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Extended-Spectrum Cephalosporin Compared to Cefazolin for Treatment of *Klebsiella pneumoniae*-Caused Liver Abscess

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From January 1995 to May 2000, a total of 107 adults with liver abscess due to *Klebsiella pneumoniae* admitted at a large medical center in northern Taiwan were reviewed. Patients were considered to have received cefazolin or an extended-spectrum cephalosporin if they received at least 3 days of that antibiotic within the first 5 days of hospitalization. Fifty-nine (55.1%) patients received cefazolin, and 48 (44.9%) patients received an extended-spectrum cephalosporin. The demographic data, clinical features, severities of illness, and rates of early drainage for the two groups were comparable. However, the rates of developing complications for the two groups were significantly different (37.3 versus 6.3%, respectively; $P < 0.001$). Furthermore, six independent factors preventing severe complications following liver abscess due to *K. pneumoniae* were identified: normal platelet count, alkaline phosphatase less than 300 U/liter, no gas formation in the abscess, APACHE III score less than 40, use of an extended-spectrum cephalosporin, and early drainage. In conclusion, cefazolin therapy may be suboptimal for patients with liver abscess due to *K. pneumoniae* despite active in vitro susceptibility. Use of an extended-spectrum cephalosporin and early drainage for patients with liver abscess due to *K. pneumoniae* are suggested.

Pyogenic liver abscess caused by *Klebsiella pneumoniae* has been increasing over the last 2 decades (1, 13, 15, 27). Severe complications including septic endogenous endophthalmitis, metastatic infections of brain and lung, and necrotizing fasciitis in patients from all over the world have been reported (2, 12, 14, 16, 19, 23). Metastatic infections and severe pulmonary complications in liver abscesses due to *K. pneumoniae* often resulted in poor outcome (8–10, 18, 20).

Over the past 20 years, *K. pneumoniae* has been identified as the leading cause (30 to 88%) of liver abscesses in Taiwan (3, 4, 6–9, 11, 25, 26). The frequency of development of metastatic infection from liver abscesses due to *K. pneumoniae* was 10 to 21%, which was much higher than that for liver abscesses due to organisms other than *K. pneumoniae* (3, 4, 7–9, 25).

K. pneumoniae, which causes community-acquired liver abscesses in Taiwan, has remained susceptible to cefazolin over the past 20 years (4, 6, 25). There is no consensus on the most appropriate antibiotic treatment for the disease. The purpose of this study is to investigate the therapy that optimizes treatment outcomes for liver abscess due to *K. pneumoniae*.

MATERIALS AND METHODS

Definitions. Liver abscess due to *K. pneumoniae* was defined by the following criteria: (i) liver abscess seen by imaging studies (abdominal ultrasonography and/or computerized tomography) or detected during laparotomy, (ii) only *K. pneumoniae* isolated from the blood or abscess aspirate, and (iii) a negative amebic serologic test.

Metastatic infection due to the disease was defined by the presence of infectious foci other than the liver and by a bacterial culture of vitreous aspirate, cerebrospinal fluid, epidural abscess, pleural effusion or other material from the tissue or organs positive for *K. pneumoniae*. Endogenous endophthalmitis was defined as pupillary hypopyon or hypopyon in addition to vitreous opacity. The diagnosis was confirmed by an ophthalmologist. Vitreous aspirate culture was also performed during the surgical management.

Pulmonary complications in the study were defined as ventilator-dependent respiratory failure, acute respiratory distress syndrome, and septic pulmonary emboli. The septic pulmonary emboli were clinically defined as present if the chest radiograph showed multiple nodular opacity lesions which disappeared after antibiotic treatment.

Severe complications were defined as occurrence of metastatic infections, pulmonary complications, or death more than 72 h after admission. Use of cefazolin versus an extended-spectrum cephalosporin was defined as administration of the antibiotic for at least 3 days within the first 5 days of hospitalization. Early drainage was defined as a drainage procedure performed within the first 3 days of diagnosis.

Patients. From January 1995 to May 2000, there were 212 adult patients with pyogenic liver abscess admitted to Tri-Service General Hospital. One hundred twenty-one patients had disease caused by *K. pneumoniae* as defined above.

