SUSCEPTIBILITY OF *STREPTOCOCCUS PNEUMONIAE* ISOLATED FROM THE RESPIRATORY TRACT OF HOSPITALIZED CHILDREN WITH RESPIRATORY TRACT INFECTIONS

SLOBODNIKOVA L, KOTULOVA D, KAPELLEROVA A, KOTZIGOVA A

CITLIVOSŤ KMEŇOV *STREPTOCOCCUS PNEUMONIAE* IZOLOVANÝCH Z RESPIRAČNÉHO TRAKTU HOSPITALIZOVANÝCH DETÍ S RESPIRAČNÝMI INFEKCIAMI

Abstract

Slobodnikova L, Kotulova D, Kapellerova A, Kotzigova A: Susceptibility of *Streptococcus pneumoniae* isolated from the respiratory tract of hospitalized children with respiratory tract infections
Bratisl Lek Listy 1999; 100 (11): 587–592

The most frequent nasopharyngeal carriers of *Streptococcus pneumoniae* are young children. Frequent use of antimicrobial therapy in children facilitates the selection of penicillin-resistant strains in this population. These strains, especially if higly resistant, may cause serious therapeutic problems.
Aim of the study was to monitor penicillin- and multidrug-resistant *S. pneumoniae* strains in hospitalized children with respiratory tract infections.
Hospitalized children up to five years were examined for *S. pneumoniae* presence in their upper respiratory tract. Susceptibility to penicillin, erythromycin, trimethoprim/sulfamethoxazole, tetracycline, and chloramphenicol was determined by the disk-diffusion method. The minimal inhibitory concentrations (MIC) of penicillin, erythromycin and trimethoprim/sulfamethoxazole were measured by the E-test.
***S. pneumoniae* strain was isolated from 60 (34.7 %) out of 173 microbiologically examined children; 2 different strains were isolated in 9 cases. Nine strains (13.0 %) were penicillin resistant with MICs ranging from 1.5 to 8 mg/L, and 17 strains (24.6 %) had intermediate susceptibility. Seventeen (24.6 %) strains were erythromycin resistant (MIC ≥1 mg/L). Eighteen strains (26.1 %) were resistant and 7 strains (10.1 %) were intermediately susceptible to trimethoprim/sulfamethoxazole. Ten strains (14.5 %) were not susceptible to tetracycline, and 11 (15.9 %) to chloramphenicol. Nonsusceptibility (resistance or intermediate susceptibility) to the tested antimicrobials was more prevalent in penicillin-nonsusceptible strains.**

Institute of Microbiology, School of Medicine, Comenius University, Bratislava. mikrobio@fmed.uniba.sk
2nd Department of Paediatrics, School of Medicine, Comenius University in Bratislava
Address for correspondence: L. Slobodnikova, RND, PhD, Institute of Microbiology, Faculty of Medicine, Comenius University, Sasinkova 4, SK-811 08 Bratislava, Slovakia.
Phone: +421.7.58357 207, Fax: +421.7.58357 583

Abstrakt

Slobodníková L., Kotulová D., Kapellerová A., Kotzigová A.: Citlivosť kmeňov *Streptococcus pneumoniae* izolovaných z respiračného traktu hospitalizovaných detí s respiračnými infekciami
Bratisl. lek. Listy, 100, 1999, č. 11, s. 587–592

Najčastejšími nazofaryngovými nosičmi *S. pneumoniae* sú malé deti. Časté používanie antimikrobiálnej terapie umožňuje selekciu kmeňov rezistentných proti penicilínu v tejto populácii. Takéto kmene, najmä ak sú vysoko rezistentné, môžu byť vážnym terapeutickým problémom.
Cieľom práce bolo monitorovanie výskytu kmeňov *S. pneumoniae* rezistentných proti penicilínu a proti ostatným antimikrobiálnym liečivám u hospitalizovaných detí s respiračnými infekciami.
Vyšetroval sa výskyt kmeňov *S. pneumoniae* v horných dýchacích cestách u hospitalizovaných detí vo veku do 5 rokov. Citlivosť izolovaných kmeňov na penicilín, erytromycín, trimetoprim/sulfametoxazol, tetracyklín a chloramfenikol sa testovala diskovým difúznym testom. Minimálne inhibičné koncentrácie (MIC) penicilínu, erytromycínu a trimetoprimu/sulfametoxazolu sa testovala E-testom.
Z celkového počtu 173 mikrobiologicky vyšetrených detí sa kmeň *S. pneumoniae* izoloval v 60 prípadoch (34,7 %). V 9 prípadoch sa izolovali dva rôzne kmene *S. pneumoniae*. 9 kmeňov (13 %) bolo rezistentných proti penicilínu s MIC v intervale 1,5—8 mg/L a 17 kmeňov (24,6 %) malo intermediárnu citlivosť. 17 kmeňov (24,6 %) bolo rezistentných proti erytromycínu (MIC ≥1 mg/L). 18 kmeňov (26,1 %) bolo rezistentných a 7 kmeňov intermediárne citlivých proti trimetoprimu/sulfametoxazolu. 10 kmeňov (14,5 %) nebolo citlivých na tetracyklín a 11 kmeňov (15,9 %) na chloramfenikol. Zmenená citlivosť (rezistencia alebo intermediárna citlivosť) na testované antimikrobiálne liečivá bola častejšia u kmeňov rezistentných alebo intermediárne citlivých na penicilín.

