

## รายการอ้างอิง

- [1] Paterson DL. Recommendation for treatment of severe infections caused by Enterobacteriaceae producing extended-spectrum  $\beta$ -lactamases (ESBLs). *Clin Microbiol Infect* 2000;6:460-3.
- [2] Burgess DS, Hall RG II, Lewis JS II, Jorgensen JH, Patterson JE. Clinical and microbiological analysis of a hospital's extended-spectrum  $\beta$ -lactamase-producing isolates over a 2-year period. *Pharmacotherapy* 2003;23:1232-7.
- [3] Paterson DL, Ko WC, Von Gottberg A. Antibiotic therapy for *K. pneumoniae pneumoniae* bacteremia: implications of production of extended-spectrum  $\beta$ -lactamases. *Clin Infect Dis* 2004;39:31-7.
- [4] Paterson DL, Ko WC, Von Gottberg A, Casellas JM, Mulazimoglu L, Klugman KP. Outcome of cephalosporin treatment for serious infections due to apparently susceptible organisms producing extended-spectrum  $\beta$ -lactamases: implications for the clinical microbiology laboratory. *J Clin Microbiol* 2001;39:2206-12.
- [5] Kang CI, Kim SH, Park WB, Lee KD, Kim HB, Kim EC. Bloodstream infections due to extended-spectrum  $\beta$ -lactamase-producing *Escherichia coli* and *K. pneumoniae pneumoniae*: risk factors for mortality and treatment outcome, with special emphasis on antimicrobial therapy. *Antimicrob Agents Chemother* 2004;48:4574-81.
- [6] Brun-Buisson C, Legrand P, Philippon A, Montravers F, Ansquer M, Duval J. Transferable enzymatic resistance to third-generation cephalosporins during nosocomial outbreak of multiresistant *K. pneumoniae pneumoniae*. *Lancet* 1987; 2:302-6.
- [7] Emery CL, Weymouth LA. Detection and clinical significance of extended-spectrum  $\beta$ -lactamases in a tertiary-care medical center. *J Clin Microbiol* 1997;35:2061-7.

- [8] Rice LB, Willey SH, Papanicolaou GA. Outbreak of ceftazidime resistance caused by extended-spectrum *b*-lactamases at a Massachusetts chronic-care facility. *Antimicrob Agents Chemother* 1990;34:2193-9.
- [9] พรรณพิศ สุวรรณกุล. แนวทางการรักษาภาวะติดเชื้อทางเดินปัสสาวะ. *Clinical Practice Guideline ทางอายุรกรรม พ.ศ.2544:295-308*
- [10] **Clinical and Laboratory Standards Institute**. Performance Standard for Antimicrobial Susceptibility Testing: Sixteenth Information Supplement 2006; 26:3
- [11] Kamonwan J, Chusana S. Prospective study of ceftriaxone treatment of acute female pyelonephritis cause by extended-spectrum betalactamase producing versus-nonproducing *Escherichia coli* or *Klebsiella*. *J Infect* 2007 (in press)
- [12] **National Committee for Clinical Laboratory Standard**. Performance Standard for Antimicrobial Susceptibility Testing: Sixteenth Information Supplement 2006; 3:
- [13] Venezia, R A F J Scarano, K E Preston, L M Steele, T P Root, R Limberger, W Archinal, and M A Kacica. Molecular epidemiology of an SHV-5 extended-spectrum beta-lactamase in enterobacteriaceae isolated from infants in a neonatal intensive care unit. *Clin Infect Dis* 1995;21:915–23
- [14] Gerald L Mandell, John E Bennett, Raphael Dolin Temperature Regulation and the Pathogenesis of Fever. *Principle and Practice of Infectious Disease Fifth Edition* 2000;1:604-7
- [15] ivermore DM. Beta-lactamase-mediated resistance and opportunities for its control. *J Antimicrob Chemother* 1998; 41 (Suppl D) :25-41.
- [16] Pitout JD, Sanders CC, Sanders WE, Jr. Antimicrobial resistance with focus on  $\beta$  - lactam resistance in Gram-negative bacilli. *Am J Med* 1997; 103:51-9.
- [17] Knothe H, Shah P, Krcmery V, Antal M, Mitsuhashi S. Transferable resistance to cefotaxime, cefoxitin, cefamandole and cefuroxime in clinical isolates of *K. pneumoniae pneumoniae* and *Serratia marcescens*. *Infection* 1983; 11:315-7.

- [18] Emery CL, Weymouth LA. Detection and clinical significance of extended-spectrum  $\beta$ -lactamases in a tertiary-care medical center. *J Clin Microbiol* 1997; 35:2061-7.
- [19] Quinn JP. Clinical significance of extended-spectrum  $\beta$  -lactamases. *Eur J Clin Microbiol Infect Dis* 1994;13 (Suppl 1) :S39-42.
- [20] Garau J.  $\beta$  -lactamases: current situation and clinical importance. *Intensive Care Med* 1994; 20 (Suppl 3) :S5-9.
- [21] Crespo MP, Woodford N, Sinclair A, Kaufmann ME, Turton J, Glover J et al. Outbreak of carbapenem-resistant *Pseudomonas aeruginosa* producing VIM-8, a novel metallo-beta-lactamase, in a tertiary care center in Cali, Colombia. *J Clin Microbiol* 2004; 42:5094-101.
- [22] Sanders CC.  $\beta$  -lactamases of Gram negative bacteria: New challenges for new drugs. *Clin Infect Dis* 1992; 14:1089-99.
- [23] Sanders CC, Sanders WE.  $\beta$  -lactam resistance in Gram negative bacteria: Global trends and clinical impact. *Clin Infect Dis* 1992; 15:824-39.
- [24] Joris B, Ghuyssen JM, Dive G, et al. The active-site-serine penicillin-recognizing enzymes as members of the *Streptomyces* R61 DD-peptidase family. *Biochem J* 1988; 250:313-24.
- [25] Garau G, García-Suñez I, Bebrone C, et al. Update of the standard numbering scheme for class B  $\beta$ -lactamases. *Antimicrob Agents Chemother* 2004; 48:2347-9.
- [26] Jacoby GA, Muñoz-Price LS. The new beta-lactamases. *N Engl J Med* 2005; 352:380-91.
- [27] Matthew M. Plasmid-mediated  $\beta$ -lactamases of Gram-negative bacteria: Properties and distribution. *J Antimicrob Chemother* 1979; 5:349-58.
- [28] Perilli M, Segatore B, Massis M.R.D, Riccio M.L, Bianchi C, Zollo A, Rossolini G.M, Amicosante G. TEM-72, a new extended spectrum  $\beta$ -lactamase detected in *P. mirabilis mirabilis* and *Morganella morganii* in Italy. *Antimicrob Agents Chemother* 2000; 44:2537-9.