For the analysis of the risk factors for developing severe complications following liver abscess due to *K. pneumoniae*, the 25 (of 121; 20.7%) patients who developed severe complications as defined above were considered. Eighty-two (67.8%) patients with liver abscess due to *K. pneumoniae* who had no complications during their hospitalization acted as controls. However, 14 patients (11.6%) who developed a complication within the first 72 h of hospitalization were excluded, because it was difficult to attribute the complications to the treatment.

The 107 patients who were enrolled were divided into two groups: those who received cefazolin and those who received an extended-spectrum cephalosporin.

Collection of medical data. Demographic data and medical information such as the presenting signs and symptoms, the underlying conditions, the laboratory data, the imaging findings, the medications administered, the drainage used, and the APACHE III score were collected (17). Information on the *K. pneumoniae* strains isolated from blood, liver abscess aspirate, or other sterile sites and their antibiograms was obtained from the medical records. MIC testing was performed according to NCCLS guidelines.

Statistical analysis. All the collected data were entered in a computerized database for analysis. The independent-sample t test, χ^2 test, or Fisher's exact test was used to assess the statistical significance of differences. The Mantel-Haenszel test was used for stratified analysis and for estimating the common odds ratio. Further logistic regression analysis by the forward stepwise method was used to identify the independent factors significantly associated with the

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TABLE 1. Demographic data, underlying illnesses, and vital signs for patients with liver abscess due to *K. pneumoniae* treated with either cefazolin or an extended-spectrum cephalosporin

Parameter or condition[a]	No. (%) of patients in:		*P*
	Cefazolin group ($n = 59$)	Extended-spectrum cephalosporin group ($n = 48$)	
Age ≥ 60 yr	31 (52.5)	23 (47.9)	0.63
Females	18 (30.5)	17 (35.4)	0.59
Underlying illnesses			
Diabetes mellitus	35 (59.3)	22 (45.8)	0.16
Liver cirrhosis	2 (3.4)	2 (4.2)	0.83
Gall bladder stone	6 (10.2)	7 (14.6)	0.49
Biliary tract stone	6 (10.2)	7 (14.6)	0.49
Biliary or GI tract operation	7 (11.9)	4 (8.3)	0.55
Peptic ulcer	9 (15.3)	5 (10.4)	0.46
Solid-organ cancer	4 (6.8)	5 (10.4)	0.50
Alcoholism	5 (8.5)	1 (2.1)	0.15
Hypertension	11 (18.6)	10 (20.8)	0.78
Vital signs			
BT > 38°C or < 36°C	27 (45.8)	22 (45.8)	0.99
HR > 90/min	30 (50.8)	22 (45.8)	0.61
RR > 20/min	21 (35.6)	20 (41.7)	0.52
MAP < 80 mm Hg	9 (15.3)	11 (22.9)	0.31
APACHE III score > 40	14 (23.7)	14 (29.2)	0.52

[a] BT, body temperature; HR, heart rate; RR, respiratory rate; MAP, mean arterial pressure; GI, gastrointestinal. Extended-spectrum cephalosporins were ceftriaxone ($n = 25$), cefotaxime ($n = 10$), moxalactam ($n = 7$), cefoperazone ($n = 5$), and ceftazidime ($n = 1$)

prevention of severe complications in patients with liver abscess due to *K. pneumoniae*. A statistically significant difference was defined as a *P* value of <0.05. Data analysis was performed using the Statistical Products of Services Solutions, version 9.0 for Windows, statistical software package (SPSS Inc., Chicago, Ill.).

RESULTS

Demographic data, underlying illnesses, vital signs, data from clinical biochemistry, and image findings for patients with liver abscess due to *K. pneumoniae* treated with either cefazolin or an extended-spectrum cephalosporin. Altogether, 107 adult patients with liver abscess due to *K. pneumoniae* were enrolled in the study. All the infections were community acquired, and all of the *K. pneumoniae* strains isolated from these patients were susceptible to cefazolin. MICs for all isolates of cefazolin, extended-spectrum cephalosporins including ceftriaxone, ceftazidime, and cefotaxime, and gentamicin were 0.5 to 2, ≤0.25, and ≤0.25 μg/ml, respectively.