Mikrobiologický ústav Lekárskej fakulty Univerzity Komenského v Bratislave a 2. detská klinika Lekárskej fakulty Univerzity Komenského v Bratislave
Adresa: RNDr. L. Slobodníková, CSc., Mikrobiologický ústav LFUK, Sasinkova 4, 811 08 Bratislava 1.

The current level of *S. pneumoniae* resistant to antimicrobial drugs in children with respiratory tract infections in the hospital department monitored in our study do not cause problems in the choice of antibacterial therapy. Penicillins still can remain the drug of choice in cases when typical bacterial causing agents of respiratory tract infections are suspected. *(Tab. 3, Fig. 2, Ref. 31.)*
Key words: *Streptococcus pneumoniae*, penicillin resistance, respiratory tract infections, hospitalized children.

Súčasný výskyt kmeňov *S. pneumoniae* rezistentných proti antimikrobiálnym liečivám u detí s respiračnými infekciami na sledovanej klinike nespôsobuje problémy pri voľbe antimikrobiálnej terapie. Penicilínové antibiotiká stále ostávajú liekom voľby v prípadoch, keď sa predpokladá typický bakteriálny pôvodca respiračnej infekcie. *(Tab.* 3*, obr.* 2*, lit.* 31*.)*
Kľúčové slová: *Streptococcus pneumoniae*, rezistencia *proti* penicilínu, respiračné infekcie, hospitalizované deti.

Streptococcus pneumoniae can be asymptomatically carried on nasopharyngeal mucosa of healthy persons. The carriers vary according to the age with higher rates in children. However, pneumococci are often isolated as the causing agents from serious diseases (pneumonia, otitis media, sinusitis, meningitis, bacteremia) (14). Young children represent one of the important risk groups (19).

Penicillin used to be the drug of choice for pneumococcal infections in the past. The first case of penicillin-resistant S. *pneumoniae* strain in patient was reported from Australia in 1967 (9). Since that time, penicillin-resistant pneumococci have emerged in most countries and many of this strains have acquired resistance to other antimicrobial drugs in addition to penicillin (1).

First penicillin-resistant and multidrug-resistant S. *pneumoniae* strains in Slovak Republic were isolated in 1981, followed by isolation of highly penicillin-resistant and multidrug-resistant serotype 14 pneumococcal strain in 1983 (13, 20).

Penicillin resistance in S. *pneumoniae* is due to alteration in the penicillin-binding proteins — the target site of penicillin and other betalactam agents (25). Increasing prevalence of such strains may significantly complicate the therapy of pneumococcal infections.

The present study deals with monitoring of penicillin- and multidrug-resistant S. *pneumoniae* strains in children with respiratory tract infections.

Material and methods

173 children up to 5 years (30 girls and 63 boys) hospitalized at the 2nd Pediatric Department of the School of Medicine, Comenius University in Bratislava, Slovak Republic, with acute respiratory tract infection (rhinitis, nasopharyngitis, pharyngitis, tonsilitis, laryngitis, epiglottitis, otitis media, pneumonia, bronchitis, tracheitis) or other diagnosis complicated by respiratory tract infection were investigated for S. *pneumoniae* presence on their respiratory tract mucosa.

Upper respiratory tract secretions were obtained using sterile calcium alginate-tipped swabs on aluminium shafts. Beside nasopharyngeal swabs, nasal and tonsilopharyngeal swabs were collected in some cases. The swabs were immediately plated on Mueller—Hinton agar with 5 % sheep blood and 0,5 mg/L of gentamicin for selective cultivation of streptococci. The inoculated agar plates were transported to laboratory for cultivation, and the swabs for further inoculation to nonselective 5 % sheep blood agar, Levinthal agar with 30 g vancomycine disk for selective cultivation of haemophili, Endo agar, and Sabouraud agar.

The streaked agar plates were incubated at 36 ˚C for 24 to 48 hours (blood agar, Mueller—Hinton blood agar, and Levinthal agar in 5 % CO_2 atmosphere).

