has abandoned the error rate–bounded method of setting breakpoints in favor of examining each species separately, in order to eliminate errors that the former method cannot handle. When a new antibiotic is introduced in Sweden, the SRGA scrutinizes documentation on it in order to recommend MIC limits, produce inhibition-zone histograms, and set zone-diameter breakpoints. Problem combinations of antibiotics and species are identified, and such species are investigated further in order to make optimal treatment recommendations. Additional tests are included in the annual surveillance to assess the quality of disk-diffusion testing. Microbiology laboratories also perform their own quality assessment, particularly for validation of the interpretive breakpoints for separating strains with different susceptibilities.

Special Technical Considerations

The Swedish approach differs from standard susceptibility-testing methods in two aspects: (1) introduction of species-specific breakpoints on a larger scale as a logical consequence of histogram studies and (2) further development of disk-diffusion testing and introduction of single-strain regression analysis (SRA). The understanding of the theory of the test and the new equations developed may provide new means to calibrate the disk-diffusion test in the individual laboratory.

Another new approach to susceptibility testing, the Etest (AB BIODISK, Solna, Sweden), is easily understood in view of theoretical considerations. It consists of a calibrated antibiotic strip for estimation of MIC values on the basis of determination of the “‘critical concentration.’” The Etest is, in fact, a diffusion method that measures the concentration of antibiotic on the strip where the inhibition zone is zero, which corresponds to the MIC. This approach has been used with good results.
International surveillance of bacterial resistance to antibiotics relies on accurate determinations of susceptibility. While the disk-diffusion method provides accurate results with species-specific interpretive zone-diameter breakpoints, the underlying theoretical basis for diffusion methods deserves further attention in light of SRA calculations and other recent developments.

Venezuela

A network for the surveillance of resistance to antimicrobial agents in routine clinical bacterial isolates from both inpatients and outpatients was established in Venezuela in 1988. As of 1993, 19 hospitals in seven regions were participating in the program, which has two main objectives in addition to the surveillance of resistance: identification of the mechanisms of resistance and formulation of recommendations for local and regional authorities regarding antibiotic use.

The surveillance network has so far identified several specific problems, including (1) an increase in resistance to oxacillin in Staphylococcus species; (2) an increase in resistance to commonly used antibiotics (ampicillin, trimethoprim-sulfamethoxazole, and first-generation cephalosporins) in E. coli; (3) an increase in resistance to third-generation cephalosporins in K. pneumoniae; and (4) an increase in resistance to quinolones in both gram-positive and gram-negative bacteria. Other points of interest include the high level of resistance to first-line anti-pseudomonal agents in P. aeruginosa and the apparent introduction of extended-spectrum β-lactamases into strains of K. pneumoniae.

Appendix

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