Table 1 shows the demographic data, underlying medical conditions, and vital signs. No significant difference between the patients treated with cefazolin and those treated with extended-spectrum cephalosporin was found. For laboratory and image findings, no significant difference was identified except that more of the patients who received an extended-spectrum cephalosporin had alkaline phosphatase levels >300 U/liter (70.8 versus 49.2%, $P = 0.02$; Table 2). The demographic data, clinical features, and severities of illness for patients treated with cefazolin were comparable to those for patients treated with an extended-spectrum cephalosporin.

TABLE 2. Laboratory findings and radiologic findings for the two groups of patients

Parameter[a]	No. (%) of patients in:		*P*
	Cefazolin group ($n = 59$)	Extended-spectrum cephalosporin group ($n = 48$)	
Laboratory data			
Albumin < 30 g/liter	17 (28.8)	19 (39.6)	0.24
Leukocyte count > 12.0×10^9 or < 4.0×10^9/liter	35 (59.3)	32 (66.7)	0.44
Platelet count < 100×10^9/liter	8 (13.6)	8 (16.7)	0.65
ALT > 80 U/liter	19 (32.2)	22 (45.8)	0.15
AST > 80 U/liter	17 (28.8)	19 (39.6)	0.24
Alkaline phosphatase > 300 U/liter	29 (49.2)	34 (70.8)	0.02
Urea nitrogen > 7.14 nmol/liter (20 mg/dl)	24 (40.7)	20 (41.7)	0.92
Creatinine > 132.6 μmol/liter (1.5 mg/dl)	9 (15.3)	12 (25.0)	0.21
K. pneumoniae bacteremia	38 (64.4)	33 (68.8)	0.64
Image findings			
Abscess size ≥ 5 cm	41 (69.5)	39 (81.3)	0.16
Gas formation	12 (20.3)	8 (16.7)	0.63
Solitary abscess	47 (79.7)	44 (91.7)	0.08
Septum formation	7 (11.9)	8 (16.7)	0.48

[a] ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Management and the incidence of developing severe complication for the patients treated with cefazolin versus those treated with an extended-spectrum cephalosporin. All 107 patients were given parenteral antibiotics once the disease was diagnosed. There was no significant difference in the mean days of fever before hospitalization between patients treated with cefazolin and those treated with extended-spectrum cephalosporins (6.7 versus 7.8 days; $P = 0.4$). Most patients received parenteral antibiotics for 2 to 4 weeks and then oral antibiotics for at least 2 weeks. The initial antibiotic used was either cefazolin or an extended-spectrum cephalosporin. The dose and dose interval for cefazolin were 1 g and 8 h, respectively. Of the 48 patients who received extended-spectrum cephalosporins, 25 received ceftriaxone (52.1%), 10 received cefotaxime (20.8%), 7 received moxalactam (14.6%), 5 received cefoperazone (10.4%), and 1 received ceftazidime (2.1%). Cefazolin, used initially for 76 patients on admission, was changed to an extended-spectrum cephalosporin for 49 patients because of persistent fever or the progression of the disease. Among the 49 patients, 17 were changed to an extended-spectrum cephalosporin within 3 days of hospitalization. When an extended-spectrum cephalosporin was used on admission, it was never changed for any patient during their first week of hospitalization. An aminoglycoside was also used for some patients on admission. No other antibiotics, including β-lactams and fluoroquinolones, were used as initial therapy for the 107 patients.

For antibiotic treatment in the two different groups of patients, a lower rate of simultaneous use of aminoglycoside (43.8 versus 84.7%; $P < 0.001$) was found for the group of patients who were treated with an extended-spectrum cephalosporin (Table 3). There was a significantly lower rate of developing severe complications in the group of patients who were treated

TABLE 3. Treatment and development of severe complications in the two groups of patients

Group (*n*)	No. (%) of patients[b]		
	Receiving:		Developing severe complications[a]
	Aminoglycoside	Early drainage	
Cefazolin (59)	50 (84.7)	29 (49.2)	22 (37.3)
Extended-spectrum cephalosporin (48)	24 (43.8)/<0.001	29 (60.4)/0.25	3 (6.3)/<0.001

[a] Severe complications included septic endophthalmitis, septic pulmonary emboli on chest X-ray, epidural abscess, meningitis, prostate abscess, renal abscess, and necrotizing fasciitis.
[b] Numbers to the right of shills are *P* values.

with an extended-spectrum cephalosporin (6.3 versus 37.3%; $P < 0.001$; Table 3).