- [29] Rosenau A, Cattier B, Gousset N, Harriau P, Philippon A, Quentin R. *Capnocytophaga ochracea*: Characterization of a plasmid-encoded extended-spectrum TEM-17  $\beta$ -lactamase in the phylum *Flavobacter-Bacteroides*. **Antimicrob Agents Chemother** 2000; 44 :760–2.
- [30] Roy C, Foz A, Segura C, Tirado M, Funster C, Reig R. Plasmid-determined  $\beta$ -lactamases identified in a group of 204 ampicillin-resistant Enterobacteriaceae. **J Gen Microbiol** 1983; 12:507–10.
- [31] Sirot D, Sirot J, Labia R, Morand A, Courvalin P, Parroux R. Transferable resistance to 3rd generation cephalosporins in clinical isolates of *K. pneumoniae pneumoniae*: Identification of CTX-1, a novel  $\beta$ -lactamase. **J Antimicrob Chemother** 1987; 38: 323–34.
- [32] Champs C.D, Sauvant M.P, Chanal C, Sirot D, Gazuy N, Malhuret R. Prospective survey of colonization and infections caused by expanded-spectrum  $\beta$ -lactamase-producing members of the family Enterobacteriaceae in an intensive care unit. **J Clin Microbiol** 1989; 12:2887–90.
- [33] Medeiros A, Evolution and dissemination of  $\beta$ -lactamases accelerated by generations of  $\beta$ -lactam antibiotics. **Clin Infect Dis** 1997; 24 (Suppl.1) : S19–45.
- [34] Livermore D.M.  $\beta$ -Lactamases in laboratory and clinical resistance. **Clin Microbiol Rev** 1995;8: 557–84
- [35] Sanders C.C, Peyret M, Moland E.S, Shubert C, Thomson K.S, Boufgras J.M, Sanders W.E. Ability of the VITEK 2 Advanced Expert system to identify  $\beta$ -lactam phenotypes in isolates of Enterobacteriaceae and *Pseudomonas aeruginosa*. **J Clin Microbiol** 2000; 38:570–4.
- [36] Bush K, Jacoby G. Nomenclature of TEM  $\beta$ -lactamases. **J Antimicrob Chemother** 1997; 40:1–3.
- [37] Bush K. New  $\beta$ -lactamases in Gram-negative bacteria: Diversity and impact on the selection of antimicrobial therapy. **Clin Infect Dis** 2001; 32:1085–9.

- [38] Ambler R.P. The structure of  $\beta$ -lactamases. *Philos Trans R Soc London B* 1980; 289:321–31.
- [39] Richmond M.H, Sykes R.B. The  $\beta$ -lactamases of Gram-negative bacteria and their possible physiological role. *Adv Microb Physiol* 1973;9:31–88.
- [40] Bush K, Jacoby G.A, Medeiros A.A. A functional classification scheme for  $\beta$ -lactamases and its correlation with molecular structure, *Antimicrob. Agents Chemother* 1995; 39:1211–33.
- [41] Jacoby GA, Medeiros AA. More extended-spectrum  $\beta$  -lactamases. *Antimicrob Agents Chemother* 1991; 35:1697-1704.
- [42] Jacoby G, Bush K. Amino acid sequences for TEM, SHV and OXA extended-spectrum and inhibitor resistant  $\beta$  -lactamases. (Accessed January 3, 2005, at <http://www.lahey.org/studies/webt.htm>.)
- [43] Bret L, Chanel C, Sirot D, Labia R, Sirot J. Characterization of an inhibitor-resistant enzyme IRT-2 derived from TEM-2  $\beta$ -lactamase produced by *P. mirabilis mirabilis* strains. *J Antimicrob Chemother* 1996; 38: 183–91.
- [44] Bonomo R.A., Rudin S.A., Shlaes D.M., Tazobactam is a potent inactivator of selected inhibitor-resistant class A  $\beta$ -lactamases. *FEMS Microbiol Lett* 1997;148:59–62
- [45] Chaibi E.B., Sirot D., Paul G., Labia R. Inhibitor-resistant TEM- $\beta$ -lactamases: Phenotypic, genetic and biochemical characteristics. *J Antimicrob Chemother* 1999; 43:447–58.
- [46] Bradford P.A, Urban C., Jaiswal A., Mariano N., Rasmussen B.A., Projan S.J., Rahal J.J., Bush K. SHV-7, a novel cefotaxime-hydrolyzing  $\beta$ -lactamase, identified in *Escherichia coli* isolates from hospitalized nursing home patients. *Antimicrob Agents Chemother* 1995; 39:899–905.
- [47] Harrif-Heraud Z. El, Arpin C., Benliman S., Quentin C. Molecular epidemiology of a nosocomial outbreak due to SHV-4 producing strains of *Citrobacter diversus*. *J Clin Microbiol* 1997; 35:2561–7.

- [48] Naas T., Philippon L., Poirel L., Ronco E., Nordman P. An SHV-derived extended-spectrum  $\beta$ -lactamase in *Pseudomonas aeruginosa*. **Antimicrob Agents Chemother** 1999; 43:1281-4.
- [49] Bonnet R. Growing group of extended-spectrum  $\beta$ -lactamases: the CTX-M enzymes. **Antimicrob Agents Chemother** 2004; 48:1-14.
- [50] Bradford PA. Extended-spectrum  $\beta$ -lactamases in the 21st century: characterization, epidemiology, and detection of this important resistance threat. **Clin Microbiol Rev** 2001;14:933-51
- [51] Naas T, Nordmann P. OXA-type  $\beta$ -lactamases. **Curr Pharm Des** 1999;5:865-79.
- [52] Danel F, Hall LM, Duke B, Gur D, Livermore DM. OXA-17, a further extended-spectrum variant of OXA-10  $\beta$ -lactamase, isolated from *Pseudomonas aeruginosa*. **Antimicrob Agents Chemother** 1999;43:1362-6.
- [53] Philippon A, Arlet G, Jacoby GA. Plasmid-determined AmpC-type  $\beta$ -lactamases. **Antimicrob Agents Chemother** 2002; 46:1-11.
- [54] Nordmann P, Poirel L. Emerging carbapenemases in Gram-negative aerobes. **Clin Microbiol Infect** 2002; 8:321-31.
- [55] Toleman MA, Rolston K, Jones RN, Walsh TR. *bla*VIM-7, An evolutionarily distinct metallo- $\beta$ -lactamase gene in a *Pseudomonas aeruginosa* isolate from the United States. **Antimicrob Agents Chemother** 2004; 48:329-32.
- [56] Poirel L, Heritier C, Tolun V, Nordmann P. Emergence of oxacillinase-mediated resistance to imipenem in *K. pneumoniae pneumoniae*. **Antimicrob Agents Chemother** 2004; 48:15-22.
- [57] Thomson KS, Smith Moland E. Version 2000: the new  $\beta$ -lactamases of Gram-negative bacteria at the dawn of the new millennium. **Microbes Infect** 2000; 2:1225-35.
- [58] Joshi SG, Litake GM, Ghole VS, Niphadkar KB. Plasmid-borne extended-spectrum  $\beta$ -lactamase in a clinical isolate of *Acinetobacter baumannii*. **J Med Microbiol** 2003; 52:1125-7.