Standard methods were used for identification of all isolates with possible role in respiratory tract diseases (18, 24).

Alpha-haemolytic colonies with typical morphology were presumptively identified as S. *pneumoniae* after detection of their susceptibility to optochin and confirmed by bile solubility testing and pneumococcal capsular antigen detection by latex agglutination test Slidex pneumo-kit (Bio-Mérieux).

S. *pneumoniae* strains were screened for susceptibility to penicillin with a 1 µg oxacillin disk by disk-diffusion method on Mueller—Hinton agar with 5 % sheep blood. Penicillin minimal inhibitory concentration (MIC) was determined in all strains with oxacillin zone sizes of ≤19 mm, as the disk test does not distinguish penicillin intermediate strains from strains that are penicillin-resistant (31).

Penicillin MICs of the nonsusceptible strains were determined by the E-test (AB Biodisk), consisting of a strip impregnated with penicillin G in a continual concentration gradient from 0.002 to 32 mg/L. Mueller-Hinton agar with 5 % of lysed horse blood was used in the test. The plates were incubated overnight at 36 ˚C in 5 % CO_2 atmosphere and read as instructed by the E-test manufacturer (29).

The tested S. *pneumoniae* strains with MICs ≤0.06 mg/L were defined as susceptible, with 1 mg/L ≥ MIC ≥ 0.1 mg/L as intermediate, and with MIC ≥ 2.0 mg/L as resistant, according to the National Committee for Clinical Laboratory Standards criteria (31).

However, strains with MICs between 0.06 and 0.1 mg/L and between 0.1 and 2 mg/L (after reading from the continual concentration gradient on the E-test strip) were included into categories of susceptibility (susceptible, intermediate, resistant) after rounding up to the closest upper dilution before susceptibility categorization, as suggested by the E-test manufacturer (29).

Susceptibility to erythromycin, trimethoprim/sulfamethoxazole, tetracycline, and chloramphenicol was determined by the disk-diffusion method according to the NCCLS guidelines (30, 31). MICs of erythromycin and trimethoprim/sulfamethoxazole of the strains nonsusceptible in the disk-diffusion test were measured by the E-test and interpreted according to the NCCLS criteria (31), after approximation described above, when necessary.

Results

Streptococcus pneumoniae was isolated from the upper respiratory tract mucosa of 60 (34.7 %) out of the 173 microbiologically examined children. Two different strains were isolated in 9 cases. Other bacterial species with possible role in respiratory tract infections (*Haemophilus influenzae, Staphylococcus aureus, Moraxella catarrhalis*, gramnegative rods or beta-haemolytic streptococci) were isolated from 34 (52.5 %) of *S. pneumoniae*-positi-

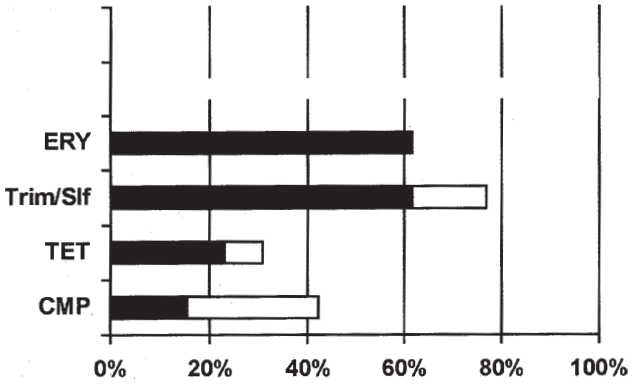

Fig. 1. Susceptibility of the 26 *S. pneumoniae* strains with changed susceptibility to penicillin. ERY — erythromycin, Trim/Slf — trimethoprim/sulfamethoxazole, TET — tetracycline, CMP — chloramphenicol. □ — intermediate, ■ — resistant.
Fig. 1. Citlivosť 26 kmeňov *S. pneumoniae* so zmenenou citlivosťou na penicilín. ERY — erytromycín, Trim/Slf — trimethoprim/sulfamethoxazole, TET — tetracyklín, CMP — chloramfenikol. □ — intermediárny, ■ — rezistentný.