To clarify the effect of an aminoglycoside combination, patients were stratified by whether they received an extended-spectrum cephalosporin or cefazolin with or without an aminoglycoside. The *P* value for the difference between the frequencies with which groups receiving an aminoglycoside for ≥3 days and <3 days developed severe complications was 0.774 (common odds ratio = 0.7; 95% confidence interval [CI] = 0.2 to 2.3; Table 4). Even treatment with the combination of cefazolin and an aminoglycoside was inferior to extended-spectrum cephalosporin treatment with respect to the development of severe complications.

Eighty-seven (81.3%) of 107 patients received drainage. Seventy-eight patients received percutaneous pigtail catheter drainage, 6 patients received surgical drainage, and 3 patients received fine-needle aspiration. Twenty patients did not receive drainage, of which 7 had an unliquefied small abscess. Fifty-eight patients received early drainage by our definition. When the comparison between cefazolin and extended-spectrum cephalosporins took into account receipt of early drainage, extended-spectrum cephalosporins remained superior to cefazolin (Table 5).

Only 6.3% (3 of 48) of patients who received an extended-spectrum cephalosporin developed severe complications, while 37.3% (22 of 59) of patients who received cefazolin developed such complications ($P < 0.001$; Table 3). Use of cefazolin versus an extended-spectrum cephalosporin resulted in a relative risk of developing severe complications following liver abscess due to *K. pneumoniae* (common odds ratio) of 6.0, and the 95% CI was 1.9 to 18.7.

TABLE 4. Duration of aminoglycoside usage and severe complications in cases of *K. pneumoniae* liver abscess, stratified by the use of cephalosporins[a]

Group (*n*)	Simultaneous use of an aminoglycoside for ≥3 days (*n*)	No. (%) of patients with severe complications
Cefazolin (59)	Yes (50)	17 (34.0)
	No (9)	5 (55.6)
Extended-spectrum cephalosporin (48)	Yes (21)	2 (9.5)
	No (27)	1 (3.7)

[a] The *P* value for the difference between rates of developing severe complications depending on whether aminoglycosides were used for ≥3 days or <3 days was 0.774. The Mantel-Haenszel common odds ratio for development of severe complications in patients treated with aminoglycosides for ≥3 days was 0.7 (95% CI: 0.2 to 2.3).

TABLE 5. Antibiotic treatment and severe complications in cases of liver abscess due to *K. pneumoniae,* stratified by APACHE III score and timing of drainage

APACHE III score (*n*)	Early drainage (*n*)	Use of an extended-spectrum cephalosporin[a] (*n*)	No. (%) of patients with severe complications
>40 (27)	Yes (12)	Yes (7)	2 (28.6)
		No (5)	2 (40.0)
	No (15)	Yes (6)	1 (16.7)
		No (9)	8 (88.9)
≤40 (80)	Yes (46)	Yes (22)	0
		No (24)	3 (12.5)
	No (34)	Yes (13)	0
		No (21)	9 (42.9)

[a] *P* for early use of a extended-spectrum cephalosporin, <0.001. The Mantel-Haenszel common odds ratio for development of severe complications in a patient with liver abscess due to *K. pneumoniae* is 0.07 (95% CI, 0.01 to 0.34).

The associations of severe complications with the risk factors APACHE III score, drainage, and the use of antibiotics. To control for the effect of early drainage and severity of illness, we used stratified analyses and the Mantel-Haenszel test to estimate the common odds ratio for the antibiotic treatment (Table 5). Extended-spectrum cephalosporins were consistently superior to cefazolin in all analyses (Table 5).

Clinical outcome and complications in all patients with liver abscess due to *K. pneumoniae*. In the enrolled patients, the incidence of metastatic infections was 6.5% (7 of 107). Endophthalmitis was the most common metastatic complication. Twenty-five of 107 patients (23.3%) developed severe complications between the 4th and 10th days after admission; among them, 7 died. The outcome and complications for all patients with liver abscess due to *K. pneumoniae* are compared in Table 6.