- [59] Vahaboglu II, Ozturk R, Aygun G, et al. Widespread detection of PER-1-type extended-spectrum  $\beta$ -lactamases among nosocomial *Acinetobacter* and *Pseudomonas aeruginosa* isolates in Turkey: a nationwide multicenter study. *Antimicrob Agents Chemother* 1997; 41:2265-9. [Erratum, *Antimicrob Agents Chemother* 1998; 42:484.
- [60] Weldhagen GF, Poirel L, Nordmann P. Ambler class A extended-spectrum  $\beta$ -lactamases lactamases in *Pseudomonas aeruginosa*: novel developments and clinical impact. *Antimicrob Agents Chemother* 2003; 47:2385-92.
- [61] Winokur PL, Canton R, Casellas JM, Legakis N. Variations in the prevalence of strains expressing an extended-spectrum  $\beta$  -lactamase phenotype and characterization of isolates from Europe, the Americas, and the Western Pacific region. *Clin Infect Dis* 2001; 32 (Suppl 2) :S94-103.
- [62] Karlowsky JA, Jones ME, Thornsberry C, Friedland IR, Sahm DF. Trends in antimicrobial susceptibilities among *Enterobacteriaceae* isolated from hospitalized patients in the United States from 1998 to 2001. *Antimicrob Agents Chemother* 2003; 47:1672-80.
- [63] Radice M, Power P, Di Conza J, Gutkind G. Early dissemination of CTX-M-derived enzymes in South America. *Antimicrob Agents Chemother* 2002; 46:602-4.
- [64] Woodford N, Tierno PM, Jr., Young K, Tysall L, Palepou MF, Ward E et al. Outbreak of *K. pneumoniae pneumoniae* producing a new carbapenem-hydrolyzing class A  $\beta$ -lactamase, KPC-3, in a New York Medical Center. *Antimicrob Agents Chemother* 2004; 48:4793-9.
- [65] Moland ES, Black JA, Hossain A, Hanson ND, Thomson KS, Pottumarthy S. Discovery of CTX-M-like extended-spectrum  $\beta$  -lactamases in *Escherichia coli* isolates from five US States. *Antimicrob Agents Chemother* 2003; 47:2382-3.
- [66] Shibata N, Doi Y, Yamane K, et al. PCR typing of genetic determinants for Metallo  $\beta$  -lactamases and integrases carried by Gramnegative bacteria isolated in Japan, with focus on the class 3 integron. *J Clin Microbiol* 2003; 41:5407-13.

- [67] Kurokawa H, Yagi T, Shibata N, Shibayama K, Arakawa Y. Worldwide proliferation of carbapenem-resistant Gram-negative bacteria. *Lancet* 1999; 354:955.
- [68] Oguri T, Igari J, Hiramatsu K, et al.  $\beta$ -lactamase-producing activity and antimicrobial susceptibility of major pathogenic bacteria isolated from clinical samples. *Jpn J Antibiot* 2002; 55: (Suppl A) :1-28.
- [69] Bradford PA, Bratu S, Urban C, et al. Emergence of carbapenem-resistant *K. pneumoniae* species possessing the class A carbapenemhydrolyzing KPC-2 and inhibitor-resistant TEM-30  $\beta$ -lactamases in New York City. *Clin Infect Dis* 2004; 39:55-60.
- [70] Kusum M, Wongwanich S, Dhiraputra C, Pongpech P, Naenna P. Occurrence of extended-spectrum  $\beta$ -lactamase in clinical isolates of *K. pneumoniae pneumoniae* in a University Hospital, Thailand. *J Med Assoc Thai* 2004;87:1029-33
- [71] Surang Dejsirilert, Anucha Apisarntharak, Rungreung Kijphati. The status of antimicrobial resistance in Thailand among Gram negative pathogen bloodstream infection: NARST data 2000-2003. Abstract from National Institute of Health, Department of medical science, Thailand
- [72] Mathai D, Lewis MT, Kugler KC, Pfaller MA, Jones RN. Antibacterial activity of 41 antimicrobials tested against over 2773 bacterial isolates from hospitalized patients with pneumonia: I-results from the SENTRY Antimicrobial Surveillance Program (North America, 1998) . *Diagn Microbiol Infect Dis* 2001; 39:105-16.
- [73] Saurina G, Quale JM, Manikal VM, Oydna E, Landman D. Antimicrobial resistance in Enterobacteriaceae in Brooklyn, NY: epidemiology and relation to antibiotic usage patterns. *J Antimicrob Chemother* 2000; 45: 895-8.
- [74] Gales AC, Sader HH, Jones RN. Respiratory tract pathogens isolated from patients hospitalized with suspected pneumonia in Latin America: frequency of occurrence and antimicrobial susceptibility profile: results from the SENTRY Antimicrobial Surveillance Program (1997-2000) . *Diagn Microbiol Infect Dis* 2002; 44:301-11.



- [75] Sader HS, Jones RN, Silva JB. Skin and soft tissue infections in Latin American medical centers: four-year assessment of the pathogen frequency and antimicrobial susceptibility patterns. *Diagn Microbiol Infect Dis* 2002; 44:281-8.
- [76] Sader HS, Jones RN, Andrade-Baiocchi S, Biedenbach DJ. Four-year evaluation of frequency of occurrence and antimicrobial susceptibility patterns of bacteria from bloodstream infections in Latin American medical centers. *Diagn Microbiol Infect Dis* 2002; 44:273- 80.
- [77] Spanu T, Luzzaro F, Perilli M, Amicosante G, Toniolo A, Fadda G. Occurrence of extended-spectrum  $\beta$ -lactamases in members of the family Enterobacteriaceae in Italy: implications for resistance to  $\beta$ -lactams and other antimicrobial drugs. *Antimicrob Agents Chemother* 2002; 46:196-202.
- [78] Oteo J, Campos J, Baquero F. Antibiotic resistance in 1962 invasive isolates of *Escherichia coli* in 27 Spanish hospitals participating in the European Antimicrobial Resistance Surveillance System (2001) . *J Antimicrob Chemother* 2002; 50:945-52.
- [79] Albertini MT, Benoit C, Berardi L, et al. Surveillance of methicillin-resistant *Staphylococcus aureus* (MRSA) and Enterobacteriaceae producing extended-spectrum  $\beta$ -lactamase (ESBL) in Northern France: a five-year multicenter incidence study. *J Hosp Infect* 2002;52:107-113
- [80] Stobberingh EE, Arends J, Hoogkamp-Korstanje JA, et al. Occurrence of extended-spectrum  $\beta$ -lactamases (ESBL) in Dutch hospitals. *Infect* 1999; 27:348-54.
- [81] Durmaz R, Durmaz B, Koroglu M, Tekerekoglu MS. Detection and typing of extended-spectrum  $\beta$ -lactamases in clinical isolates of the family Enterobacteriaceae in a medical center in Turkey. *Microb Drug Resist* 2001; 7:171-5.
- [82] Bell JM, Turnidge JD, Gales AC, Pfaller MA, Jones RN. Prevalence of extended spectrum  $\beta$ -lactamase (ESBL) -producing clinical isolates in the Asia-Pacific region and South Africa: regional results from SENTRY Antimicrobial Surveillance Program (1998-99) . *Diagn Microbiol Infect Dis* 2002; 42:193-8.