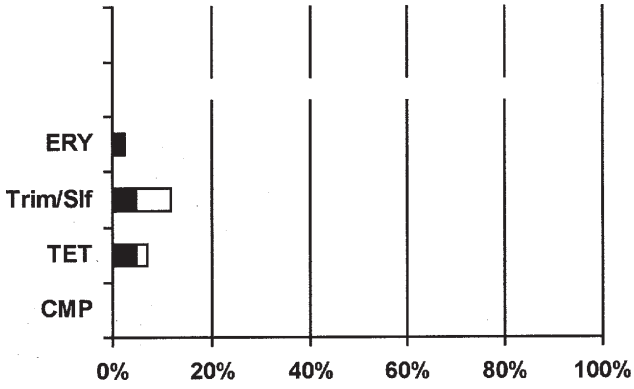

Fig. 2. Susceptibility values of the 43 *S. pneumoniae* strains susceptible to penicillin. ERY — erythromycin, Trim/Slf — trimethoprim/sulfamethoxazole, TET — tetracycline, CMP — chloramphenicol. □ — intermediate, ■ — resistant.
Obr. 2. Citlivosť 43 kmeňov *S. pneumoniae* citlivých na penicilín. ERY — erytromycín, Trim/Slf — trimethoprim/sulfamethoxazole, TET — tetracyklín, CMP — chloramfenikol. □ — intermediárny, ■ — rezistentný.

ve samples. Pathogenic or potentially pathogenic bacterial species other than *S. pneumoniae* were isolated from the respiratory tract of 76 (43.9 %) patients. In 37 (21.4 %) children physiological flora was found only.

Thirty-five (50.7 %) out of 69 isolated *S. pneumoniae* strains were susceptible to all tested antimicrobial drugs. Penicillin nonsusceptibility in the screening disk-diffusion test was documented in 26 (37.6 %) out of the 69 *S. pneumoniae* isolates; the results of the subsequent quantitative susceptibility tests to penicillin showed 17 (24.6 %) strains to be intermediately susceptible, and only 9 (13.1 %) strains penicillin-resistant with MICs ranging from 1.5 to 8 mg/L (Tab. 1, 2).

Resistance to erythromycin was observed in 17 (24.6 %) strains. 7 (10.1 %) strains had intermediate susceptibility and 18 (26.1 %) were resistant to trimethoprim/sulfamethoxazole. Ten (14.5 %) strains were nonsusceptible to tetracycline, and 11 (15.9 %) to chloramphenicol (Tab. 1).

Resistance or intermediate susceptibility to the tested antimicrobial agents was more prevalent in penicillin-nonsusceptible (i.e. penicillin-resitant or intermediate) S. *pneumoniae* strains in comparison with penicillin-susceptible strains (Fig. 1, 2). Twenty-one penicillin-nonsusceptible strains (80.8 %) out of 26 were resistant or had intermediate susceptibility to the tested drugs other than penicillin, versus 8 strains (18.6 %) out of 43 penicillin-susceptible strains. Erythromycin resistance (MIC ≥1 mg/L) was documented in 61.5 % of penicillin-nonsusceptible versus 2.3 % of penicillin-susceptible strains. Resistance to trimethoprime/sulfamethoxazole was observed in 61.5 % of penicillin-nonsusceptible versus 4.7 % of penicillin-susceptible strains, whereas intermediate susceptibility to trimethoprime/sulfamethoxazole was seen in 15.4 % of penicillin-nonsusceptible and only in 7 % of penicillin-susceptible strains. Nonsusceptibility to tetracycline was detected in 30.8 % of penicillin-nonsusceptible versus in 7 % of penicillin-susceptible strains, and to chloramphenicol in 42.3 % of penicillin-susceptible versus none of the penicillin-susceptible strains.

Table 3 shows the patterns of resistance of the 9 penicillin-resistant S. *pneumoniae* strains. Multiple resistant strains (resistant at least to three of the tested antimicrobials with different mechanisms of antibacterial activity) were isolated in 5 cases.

Respiratory tract infections of children included in our study were treated with antimicrobials only in cases when the bacterial etiology of the disease was suspected by the clinical status, the laboratory parameters used to obtain nonspecific evidence for bacterial infection — leukocytes count over 12.10^9/L, erythrocyte sedimentation rate over 25 mm/h, C-reactive protein level over 12

Tab. 1. Susceptibility of the 69 S. *pneumoniae* strains to the tested antimicrobial agents.
Tab. 1. Citlivosť 69 kmeňov *S. pneumoniae* na testované antimikróbne liečivá.

Tested agent Testované liečivo	Susceptible Citlivý	Intermediate Intermediárny	Resistant Rezizstentný
Penicillin[1]	43 (62.3%)	17 (24.6%)	9 (13.1%)
Erythromycin[1]	52 (75.4%)	0	17 (24.6%)
Trimethoprim/ sulfamethoxazole[1]	44 (63.8%)	7 (10.1%)	18 (26.1%)
Tetracycline[2]	59 (85.5%)	2 (2.9 %)	8 (11.6%)
Chloramphenicol[2]	58 (84.1%)	6 (8.7%)	5 (7.2%)

[1]tested by disk-diffusion method, and E-test when nonsusceptible
[2]tested by disk-diffusion method only; the tested strains were included into the categories of antimicrobial susceptibility according to the NCCLS (31)
[1]citlivosť testovaná diskovou difúznou metódou a v prípade zmenenej citlivosti E-testom
[2]citlivosť testovaná iba diskovou difúznou metódou, kmene boli zaradené do kategórií citlivý, intermediárny, rezistentný podľa NCCLS (31)

Tab. 2. Values of MIC of penicillin in the 9 penicillin-resistant S. *pneumoniae* strains.
Tab. 2. Hodnoty MIC penicilínu 9 kmeňov *S. pneumoniae* rezistentných proti penicilínu.