Factors significantly associated with the prevention of the development of severe complications. Among the 107 patients, 25 developed severe complications later than 3 days after admission and 82 did not have any complication during their hospitalization. We found some variables significantly associated with developing severe complications by way of univariate analysis ($P < 0.05$). They included tachypnea (respiratory rate > 20/min), thrombocytopenia (platelet count $< 100 \times 10^9$/

TABLE 6. Outcome and complications in all patients with liver abscess due to *K. pneumoniae*

Severe complication	No. (%) of patients treated with:		*P*
	Cefazolin (*n* = 59)	Extended-spectrum cephalosporin (*n* = 48)	
Metastatic infections	7[a] (11.9)	0	0.02
Pulmonary complications	17[b] (28.8)	3 (6.3)	<0.01
Death	5 (8.5)	2 (4.2)	0.42

[a] Among the seven patients with endophthalmitis, one had concomitant septic pulmonary emboli, prostate abscess, and renal abscess, one had concomitant septic pulmonary emboli, and epidural abscess, and one had concomitant necrotizing fasciitis on left index finger.
[b] Two patients had only septic pulmonary emboli, and two patients with ventilator-dependent respiratory failure also had metastatic infections.

TABLE 7. Adjusted odds ratios for significant factors for preventing severe complications in patients with liver abscess due to *K. pneumoniae*[a]:

Factor	Adjusted odds ratio	95% CI
Platelet count $> 100 \times 10^9$/liter	0.03	0.004–0.28
Alkaline phosphatase < 300 U/liter	0.19	0.04–0.78
No gas formation in abscess	0.2	0.05–0.92
APACHE III score < 40	0.07	0.01–0.39
Extended-spectrum cephalosporin treatment[b]	0.01	0.001–0.12
Early drainage[c]	0.11	0.02–0.53

[a] In addition to the six factors in this table, age, sex, history of diabetes and peptic ulcer, tachypnea, tachycardia, albumin, blood urea nitrogen, and creatinine levels, and large abscess were all included in the logistic regression analysis. They were all eliminated in the final model.
[b] Patients received an extended-spectrum cephalosporin for at least 3 days within the first 5 days of hospitalization.
[c] Patients received early drainage within 3 days of diagnosis.

liter), low albumin (<3.0 g/dl), high blood urea nitrogen (>20 mg/dl), high creatinine (>1.5 mg/dl), use of cefazolin, nonearly drainage, and an APACHE III score higher than 40. A further analysis with logistic regression using the forward stepwise method identified six independent factors significantly associated with the prevention of severe complications: platelet count of $>100 \times 10^9$/liter, alkaline phosphatase level of <300 U/liter, no gas formation in the abscess, APACHE III score of <40, use of an extended-spectrum cephalosporin, and early drainage (Table 7).

DISCUSSION

The purpose of this cohort study was to find the optimal therapy and to assess the difference between two currently used therapies for the treatment of liver abscess due to *K. pneumoniae*. Our study has observed that cefazolin is less efficacious than extended-spectrum cephalosporins for preventing the development of severe complications. Although *K. pneumoniae*, which causes community-acquired liver abscess, remains susceptible to cefazolin (4, 6, 25), this study shows that cefazolin may not be the optimal treatment for the disease.

This study identified six independent factors associated with preventing the development of severe complications in liver abscess due to *K. pneumoniae*: platelet count of $>100 \times 10^9$/liter, alkaline phosphatase level of <300 U/liter, no gas formation in the abscess, an APACHE III score of <40, use of an extended-spectrum cephalosporin, and early drainage. Although more patients in the group that received an extended-spectrum cephalosporin had alkaline phosphatase levels higher than 300 U/liter, an independent risk factor predicting severe complications, the rate of severe complications was lower in this group. Patients who received cefazolin had a higher rate of concomitant use of an aminoglycoside, but this group of patients was statistically associated with a higher rate of development of severe complications than the group of patients with extended-spectrum cephalosporin treatment. In the present investigation, the dose and dose interval were 1 g and 8 h, respectively, for patients treated with cefazolin whereas the gentamicin dosage was 4 mg/kg of body weight/day for patients with normal renal function (dosage was adjusted if renal function was impaired). Since the in vitro cefazolin MICs for isolates ranged from 0.5 to 2 μg/ml and the aminoglycoside (gentamicin) MIC was ≤0.25 μg, the reason for the unfavorable outcome is probably not that cefazolin and aminoglycoside concentrations were below the MICs.