- [83] Xiong Z, Zhu D, Zhang Y, Wang F. Extended-spectrum  $\beta$ -lactamase in *K. pneumoniae pneumoniae* and *Escherichia coli* isolates. *Zhonghua Yi Xue Za Zhi* 2002; 82:1476-9.
- [84] Hsueh PR, Liu YC, Yang D, et al. Multicenter surveillance of antimicrobial resistance of major bacterial pathogens in intensive care units in 2000 in Taiwan. *Microb Drug Resist* 2001; 7:373-82.
- [85] Ho PL, Tsang DN, Que TL, Ho M, Yuen KY. Comparison of screening methods for detection of extended-spectrum  $\beta$ -lactamases and their prevalence among *Escherichia coli* and *K. pneumoniae* species in Hong Kong. *APMIS* 2000; 108:237-40.
- [86] Kim J, Lee H-J. Rapid discriminatory detection of genes coding for SHV  $\beta$ -lactamase by ligase chain reaction. *Antimicrob Agents Chemother* 2000;44:1860-4
- [87] Bradford PA. Automated thermal cycling is superior to traditional methods for nucleotide sequencing of *bla<sub>shv</sub>* genes. *Antimicrob Agents Chemother* 1999;43:2960-3
- [88] National Committee for Clinical Laboratory Standard. Performance Standard for Antimicrobial Susceptibility Testing: Fourteenth Information Supplement 2004; 2:35
- [89] National Committee for Clinical Laboratory Standard. Performance Standard for Antimicrobial Susceptibility Testing: Fourteenth Information Supplement 2004; 2:100
- [90] Jarlier V, Nicolas MH, Fournier G, Philippon A. Extended board-spectrum  $\beta$ -lactamase conferring transferable resistance to newer  $\beta$ -lactam agents in *Enterobacteriaceae*: hospital prevalence and susceptibility pattern. *Rev Inf Dis* 1988;10:867-78
- [91] Thomson KS, Sander CC. Detection of extended-spectrum  $\beta$ -lactamases in member of family *Enterobacteriaceae*: Comparison of the double-disc and three dimensional tests. *Antimicrob Agents Chemother* 1992; 36:1877-82

- [92] M'Zali FH, Chanawong A, Kerr KG, et al. Detection of extended-spectrum  $\beta$ -lactamase in members of the family Enterobacteriaceae: a comparison of the Mast DD method, the double disc and E test ESBL. **J Antimicrob Chemother** 2000;45:881-5
- [93] Caster MW, Oakton KJ, Warner M, Livermore DM. Detection of extended-spectrum  $\beta$ -lactamase in *K. pneumoniae* with oxoid combination disc method. **J Clin Microbiol** 2000;38:4228-32
- [94] Jacoby GA, Han P. Detection of extended-spectrum  $\beta$ -lactamases in clinical isolates of *K. pneumoniae pneumoniae* and *Escherichia coli*. **J Clin Microbiol** 1996; 34:908-11.
- [95] Vercauteren E, Descheemaeker P, Leven M, et al. Comparison of screening methods for the detection of extended-spectrum  $\beta$ -lactamases and their prevalence among blood isolates of *Escherichia coli* and *K. pneumoniae*, *K. oxytoca* in Belgian teaching hospital. **J Clin Microbiol** 1997;35:219-7
- [96] Rice LB, Carias LL, Hujer AM, et al. High-level expression of chromosomally encoded SHV-1 extended-spectrum  $\beta$ -lactamases and outer membrane protein change confer resistance to ceftazidime and piperacillin-tazobactam in a clinical isolate of *K. pneumoniae pneumoniae*. **Antimicrob Agents Chemother** 2000;44:326-7
- [97] Bush K. Is important to identify extended-spectrum  $\beta$ -lactamase-producing isolates? **Eur J Clin Microbiol Inf Dis** 1996;15:361-4
- [98] Rasheed JK, Jay C, Metchock B, et al. Evolution of extended-spectrum  $\beta$ -lactam resistance (SHV-8) in strain *Escherichia coli* during multiple episodes of bacteremia. **Antimicrob Agents Chemother** 1997;41:647-53
- [99] Braford PA, Urban C, Mariano N, et al. Imipenem resistance in *K. pneumoniae pneumoniae* is associated with the combination of ACT-1, a plasmid mediated AmpC  $\beta$ -lactamases and the loss of an outer membrane protein. **Antimicrob Agents Chemother** 1997;41:563-9
- [100] Steward CD, Rasheed JK, Hubert SK, Biddle JW, Raney PM, Anderson GJ et al. Characterization of clinical isolates of *K. pneumoniae pneumoniae* from 19

- laboratories using the National Committee for Clinical Laboratory Standards extended-spectrum  $\beta$ -lactamase detection methods. *J Clin Microbiol* 2001; 39:2864-72.
- [101] Safdar N, Maki DG. The commonality of risk factors for nosocomial colonization and infection with antimicrobial-resistant *Staphylococcus aureus*, enterococcus, Gramnegative bacilli, *Clostridium difficile*, and *Candida*. *Ann Intern Med* 2002; 136:834-44.
- [102] Mangeney N, Niel P, Paul G, et al. A 5-year epidemiological study of extended-spectrum  $\beta$ -lactamase-producing *K. pneumoniae pneumoniae* isolates in a medium- and longstay neurological unit. *J Appl Microbiol* 2000; 88:504-11.
- [103] Bisson G, Fishman NO, Patel JB, Edelstein PH, Lautenbach E. Extended-spectrum  $\beta$ -lactamase-producing *Escherichia coli* and *K. pneumoniae* species: risk factors for colonization and impact of antimicrobial formulary interventions on colonization prevalence. *Infect Control Hosp Epidemiol* 2002; 23:254-60.
- [104] Lucet JC, Chevret S, Decre D et al. Outbreak of multiple resistant Enterobacteriaceae in an intensive care unit epidemiology and risk factors for acquisition. *Clin Infect Dis* 1996;22:430-6
- [105] De Champs C, Rouby D, Guelon D, et al. A case-control study of an outbreak of infections caused by *K. pneumoniae pneumoniae* strains producing CTX-1 (TEM-3)  $\beta$ -lactamase. *J Hosp Infect* 1991; 18:5-13.
- [106] Pena C, Pujol M, Ricart A, et al. Risk factors for faecal carriage of *K. pneumoniae pneumoniae* producing extended spectrum  $\beta$ -lactamase (ESBL-KP) in the intensive care unit. *J Hosp Infect* 1997; 35:9-16.
- [107] Ho PL, Chan WM, Tsang KW, Wong SS, Young K. Bacteremia caused by *Escherichia coli* producing extended-spectrum  $\beta$ -lactamase: a case-control study of risk factors and outcomes. *Scand J Infect Dis* 2002; 34:567-73.
- [108] Schiappa DA, Hayden MK, Matushek MG, Hashemi FN, Sullivan J, Smith KY et al. Ceftazidime-resistant *K. pneumoniae pneumoniae* and *Escherichia coli*