MIC (mg/L)	1.5	2.0	3.0	4.0	8.0
No. of strains Počet kmeňov	3	3	1	1	1

Tab. 3. The patterns of resistance of the 9 penicillin-resistant S. *pneumoniae* strains.
Tab. 3. Rezistencia 9 kmeňov *S. pneumoniae* rezistentných proti penicilínu.

Resistance to combinations of the tested antimicrobial agents Rezistencia proti kombinácii testovaných antimikrobiálnych liečiv	No of strains Počet kmeňov
Penicillin + erythromycin	1
Penicillin + trimethoprim/sulfamethoxazol	3
Penicillin + erythromycin + trimethoprim/sulfamethoxazol	4
Penicillin + trimethoprim/sulfamethoxazol + tetracycline	1

mg/L (23) — and pulmonary infiltrate on chest radiography in cases with indication for chest X-ray. The initial antimicrobial therapy was chosen mainly on empiric basis.

In the group of antimicrobial-treated children, 28 had positive cultures for S. *pneumoniae* (in this group, amoxicillin with clavulanate was used in 8 children, penicillin in 1, cefuroxime-axetil in 2, josamycin in 1, and azithromycin in 18 children). S. *pneumoniae* with intermediate susceptibility to penicillin and penicillin-resistant strain was isolated from the resppiratory tract mucosa of 10 and of 3 antimicrobials-treated children, respectively. However, no failure of antimicrobial therapy was caused because of their presence.

Discussion

All S. *pneumoniae* strains, isolated during the study, originated from the upper respiratory tract mucosa of patients. Therefore, their role in the respiratory tract diseases of examined children, especially of those with lower respiratory tract infections, can be neither proved, nor excluded. Isolation of pneumococci from bronchoalveolar lavage fluid, bronchoscopic-specimen brushing, transthoracic needle aspiration sample, pleural fluid, or blood (in case of bacteremic pneumonia) would confirm their etiologic role in lower respiratory tract infections (17). However, the sampling techniques mentioned above are used in young children only in strictly indicated cases (5).

Nevertheless, our results are important from the epidemiological point of view, and give an overview of S. *pneumoniae* antimicrobial susceptibility at the local level. The information about the presence of S. *pneumoniae* in the upper respiratory tract mucosa of children with respiratory tract infections may be important even in cases of colonisation, as pneumococcal pneumonia most likely develops after inhalation of pneumococci which have colonized the nasopharynx, and even a simple colonisation of respiratory tract mucosa belong to the important risk factors for development of severe diseases (22, 28).

Over 50 % of S. *pneumoniae*-positive samples yielded additional bacterial species with probable role in respiratory tract infections. Many of them are potential beta-lactamase producers (11). This finding is important for decision-making in the choice of the initial antibacterial therapy of serious cases. Use of penicillin antibiotics in combination with beta-lactamase inhibitors, or cephalosporins, macrolides, or azalides seems to be more appropriate initial antibacterial therapy of severe cases even if penicillin-susceptible S. *pneumoniae* strain is expected in the culture.

The rate of S. *pneumoniae* strains resistant to penicillin in samples of our patients was 13.1 % (9 strains). Their MICs were near or slightly above the breakpoint level of resistance (2 mg/L). Opinions about the therapy of infections caused by penicillin-resistant strains are not uniform. It is without any doubt, that in the therapy of pneumococcal meningitis caused by penicillin-resistant strain alternative antibacterial agents must be used (third generation cefalosporins in regions without cefalosporin-resistant pneumococci, vancomycine, or rifampine) (8, 10). However, there are several literary data about successful therapy of respiratory tract infections caused by penicillin-resistant S. *pneumoniae* strains (MIC ≥2 mg/L) with high doses of penicillin, ampicillin, or amoxicillin (6, 15). According to some authors, the MIC breakpoint above which penicillin therapy is likely to be ineffective for non-meningeal infections is probably 4 mg/L (26). In our study, only one S. *pneumoniae* strain out of 69 exhibited MIC of penicillin over this value (its MIC was 8 mg/L). Concerning the most appropriate choice of drug, many authors have been giving priority to amoxicillin for its higher levels obtainable in inflamed tissue of respiratory tract and lower MICs for penicillin-resistant strains in comparison with penicillin and cephalosporins (3, 12). Nonetheless, in severe respiratory tract infections or in highly immunocompromised patients, therapy with alternative antimicrobial drugs should be considered, as therapy with penicillins may not always be successful in such cases (7).