When the patients were further stratified by disease severity and timing of drainage, patients who received cefazolin still had more severe complications than those who received an extended-spectrum cephalosporin during their hospitalization (Table 5). All the univariate and multivariate analyses lead to the conclusion that an extended-spectrum cephalosporin is better than cefazolin for the treatment of liver abscess due to *K. pneumoniae*.

On the basis of an animal model, it has previously been suggested that the inoculum effect, a significant increase in the MIC when the inoculum size is increased, has important predictive value for in vivo efficacy. A correlation between MIC and in vivo response is predicted only if the MIC is determined with a large inoculum instead of the standard one (24). In most microbiology laboratories, the MIC is based on the susceptibility result from a standard inoculum and all *K. pneumoniae* isolates have an ubiquitous chromosomally mediated SHV-1 β-lactamase (5), which inactivates the cefazolin in an inoculum-dependent manner (21). As a result, the use of a cefazolin predisposes patients to severe infective complications in liver abscess due to *K. pneumoniae*. In contrast, the extended-spectrum cephalosporins have better penetration into the aqueous humor of the eye, the cerebrospinal fluid, the synovial fluid, and the pericardial fluid (22). Also, the maximum concentrations of the extended-spectrum cephalosporins in serum greatly exceeded the MIC and ratio of the area under the concentration-time curve to the MIC was large even when the MICs were determined with a large inoculum (24). The extended-spectrum cephalosporins are thus more effective than cefazolin when an obscure metastatic infection exists in the early stage of the disease. This is relevant to the treatment of an abscess, which contains the equivalent of a high inoculum.

In conclusion, use of an extended-spectrum cephalosporin instead of the cephalosporin cefazolin optimizes the outcome for liver abscess due to *K. pneumoniae*.

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REFERENCES

1. **Barton, E. N., H. Daisley, D. T. Gilbert, and L. Roberts.** 1991. Diabetes mellitus and *Klebsiella pneumoniae* liver abscess in adults. Trop. Geogr. Med. **43:**100–104.
2. **Casanova, C., J. A. Lorente, F. Carrillo, E. Perez-Rodriguez, and N. Nunez.** 1989. *Klebsiella pneumoniae* liver abscess associated with septic endophthalmitis. Arch. Intern. Med. **149:**1467.
3. **Chang, F. Y., and M. Y. Chou.** 1995. Comparison of pyogenic liver abscess caused by *Klebsiella pneumoniae* and non-*Klebsiella pneumoniae* pathogens. J. Formos. Med. Assoc. **95:**232–237.
4. **Chang, F.-Y., M. Y. Chou, R. L. Fan, and M. F. Shaio.** 1988. A clinical study of *Klebsiella* liver abscess. Taiwan. Yi. Xue. Hui. Za Zhi. **87:**282–287.
5. **Chaves, J., M. G. Ladona, C. Segura, A. Coira, R. Reig, and C. Ampurdanes.** 2001. SHV-1 beta-lactamase is mainly a chromosomally encoded species-specific enzyme in *Klebsiella pneumoniae*. Antimicrob. Agents Chemother. **45:**2856–2861.
6. **Cheng, D. L., Y. C. Liu, M. Y. Yen, C. Y. Liu, F. W. Shi, and L. S. Wang.** 1989. Causal bacteria of pyogenic liver abscess. Taiwan. Yi. Xue. Hui. Za Zhi. **88:**1008–1011.
7. **Cheng, D. L., Y. C. Liu, M. Y. Yen, C. Y. Liu, F. W. Shi, and L. S. Wang.** 1990.