- bloodstream infection: a case-control and molecular epidemiologic investigation. **J Infect Dis** 1996; 174:529-36.
- [109] Menashe G, Borer A, Yagupsky P, Peled N, Gilad J, Fraser D et al. Clinical significance and impact on mortality of extended-spectrum  $\beta$ -lactamase-producing Enterobacteriaceae isolates in nosocomial bacteremia. **Scand J Infect Dis** 2001;33:188-93
- [110] Piroth L, Aube H, Doise JM, Vincent-Martin M. Spread of extended-spectrum  $\beta$ -lactamase-producing *K. pneumoniae pneumoniae*: are  $\beta$ -lactamase inhibitors of therapeutic value? **Clin Infect Dis** 1998; 27:76-80.
- [111] D'Agata E, Venkataraman L, DeGirolami P, Weigel L, Samore M, Tenover F. The molecular and clinical epidemiology of Enterobacteriaceae-producing extended-spectrum  $\beta$ -lactamase in a tertiary care hospital. **J Infect** 1998; 36:279-85.
- [112] Pena C, Pujol M, Ardanuy C, et al. Epidemiology and successful control of a large outbreak due to *K. pneumoniae pneumoniae* producing extended-spectrum  $\beta$ -lactamases. **Antimicrob Agents Chemother** 1998; 42:53-8.
- [113] Paterson DL, Ko WC, Von Gottberg A, et al. International prospective study of *K. pneumoniae pneumoniae* bacteremia: implications of extended-spectrum  $\beta$ -lactamase production in nosocomial infections. **Ann Intern Med** 2004; 140:26-32.
- [114] Du B, Long Y, Liu H, Chen D, Liu D, Xu Y et al. Extended-spectrum  $\beta$ -lactamase-producing *Escherichia coli* and *K. pneumoniae pneumoniae* bloodstream infection: risk factors and clinical outcome. **Intensive Care Med** 2002; 28:1718-23.
- [115] Kim YK, Pai H, Lee HJ, Park SE, Choi EH, Kim J et al. Bloodstream infections by extended-spectrum  $\beta$ -lactamase-producing *Escherichia coli* and *K. pneumoniae pneumoniae* in children: epidemiology and clinical outcome. **Antimicrob Agents Chemother** 2002; 46:1481-91.

- [116] Lin MF, Huang ML, Lai SH. Risk factors in the acquisition of extended-spectrum  $\beta$ -lactamase *K. pneumoniae pneumoniae*: a case-control study in a district teaching hospital in Taiwan. *J Hosp Infect* 2003; 53:39-45.
- [117] Lautenbach E, Patel JB, Bilker WB, Edelstein PH, Fishman NO. Extended-spectrum  $\beta$ -lactamase-producing *Escherichia coli* and *K. pneumoniae pneumoniae*: risk factors for infection and impact of resistance on outcomes. *Clin Infect Dis* 2001;32:1162-71
- [118] Jett BD, Ritchie DJ, Reichley R, Bailey TC, Sahm DF. In vitro activities of various  $\beta$ -lactam antimicrobial agents against clinical isolates of *Escherichia coli* and *K. pneumoniae*, *K. oxytoca* resistant to oxyimino cephalosporins. *Antimicrob Agents Chemother* 1995; 39:1187-90.
- [119] Thomson KS, Moland ES. Cefepime, piperacillin-tazobactam, and the inoculum effect in tests with extended-spectrum  $\beta$ -lactamase-producing *Enterobacteriaceae*. *Antimicrob Agents Chemother* 2001; 45:3548-54.
- [120] Jacoby GA, Carreras I. Activities of  $\beta$ -lactam antibiotics against *Escherichia coli* strains producing extended-spectrum  $\beta$ -lactamases. *Antimicrob Agents Chemother* 1990; 34:858-62.
- [121] Martinez-Martinez L, Pascual A, Hernandez-Alles S, Alvarez-Diaz D, Suarez AI, Tran J et al. Roles of  $\beta$ -lactamases and porins in activities of carbapenems and cephalosporins against *K. pneumoniae pneumoniae*. *Antimicrob Agents Chemother* 1999; 43:1669-73.
- [122] Paterson DL, Mulazimoglu L, Casellas JM, et al. Epidemiology of ciprofloxacin resistance and its relationship to extended spectrum  $\beta$ -lactamase production in *K. pneumoniae pneumoniae* isolates causing bacteremia. *Clin Infect Dis* 2000; 30:473-8.
- [123] Lautenbach E, Strom BL, Bilker WB, Patel JB, Edelstein PH, Fishman NO. Epidemiological investigation of fluoroquinolone resistance in infections due to extended-spectrum  $\beta$ -lactamase-producing *Escherichia coli* and *K. pneumoniae pneumoniae*. *Clin Infect Dis* 2001;33:1288-94

- [124] Mehlhaff DL, Breiceland L, Tobin E, Venezia R, et al. Abstr 36<sup>th</sup> Intersci Conf **Antimicrob Agents Chemother** 1996; abstr. J-098
- [125] Wong-Beringer A. Therapeutic challenges associated with extended-spectrum,  $\beta$ -lactamase-producing *Escherichia coli* and *K. pneumoniae pneumoniae*. **Pharmacotherapy** 2001; 21:583-92.
- [126] Wong-Beringer A, Hindler J, Loeloff M, Queenan AM, Lee N, Pegues DA et al. Molecular correlation for the treatment outcomes in bloodstream infections caused by *Escherichia coli* and *K. pneumoniae pneumoniae* with reduced susceptibility to ceftazidime. **Clin Infect Dis** 2002;34:135-46
- [127] Zanetti G, Bally F, Greub G, et al. Cefepime versus imipenem-cilastatin for treatment of nosocomial pneumonia in intensive care unit patients: a multicenter, evaluator-blind, prospective, randomized study. **Antimicrob Agents Chemother** 2003; 47:3442-7.
- [128] Burgess DS, Hall RG II, Lewis JS II, Jorgensen JH, Patterson JE. Clinical and microbiological analysis of a hospital's extended-spectrum  $\beta$ -lactamase-producing isolates over a 2-year period. **Pharmacotherapy** 2003; 23:1232-7.
- [129] Ahmad M, Urban C, Mariano N, Bradford PA, Calcagni E, Projan SJ et al. Clinical characteristics and molecular epidemiology associated with imipenem-resistant *K. pneumoniae pneumoniae*. **Clin Infect Dis** 1999; 29:352-5.
- [130] Chong Y, Lee K. Present situation of antimicrobial resistance in Korea. **J Infect Chemother** 2000;6:189-95
- [131] Kang CI, Kim SH, Park WB, Lee KD, Kim HB, Kim EC et al. Bloodstream infections due to extended-spectrum  $\beta$ -lactamase-producing *Escherichia coli* and *K. pneumoniae pneumoniae*: risk factors for mortality and treatment outcome, with special emphasis on antimicrobial therapy. **Antimicrob Agents Chemother** 2004; 48:4574-81.
- [132] Brun-Buisson C, Legrand P, Philippon A, Montravers F, Ansquer M, Duval J. Transferable enzymatic resistance to third-generation cephalosporins during nosocomial outbreak of multiresistant *K. pneumoniae pneumoniae*. **Lancet** 1987; 2:302-6.