Additional 17 S. *pneumoniae* strains (24.6 %) from our study expressed intermediate susceptibility (MIC between 0.1 mg/L and 1 mg/L). Respiratory tract infections caused by intermediately susceptible strains can be safely and effectively treated with higher (4, 17) or even standard (10, 26) doses of penicillins that produce serum and tissue levels above the MIC for strains of pneumococci intermediately susceptible to penicillin.

When comparing the occurrence of penicillin-resistant S. *pneumoniae* strains in the department monitored in our study with available data about the antimicrobial susceptibility in other regions of Slovak Republic, the data more or less differ: 33.8 % resistance to penicillin in Topolcany District Hospital and 0.8 % in outpatients clinics or day care centres during the period from January to February 1991 (21), and penicillin resistance ranging from 0 to 52 % (the mean incidence 8.5) from clinical samples of inpatients and from 0 to 21 % in outpatients in different regions of Slovakia during the period from September to December 1993 (27). Hovewer, the last mentioned study gives a survey of penicillin resistant pneumococci without respect to the age categories of patients.

Therefore, current data on the epidemiology and resistance patterns of pneumococcal strains not only on the central level, but first of all on the regional and local level might guide physicians

in the choice of initial antibacterial therapy of patients with respiratory tract diseases before the culture results are available.

Summary

The current levels of penicillin resistance of S. *pneumoniae* strains in children with respiratory tract infections in the hospital department monitored in our study do not cause problems in the choice of antibacterial therapy. Penicillins (penicillin, or amoxycillin, preferentially combined with beta-lactamase inhibitors) still remain the drug of choice in cases when typical bacterial causing agents of respiratory tract infections are suspected.

E-test seems to be useful in the routine testing of susceptibility of S. *pneumoniae* strains nonsusceptible to penicillin in the screening disk-diffusion test. However, newer molecular biological assays have been developing with future prospects of more exact and rapid detection of resistance to penicillin directly from the sampled material (3, 24).*

References

1. Appelbaum P.C., Gladkova C., Hryniewicz W., Kojouharov B., Kotulová D., Mihalcu F., Schindler J., Setchanova L., Semina N., Trupl J., Tyski S., Urbášková P., Jacobs M.R.: Carriage of antibiotic-resistant Streptococcus pneumoniae by children in Eastern and Central Europe — A multicenter study using standardized methods. Clin. Infect. Dis., 23, 1996, s. 1—5.

2. Beall B., Facklam R.R., Jackson D.M., Starling H.H.: Rapid screening for penicillin susceptibility of systemic pneumococcal isolates by restriction enzyme profiling of the pbp2B gene. J. Clin. Microbiol., 36, 1998, s. 2359—2362.

3. Barry B., Muffat-Joly M., Gehanno P., Pocidalo J.J.: Effect of increased dosages of ampicillin and amoxicillin in the treatment of experimental middle ear otitis induced by highly penicillin-resistant Streptococcus pneumoniae. 6th International Congress for Infectious Diseases, April 26—30, 1994, Prague, Czech Republic.

4. Bradley J.S., Kaplan S.L., Klugman K.P., Leggiadro R.J.: Consensus: management of infections in children caused by Streptococcus pneumoniae with decreased susceptibility to penicillin. Pediat. Infect. Dis. J., 14, 1995, s. 1037—1041.

5. Brown P.D., Lerner S.A.: Community-acquired pneumonia. Lancet, 352, 1998, s. 1295—1302.

6. Bryan Ch.S., Talwani R., Stinson M.S.: Penicillin dosing for pneumococcal pneumonia. Chest, 12, 1997, s. 1657—1664.

7. Carratala J., Marron A., Fernandez-Sevilla A., Linares J., Guidal F.: Treatment of penicillin-resistant pneumococcal bacteremia in neutropenic patients with cancer. Clin. Infect. Dis., 24, 1996, s. 148—152.

8. Friedland I.R., McCracken Jr.G.H.: Management of infections caused by antibiotic-resistant Streptococcus pneumoniae. New Engl. J. Med., 331, 1994, s. 377—382.

9. Hansman D., Bullen M.M.: A resistant pneumococcus. Lancet, ii, 1967, s. 264—265.

10. Jacobs M.R.: Treatment and diagnosis of infections caused by drug-resistant Streptococcus pneumoniae. Clin. Infect. Dis.,15, 1992, s. 112—118.