Pyogenic liver abscess: clinical manifestations and value of percutaneous catheter drainage treatment. J. Formos. Med. Assoc. **89:**571–576.
8. **Cheng, D. L., Y. C. Liu, M. Y. Yen, C. Y. Liu, and R. S. Wang.** 1991. Septic metastatic lesions of pyogenic liver abscess. Their association with *Klebsiella pneumoniae* bacteremia in diabetic patients. Arch. Intern. Med. **151:**1557–1559.
9. **Chiu, C. T., D. Y. Lin, and Y. F. Liaw.** 1988. Metastatic septic endophthalmitis in pyogenic liver abscess. J. Clin. Gastroenterol. **10:**524–527.
10. **Chou, F. F., and H. K. Kou.** 1996. Endogenous endophthalmitis associated with pyogenic hepatic abscess. J. Am. Coll. Surg. **182:**33–36.
11. **Chou, F. F., S. M. Sheen-Chen, Y. S. Chen, and T. Y. Lee.** 1995. The comparison of clinical course and results of treatment between gas-forming and non-gas-forming pyogenic liver abscess. Arch. Surg. **130:**401–405.
12. **Cobo, M. F., M. L. Aliaga, M. F. Diaz, J. D. Mediavilla Garcia, J. P. Arrebola Nacle, and F. M. de la Rosa.** 1999. Liver abscess caused by *Klebsiella pneumoniae* in diabetic patients. Rev. Clin. Esp. **199:**517–519.
13. **de la Maza, L. M., F. Naceim, and L. D. Berman.** 1974. The changing etiology of liver abscess. Further observations. JAMA **227:**161–163.
14. **Dylewski, J. S., and I. Dylewski.** 1998. Necrotizing fasciitis with *Klebsiella* liver abscess. Clin. Infect. Dis. **27:**1561–1562.
15. **Hansen, N., and T. Vargish.** 1993. Pyogenic hepatic abscess: a case for open drainage. Am. Surg. **59:**219–222.
16. **Higashi, T., Y. Makino, and K. Katsurada.** 1995. A case of gas-containing liver abscess with multiple metastatic lesions. Kansenshogaku Zasshi **69:**1017–1020.
17. **Knaus, W. A., D. P. Wagner, E. A. Draper, J. E. Zimmerman, M. Bergner, P. G. Bastos, C. A. Sirio, D. J. Murphy, T. Lotring, and A. Damiano.** 1991. The APACHE III prognostic system. Risk prediction of hospital mortality for critically ill hospitalized adults. Chest **100:**1619–1636.
18. **Liao, H. R., H. W. Lee, H. S. Leu, B. J. Lin, and C. J. Juang.** 1992. Endogenous *Klebsiella pneumoniae* endophthalmitis in diabetic patients. Can. J. Ophthalmol. **27:**143–147.
19. **Lindstrom, S. T., P. R. Healey, and S. C. Chen.** 1997. Metastatic septic endophthalmitis complicating pyogenic liver abscess caused by *Klebsiella pneumoniae*. Aust. N. Z. J. Med. **27:**77–78.
20. **Liu, Y. C., D. L. Cheng, and C. L. Lin.** 1986. *Klebsiella pneumoniae* liver abscess associated with septic endophthalmitis. Arch. Intern. Med. **146:**1913–1916.
21. **Livermore, D. M.** 1995. β-Lactamases in laboratory and clinical resistance. Clin. Microbiol. Rev. **8:**557–584.
22. **Mandell, G. L., and M. A. Sande.** 2002. Antimicrobial agents: penicillins, cephalosporins, and beta-antibiotics, p. 1088. *In* A. G. Gilman, T. W. Rall, A. Nies, and P. Taylor (ed.), Goodman and Gilman's the pharmacological basis of therapeutics, 8th ed. Pergamon Press, New York, N.Y.
23. **Saccente, M.** 1999. *Klebsiella pneumoniae* liver abscess, endophthalmitis, and meningitis in a man with newly recognized diabetes mellitus. Clin. Infect. Dis. **29:**1570–1571.
24. **Soriano, F., P. Garcia-Corbeira, C. Ponte, R. Fernandez-Roblas, and I. Gadea.** 1996. Correlation of pharmacodynamic parameters of five beta-lactam antibiotics with therapeutic efficacies in an animal model. Antimicrob. Agents Chemother. **40:**2686–2690.
25. **Wang, J. H., Y. C. Liu, S. S. Lee, M. Y. Yen, Y. S. Chen, J. H. Wang, S. R. Wann, and H. H. Lin.** 1998. Primary liver abscess due to *Klebsiella pneumoniae* in Taiwan. Clin. Infect. Dis. **26:**1434–1438.
26. **Yang, C. C., C. Y. Chen, X. Z. Lin, T. T. Chang, J. S. Shin, and C. Y. Lin.** 1993. Pyogenic liver abscess in Taiwan: emphasis on gas-forming liver abscess in diabetics. Am. J. Gastroenterol. **88:**1911–1915.
27. **Yeoh, K. G., I. Yap, S. T. Wong, A. Wee, R. Guan, and J. Y. Kang.** 1997. Tropical liver abscess. Postgrad. Med. J. **73:**89–92.