- [133] Rice LB, Willey SH, Papanicolaou GA, et al. Outbreak of ceftazidime resistance caused by extended-spectrum *b*-lactamases at a Massachusetts chronic-care facility. **Antimicrob Agents Chemother** 1990; 34:2193-9.
- [134] Kim BN, Woo JH, Kim MN, Ryu J, Kim YS. Clinical implications of extended-spectrum  $\beta$ -lactamase-producing *K. pneumoniae pneumoniae* bacteraemia. **J Hosp Infect** 2002; 5:99-106.
- [135] Casellas J.M. Abstract 36<sup>th</sup> Interscience Conference Antimicrobial Agents Chemotherapy 1996: abstract E89.
- [136] Venezia, R. A., F. J. Scarano, K. E. Preston, L. M. Steele, T. P. Root, R. Limberger, W. Archinal, and M. A. Kacica. Molecular epidemiology of an SHV-5 extended-spectrum beta-lactamase in enterobacteriaceae isolated from infants in a neonatal intensive care unit. **Clin Infect Dis** 1995; 21:915-23.
- [137] Pangon, B., C. Bizet, A. Bure, F. Pichon, A. Philippon, B. Regnier, and L. Gutmann. In vivo selection of a cephamycin-resistant porin-deficient mutant of *K. pneumoniae pneumoniae* producing a TEM-3 *b*-lactamase. **J Infect Dis** 1989; 159:1005-6.
- [138] Siu, L. K., P. L. Lu, P. R. Hsueh, F. M. Lin, S. C. Chang, K. T. Luh, M. Ho, and C. Y. Lee. Bacteremia due to extended-spectrum beta-lactamase-producing *Escherichia coli* and *K. pneumoniae pneumoniae* in a pediatric oncology ward: clinical features and identification of different plasmids carrying both SHV-5 and TEM-1 genes. **J Clin Microbiol** 1999; 7:4020-7.
- [139] Quinn, J. P., D. Miyashiro, D. Sahm, R. Flamm, and K. Bush. Novel plasmid-mediated beta-lactamase (TEM-10) conferring selective resistance to ceftazidime and aztreonam in clinical isolates of *K. pneumoniae pneumoniae*. **Antimicrob Agents Chemother** 1989; 33:1451-6.
- [140] Rice, L. B., E. C. Eckstein, J. DeVente, and D. M. Shlaes. Ceftazidime resistant *K. pneumoniae pneumoniae* isolates recovered at the Cleveland Department of Veterans Affairs Medical Center. **Clin Infect Dis** 1996; 23:118-24.
- [141] Karas, J. A., D. G. Pillay, D. Muckart, and A. W. Sturm. Treatment failure due to extended spectrum *b*-lactamase. **J Antimicrob Chemother** 1996; 37:203-4.



- [142] Smith, C. E., S. Tillman, A. W. Howell, R. N. Longfield, and J. H. Jørgensen. Failure of ceftazidime-amikacin therapy for bacteremia and meningitis due to *K. pneumoniae pneumoniae* producing an extended-spectrum b-lactamase. **Antimicrob Agents Chemother** 1990; 34:1290-3.
- [143] Kang CI, Kim SH, Kim DM, Park WB, Lee KD, Kim HB et al. Risk factors for and clinical outcomes of bloodstream infections caused by extended-spectrum beta-lactamase-producing *K. pneumoniae pneumoniae*. **Infect Control Hosp Epidemiol** 2004; 25:860-7
- [144] Gerald L. Mandell, John E. Bennett, Raphael Dolin. Temperature Regulation and the Pathogenesis of Fever. **Principle and Practice of Infectious Disease Fifth Edition** 2000; 1:604-7.
- [145] สุรภี เทียนกริม. Antimicrobial resistance ใน: พรรณพิศ สุวรรณกุล, ธีระพงษ์ ตัณฑวิเชียร, บรรณาธิการ. **An update on infectious disease** 2547:484.
- [146] Lucet JC, Decre D, Fichelle A et al. Control of a prolonged outbreak of extended spectrum beta-lactamase producing Enterobacteriaceae in a university hospital. **Clin Infect Dis** 1999; 29:1411-8.
- [147] Livermore DM, Yuan M. Antibiotic resistance and production of extended-spectrum beta-lactamases amongst *K. pneumoniae*, *K. oxytoca* from intensive care units in Europe. **J Antimicrob Chemother** 1996; 38:409-24.
- [148] Eisen D, Russell EG, Tymms M, Roper EJ, Grayson ML, Turnidge J. Random amplified polymorphic DNA and plasmid analyses used in investigation of an outbreak of multiresistant *K. pneumoniae pneumoniae*. **J Clin Microbiol** 1995; 33:713-7.
- [149] Leibovici L, Wysenbeek AJ, Konisberger H, Samra Z, Pitlik SD, Drucker M. Patterns of multiple resistance to antibiotics in Gram-negative bacteria demonstrated by factor analysis. **Eur J Clin Microbiol Infect Dis** 1992; 11:782-8.
- [150] McGowan JE, Jr., Hall EC, Parrott PL. Antimicrobial susceptibility in Gram-negative bacteremia: are nosocomial isolates really more resistant? **Antimicrob Agents Chemother** 1989; 33:1855-9.

- [151] Martinez-Martinez L, Pascual A, Jacoby GA. Quinolone resistance from a transferable plasmid. *Lancet* 1998; 351:797-9.
- [152] Chong Y, Lee K. Present situation of antimicrobial resistance in Korea. *J Infect Chemother* 2000;6:189-95

ภาคผนวก

## ภาคผนวก ก

### คำอธิบายของคำจำกัดความต่าง ๆ ในการศึกษา

**AmpC *beta*-lactamase:** This type of broad-spectrum enzyme, usually encoded on the bacterial chromosome, is active on cephamycins as well as oxyimino *beta*-lactams.

***Beta*-lactam-*beta*-lactamase inhibitor combinations:** Clavulanic acid, sulbactam, and tazobactam are inhibitory *beta*-lactams that bind to and block the action of class A, and to a lesser extent, class D *beta*-lactamases. The inhibitors are available in combinations with otherwise *beta*-lactamase-susceptible antibiotics, such as ticarcillin-clavulanic acid, ampicillin-sulbactam, and piperacillin-tazobactam.

**Carbapenems:** Compounds with a fused *beta*-lactam system in which the sulfur atom of the five-member ring is replaced by carbon. Examples include imipenem, meropenem, and ertapenem.

**Cephamycins:** Cephalosporins with a 7- $\alpha$ -methoxy side chain that blocks hydrolysis by class A and class D *beta*-lactamases. Examples include cefoxitin, cefotetan, and cefmetazole.

**Extended-spectrum *beta*-lactamase (ESBL) :** This name was originally coined to reflect the expanded substrate spectrum of enzymes derived from narrower-spectrum TEM, SHV, or OXA *beta*-lactamases. The term now also refers to *beta*-lactamases, such as those in the CTX-M family, with a similar phenotype but a separate heritage.

**Inhibitor-resistant *beta*-lactamase:** Enzyme variants in the TEM family (and, less often, the SHV family) with reduced sensitivity to clavulanic acid, sulbactam, and tazobactam inhibitors as a result of amino acid substitutions.

**Inoculum effect:** Increased resistance with increasing numbers of test bacteria. One possible mechanism is increased hydrolysis with larger inocula of *beta*-lactamase-producing organisms.

**Integron:** A unit of DNA containing a gene for a site-specific integrase (*intI*) and a recombination site (*attI*) , into which gene cassettes made up of an antibiotic-resistance gene linked to a 59-base element (or *attC* site) can be integrated. A strong promoter adjacent to the *attI* site ensures that the integrated genes will be efficiently expressed.

Integrans can be part of a transposon or a defective transposon and thus have an additional potential for mobility.