11. Mandell L.A.: Introduction: Evolving needs in respiratory tract infections. Clin. Microbiol. Infect., 4, Suppl. 1, 1998, s. S1—S8.

12. Marchese A., Debbia E., Pesce A., Schito G.C.: Comparative activities of amoxicillin and 10 other oral drugs against penicillin-susceptible and –resistant Streptococcus pneumoniae strains recently isolated in Italy. Clin. Microbiol. Infect., 4, 1998, s. 170—173.

13. Moravčík P., Čechová A., Galanda V., Marčeková D., Zavarská L.: Izolácia multirezistentných pneumokokov z klinického materiálu. Bratisl. lek. Listy, 80, 1983, s. 176—183.

14. Musher D.M.: Infections caused by Streptococcus pneumoniae: clinical spectrum, pathogenesis, immunity, and treatment. Clin. Infect. Dis., 14, 1992, s. 801—809.

15. Nelson Ch.T., Mason E.O., Kaplan Sh.L.: Activity of oral antibiotics in middle ear and sinus infections caused by penicillin resistant Streptococcus pneumoniae: implications treatment. Pediat. Infect. Dis. J., 3, 1994, s. 585—589.

16. O'Neill A.M., Gillespie S.H., Whiting G.C.: Detection of penicillin susceptibility in Streptococcus pneumoniae by pbp2b PCR-restriction fragment length polymorphism analysis. J. Clin. Microbiol., 37, 1999, s. 157—160.

17. Pallares R., Linares J., Vadillo M., Cabellos C., Manresa F., Viladrich P.F., Martin R., Gudiol F.: Resistance to penicillin and cephalosporin and mortality from severe pneumococcal pneumonia in Barcelona, Spain. New Engl. J. Med., 333, 1995, s. 474—480.

18. Pratt-Rippin K., Pezzlo M.: Identification of commonly isolated gram-positive bacteria. S. 1.20.1—1.20.44. In: Isenberg H.D. (Ed.): Clinical Microbiology Procedures Handbook. ASM Press, Washington,D.C., 1992.

19. Primhak R.A., Tanner M.S., Spencer R.C.: Pneumococcal infection in the newborn. Arch. Dis. Child., 69, 1993, s. 317—318.

20. Reichler M.R., Rakovský J., Sobotová A., Sláčiková M., Hlavačová B., Hill B., Krajčiková L., Tarina P., Facklam R.R., Breiman R.F.: Multiple antimicrobial resistance of pneumococci in children with otitis media, bacteremia, and meningitis in Slovakia. J. Infect. Dis., 171, 1995, s. 1491—1496.

21. Reichler M.R., Rakovský J., Sláčiková M., Hlavačová B., Krajčiková L., Tarina P., Sobotová A., Facklam R.R., Breiman R.F.: Spread of multidrug-resistant Streptococcus pneumoniae among hospitalized children in Slovakia. J. Infect. Dis., 173, 1996, s. 374—379

22. Salyers A.A., Whitt D.D.: Bacterial pathogenesis; a molecular approach. ASM Press, Washington,D.C., 1994.

23. Šašinka M., Filka J.: Pediatrická infektológia a antimikrobiálna liečba. S. 915—928. In: Dzúrik R., Trnovec T. (Eds.): Štandardné terapeutické postupy. Martin, Osveta 1997.

24. Shigei J.: Test methods used in the identification of commonly isolated aerobic gram-negative bacteria. S. 1.19.1—1.19.100. In: Isenberg H.D. (Ed.): Clinical Microbiology Procedures Handbook. Washington, D.C., ASM Press 1992.

25. Spratt B.G.: Resistance to antibiotics mediated by target alterations. Science, 264, 1994, s. 388—393.

*Part of this study was presented at the 98th General Meeting of the American Society for Microbiology in Atlanta on May 17—21, 1998 in poster format.
This investigation was supported by grant No 1/2134/95 from the Scientific Grant Agency of Ministry of Education of Slovak Republic and Slovak Academy of Sciences.
The authors would like to express their cordial thanks to Mrs. A. Horecka, V. Makoova, and M. Mercellova for brilliant technical cooperation.

26. Strachon S.A., Friedlam I.R.: Therapy for penicillin-resistant Streptococcus pneumoniae. J. Med. Microbiol., 43, 1995, s. 237—238.

27. Trupl J., Hupková H., Appelbaum P.C., Jacobs M.R.: The incidence of penicillin-resistant pneumococci in the Slovak Republic. Chemotherapy, 43, 1997, s. 316—322.

28. Tuomanen E., Austrian R., Masure H.R.: Pathogenesis of pneumococcal disease. New Engl. J. Med., 332, 1995, s. 1280—1283.