**Monobactam:** A monocyclic *beta*-lactam. The single commercially available example is aztreonam, which has an oxyimino side chain and is therefore also an oxyimino *beta*-lactam.

**Oxyimino *beta*-lactams:** *beta*-Lactams with an oxyiminoside chain designed to block the action of *beta*-lactamase. Sometimes referred to as "third-generation cephalosporins," they include cefotaxime, ceftriaxone, ceftazidime, and cefepime (a "fourth-generation" derivative).

**Plasmid:** An extrachromosomal segment of DNA, usually circular, varying in size from a few kilobases to a 10th or more of the size of the bacterial chromosome. Plasmids larger than 20 kb are often conjugative and can promote their transfer between bacterial hosts. Resistance plasmids carry resistance genes, often organized into integrans or carried on transposons. Other plasmids carry metabolic genes or act as sex factors to promote transfer of the bacteria chromosome.

**SHV, TEM, OXA, IMP, VIM, and KPC:** *beta*-Lactamase families with members (denoted by numerals, as in SHV-1) that are related by a few amino acid substitutions. *Beta*-Lactamase nomenclature is not standardized. SHV denotes a variable response to sulfhydryl inhibitors; TEM was named after the patient (Temoneira) from whom the first sample was obtained; CTX-M, OXA, and IMP reflect an ability to hydrolyze cefotaxime, oxacillin, and imipenem, respectively; VIM denotes Verona integron-encoded Metallo *beta*-lactamase; and KPC is derived from *K. pneumoniae pneumoniae* carbapenemase.

The origin of names for other *beta*-lactamases is just as variable and arcane.

**Transposon:** A mobile unit of DNA that can jump, or transpose, from one DNA molecule to another - for example, from a plasmid to a chromosome or from a plasmid to a plasmid, usually without site specificity. In class I transposons, a pair of insertion sequences (segments of DNA that can replicate and insert more or less randomly at other sites) flank a resistance gene. In class II transposons, terminal inverted-repeat segments enclose the genes for a transposase (*tnpA*), a resolvase (*tnpR*), and one or more antibiotic-resistance genes. Some transposons are conjugative.

## ภาคผนวก ข

วิธีการตรวจหาเ็นไซม์เบต้าแลกตาเมสด้วยวิธี combination disc ตามมาตรฐานของ CLSI 2004

Screening and Confirmatory Tests for ESBLs in *Klebsiella pneumoniae*, *K. oxytoca*, and *Escherichia coli*

Method	Initial Screen Test	Phenotypic Confirmatory Test
Medium	Mueller-Hinton Agar	Mueller-Hinton Agar
Antimicrobial Disk Concentration	Cefpodoxime 10 µg or ceftazidime 30 µg or aztreonam 30 µg or cefotaxime 30 µg or ceftriaxone 30 µg  (The use of more than one antimicrobial agent for screening improves the sensitivity of detection.)	ceftazidime 30 µg ceftazidime-clavulanic acid <sup>a</sup> 30/10 µg <b>and</b> cefotaxime 30 µg cefotaxime-clavulanic acid <sup>a</sup> 30/10 µg  (Confirmatory testing requires use of both cefotaxime and ceftazidime, alone and in combination with clavulanic acid.)
Inoculum		
Incubation conditions	Standard disk diffusion recommendations	Standard disk diffusion recommendations
Incubation length		
Results	Cefpodoxime zone ≤ 17 mm Ceftazidime zone ≤ 22 mm Aztreonam zone ≤ 27 mm Cefotaxime zone ≤ 27 mm Ceftriaxone zone ≤ 25 mm = may indicate ESBL production	A ≥ 5-mm increase in a zone diameter for either antimicrobial agent tested in combination with clavulanic acid versus its zone when tested alone = ESBL (e.g., ceftazidime zone = 16; ceftazidime-clavulanic acid zone = 21)
QC Recommendations	<i>E. coli</i> ATCC <sup>®</sup> 25922 (see control limits in Table 3) <i>Klebsiella pneumoniae</i> ATCC <sup>®</sup> 700603:  cefepodoxime zone 9-16 mm ceftazidime zone 10-18 mm aztreonam zone 9-17 mm cefotaxime zone 17-25 mm ceftriaxone zone 16-24 mm	<i>E. coli</i> ATCC <sup>®</sup> 25922: ≤ 2-mm increase in zone diameter for antimicrobial agent tested alone versus its zone when tested in combination with clavulanic acid <i>Klebsiella pneumoniae</i> ATCC <sup>®</sup> 700603: ≥5-mm increase in ceftazidime-clavulanic acid zone diameter; ≥ 3-mm increase in cefotaxime-clavulanic acid zone diameter.

## Footnote

- a. Preparation of ceftazidime-clavulanic acid (30 µg/10 µg) and cefotaxime-clavulanic acid (30 µg/10 µg) disks: Using a stock solution of clavulanic acid at 1,000 µg/mL (either freshly prepared or taken from small aliquots that have been frozen at -70 °C), add 10 µL of clavulanic acid to ceftazidime (30 µg) and cefotaxime (30 µg) disks. Use a micropipette to apply the 10 µL of stock solution to the ceftazidime and cefotaxime disks within one hour before they are applied to the plates, allowing about 30 minutes for the clavulanic acid to absorb and the disks to be dry enough for application. Use disks immediately after preparation or discard; do not store.

## ภาคผนวก ค

วิธีการตรวจหาเอ็นไซม์เบต้าแลกตาเมสด้วยวิธี broth dilution ตามมาตรฐานของ CLSI

2004

Screening and Confirmatory Tests for ESBLs in *Klebsiella pneumoniae*, *K. oxytoca*, and *Escherichia coli*

Method	Initial Screen Test	Phenotypic Confirmatory Test
Medium	CAMHB	CAMHB
Antimicrobial Concentration	cefpodoxime 4 µg/mL or ceftazidime 1 µg/mL or aztreonam 1 µg/mL or cefotaxime 1 µg/mL or ceftriaxone 1 µg/mL  (The use of more than one antimicrobial agent for screening will improve the sensitivity of detection.)	ceftazidime 0.25-128 µg/mL ceftazidime-clavulanic acid 0.25/4-128/4 µg/mL <b>and</b> cefotaxime 0.25-64 µg/mL cefotaxime-clavulanic acid 0.25/4-64/4 µg/mL  (Confirmatory testing requires use of both cefotaxime and ceftazidime, alone and in combination with clavulanic acid.)
Inoculum	Standard broth dilution recommendations	Standard broth dilution recommendations
Incubation Conditions		
Incubation Length		
Results	Growth = may indicate ESBL production (i.e., MIC ≥ 2 µg/mL for ceftazidime, aztreonam, cefotaxime, or ceftriaxone; or MIC ≥ 8 µg/mL for cefpodoxime)	A ≥ 3 twofold concentration decrease in an MIC for either antimicrobial agent tested in combination with clavulanic acid versus its MIC when tested alone = ESBL (e.g., ceftazidime MIC= 8 µg/mL; ceftazidime-clavulanic acid MIC = 1 µg/mL).
QC Recommendations	<i>E. coli</i> ATCC* 25922 = No growth (also refer to control limits listed in M7 Table 3)  <i>Klebsiella pneumoniae</i> ATCC* 700603 = Growth:  cefpodoxime MIC ≥ 8 µg/mL ceftazidime MIC ≥ 2 µg/mL aztreonam MIC ≥ 2 µg/mL cefotaxime MIC ≥ 2 µg/mL ceftriaxone MIC ≥ 2 µg/mL	<i>Klebsiella pneumoniae</i> ATCC* 700603: ≥ 3 twofold concentration decrease in an MIC for an antimicrobial agent tested in combination with clavulanic acid versus its MIC when tested alone.





13. DM 1.yes 2.no
14. cerebrovascular disease 1.yes 2. no
15. previous medication 1.yes, specify.....  
2.no
16. previous antibiotic use (within 1 month) 1.yes, specify.....  
2. no
17. previous hospital admission 1. yes, duration..... 2. no
18. renal disease 1.yes, specify..... 2. no
19. history previous UTI 1. yes, duration..... 2. no
20. drug allergy 1.yes, specify..... 2. no

### Symptoms

21. fever 1.yes, duration....., . grade..... 2. no
22. nausea 1. yes, . grade..... 2. no
23. vomiting 1. yes, . grade..... 2. no
24. chill 1. yes 2. no
25. back pain 1. yes 2. no
26. dysuria 1. yes 2. no
27. urinary frequency 1. yes 2. no
28. urgency 1. yes 2. no
29. hematuria 1. yes 2. no

### Physical examination

30. body temperature .....C
31. BP ..... mm/Hg
32. pulse ...../min
33. RR ...../min
34. pale 1. yes 2. no
35. jaundice 1. yes 2. no
36. CVA tender 1. yes 2. no
37. respiratory system 1. abnormal 2. normal
38. abdominal system 1. abnormal 2. normal
- Hepatomegaly 1. yes 2. no
- Splenomegaly 1. yes 2. no

## 39. clinical severity

mild (absence of criteria for moderate and severe)

moderate ( fever > 39 C, severe flank pain, nausea or vomiting, leukocytosis

wbc>15, 000 : 2 ใน 4 ข้อ)

severe (vital signs unstable or sepsis)

Laboratory finding

## 40. CBC

Haemoglobin ..... g/dl Hct ..... %

White blood cell ...../mm<sup>3</sup>

Absolute neutrophil count .....%.

Platelet ...../mm<sup>3</sup>

41. leukocytosis (wbc>15, 000) 1. yes 2. no

## 42. UA

Wbc...../mm<sup>3</sup> rbc...../mm<sup>3</sup> Wbc cast.....

protein..... sugar.....

## 43. Urine Gram stain

1. Gram negative 2. organism not found

44. Urine culture 1.positive 2. no growth

1. *E. coli* 2. *K. pneumoniae* 3. *K. oxytoca* 4. other, specify

sensitivity.....

resist.....

45. hemoculture 1.positive 2. no growth

1. *E. coli* 2. *K. pneumoniae* 3. *K. oxytoca* 4. other, specify

sensitivity.....

resist.....

46. CXR 1. abnormal, specify..... 2. normal

47. USG kidney 1. yes 2. no

If yes, specified result .....

48. CT abdomen 1. yes 2. no

If yes, specified result .....

49. IVP 1. yes 2. no

If yes, specified result .....

50. MIC ceftriaxone .....

51. ESBL producing 1. yes 2. no

52. creatinine .....mg/dl

53. Na .....

54. K .....

55. HCO<sub>3</sub> .....

56. Blood sugar .....

**Assessment Day 1, date**.....

57. Fever, oral  $\geq 37.8$  1.yes, grade.....2. no, time.....hr after antibiotic

58. Chill 1.yes 2. no

59. Nausea 1.yes , grade..... 2. no

60. Vomiting 1.yes , grade..... 2. no

61. CVA tender 1.yes 2. no

**Assessment Day 2, date**.....

62. Fever, oral  $\geq 37.8$  1.yes, grade.....2. no , time..... hr after antibiotic

63. Chill 1.yes 2. no

64. Nausea 1.yes, grade..... 2. no

65. Vomiting 1.yes , grade..... 2. no

66. CVA tender 1.yes 2. no

**Assessment Day 3, date**.....

**Clinical outcome**

67. Fever, oral  $\geq 37.7$  1.yes, grade..... 2. no, time.....hr after antibiotic

68. Chill 1.yes 2. no

69. Nausea 1.yes, grade..... 2. no

70. Vomiting 1.yes, grade..... 2. no

71. CVA tender 1.yes 2. no

**Microbiological outcome**

72. leukocytosis 1.yes 2. no

73. wbc in urine 1.yes , จำนวน..... 2. no

74. urine Gram stain 1. Gram negative 2. organism not found

75. urine culture 1.positive 2. no growth

1. *E. coli*                      2. *K. pneumoniae*                      3. other, specify  
 sensitivity.....  
 resist.....

76. change antibiotic      1. yes, specify.....      2. no

77. complication      1. yes                      2. no  
 if yes, specify.....

#### response for treatment

78. fever clearance time ..... Hr (ระยะเวลาตั้งแต่เริ่มให้ยาจนถึงตรวจพบไม่มีไข้)

79. outcome      1 cured      2 improved      3 recurrent      4 death

Assessment day 10-14, date.....

#### Clinical outcome

80. Fever, oral  $\geq 37.7$  1. yes, grade..... 2. no, time.....hr after antibiotic

81. Chill      1. yes                      2. no

82. Nausea      1. yes, grade..... 2. no

83. Vomiting      1. yes, grade..... 2. no

84. CVA tender      1. yes                      2. no

#### Microbiological outcome

85. leukocytosis      1. yes                      2. no

86. wbc in urine      1. yes , จำนวน..... 2. no

87. urine Gram stain      1. Gram negative 2. organism not found

88. urine culture      1. positive                      2. no growth

1. *E. coli*                      2. *K. pneumoniae*                      3. other, specify  
 sensitivity.....  
 resist.....

89. complication      1. yes                      2. no  
 if yes, specify.....

## ประวัติผู้เขียนวิทยานิพนธ์



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ประวัติการศึกษาและการทำงาน

นิสิตคณะแพทยศาสตร์จุฬาลงกรณ์	2534-2540
แพทย์เพิ่มพูนทักษะ โรงพยาบาลสรรพสิทธิประสงค์	2540-2541
แพทย์ประจำโรงพยาบาลตากสิน	2541
แพทย์ประจำบ้านอายุรศาสตร์ โรงพยาบาลจุฬาลงกรณ์	2543-2546

ปริญญาและประกาศนียบัตร

แพทยศาสตรบัณฑิต (เกียรตินิยมอันดับ2) จุฬาลงกรณ์	2540
วุฒิบัตรแพทย์ผู้เชี่ยวชาญสาขาอายุรศาสตร์	2546
อนุมัติบัตรแพทย์เวชศาสตร์ครอบครัว แพทยสภา	2547

สมาชิกสมาคมวิชาชีพ

- สมาชิกราชวิทยาลัยอายุรแพทย์แห่งประเทศไทย
- สมาชิกสมาคมโรคติดเชื้อแห่งประเทศไทย
- สมาชิกสมาคมทางเดินอาหารแห่งประเทศไทย
- สมาชิกสมาคมต่อมไร้ท่อแห่งประเทศไทย
- สมาชิกแพทยสภา