29. MIC determination. E—test technical guide No. 3, May 1993. AB BIODISK, Solna, Sweden.

30. National Committee for Clinical Laboratory Standards: Performance Standards for Antimicrobial Disk Susceptibility Tests. NCCLS Document M2-A5. NCCLS, Villanova, PA, 1993.

31. National Committee for Clinical Laboratory Standards: Performance Standards for Antimicrobial Susceptibility Testing — Sixth Informational Supplement. NCCLS Document M100-S6. NCCLS, Villanova, PA, 1995.

Received July 30, 1999.
Accepted September 24, 1999.

BOOK REVIEW

Hahn H., Falke D., Kaufmann S.H., Ullmann U. (Eds.): Medizinische Mikrobiologie und Infektologie (Medicinal Microbiology and Infectology). 3rd edition, reedited and updated. Berlin, Heidelberg, New York, Barcelona, Hong Kong, London, Milan, Paris, Singapore, Tokyo, Springer Verlag

Infectious diseases are the globally most frequent cause of death, and any changes of this fact in the near future appear to be unlikely. Smallpox, one of the diseases, could be eradicated in this century and vaccines against others were prepared; at the same time, however, new agents appeared, as e.g. HIV-AIDS, Helicobacter pylori, Bartonella henselae.

Thanks to improved diagnostics, pathogenesis of several diseases was found to involve microbial infections. Resistant bacterial strains have been appearing and spreading, forcing humankind to search out new drugs and new methods of prevention.

These are the introductory words of the authors of a textbook of microbiology and infectology, appearing in its third edition with a modern interdisciplinary concept.

The authors of the first edition, H. Hahn, D. Falke and Professor P. Klein, outstanding teacher of microbiology in Mainz wrote their textbook already in 1991 with clear medical targeting and useful practical knowledge in mind. The third edition, fully updated by authors and editors – Professors H. Hahn (Freie Universität Berlin, Institut für Infektionsmedizin), D. Falke (Institut für Virologie, Johannes Gutenberg Universität, Mainz), E.H. Kaufmann (Max Planck Institut für Infektionsbiologie, Berlin) and U. Ullmann (Institut für Medizinische Mikrobiologie und Virologie, Klinikum der Christian Albrechts Universität zu Kiel) presents the results of cooperation with further 34 distinguished experts in the fields of general and clinical microbiology, immunology, infectology, internal medicine, neurology and pathology.

The book is divided into 17 chapters. The introduction contains the characteristics of infectious diseases, definitions of the fundamental properties of the agents – viruses, bacteria, microscopic fungi, one-cell and multiple-cell parasites. Explanations of the general principles of the pathogenesis of microbial diseases caused by obligatorily and opportunely pathogenic microorganisms are offered in the third chapter, followed by a section concerning the immune system, antiinfective immunity and immunopathological conditions. Chapter IV explains the essential terms in the field of epidemiology, primary and secondary prevention, disinfection and sterilisation.

The general part of the chapter on bacteria discusses their morphology, physiology, genotype changes and metabolism in link with possibilities of in vitro cultivation. Special bacteriology is included in the form of 27 subchapters, describing in accordance with valid nomenclature the individual bacterial species and types involved in human diseases.

The chapter on virology is itemised in a similar manner. The structure and replication of viruses, origin and course of viral diseases, diagnostics and therapy with virostatic agents are described in the general part. A special section is concerned with the relationship between viruses and the development of tumours. Individual viral groups and the diseases caused by them are characterised in the special part. Four chapters are dedicated to the area of general and special mycology and parasitology.

The next part presents a review of antibacterial. antimycotic and antiparasitis drugs, with mechanism and spectrum of effects and potential therapeutical use.

The remaining chapters offer a comprehensive view of the infection phenomenon, describing diseases by systems and syndromes: sepsis, endocarditis, meningitis, infections of the respiratory tract, of the uropoetic system, sexually transmitted diseases, diseases of the gastrointestinal system, intraabdominal infections, skin and soft-tissue infections, eye and nosocomial infections. These chapters provide valuable information not only to infectologists but also to specialists in all medicinal areas confronting infections of organs and systems.

The textbook is written in a clear style, containing latest information on infectious diseases. Study is greatly alleviated by pictures and schemes presenting a suitable completion of texts, and by conclusions containing the most important points of the individual chapters.

The book represents the result of cooperation of foremost specialists who at the same time are excellent pedagogical workers. Its study is sincerely recommended to all German-speaking physicians and medical school students who wish to update their knowledge of microbial diseases. All of us will find much new information in it, presented in a concentrated and clearly comprehensible form.

Kotulová D.