- Non-extended-spectrumbeta-lactamase-producing Klebsiellae are likely to be sensitive to awide range of agents active against Gram-negative organisms.
- These include fluoroquinolones, aminoglycosides, the antipseudomonal betalactams (piperacillin-tazobactam, ticarcillin-clavulanic acid, cefepime, cefpirome and ceftazidime) and often other second and third generation cephalosporins and broadspectrum penicillins.
  - The drugs of choice for extended-spectrum beta-lactamaseproducing strains are the carbapenems, imipenem and meropenem.
  - Although in vitro testing may indicate susceptibility to one or more third generation cephalosporins, the clinical outcome is poor when they are used even in the presence of apparent susceptibility. The use of a beta-lactam / beta-lactamase inhibitor combination such as piperacillin-tazobactam is also not recommended for extended-spectrum beta-lactamase-producing strains except possibly for urinary tract infections. Clinical evidence to support their use for treatment of bloodstream infections is lacking.
  - Extended-spectrum beta-lactamase-producing Klebsiellae are often resistant to fluoroguinolones, and their prevalence is increasing. The exact mechanism for the association is still unclear, but is thought to arise through prior exposure to both cephalosporins and quinolones

Klebsiella created by therapy

- Klebsiella species belong to the family Enterobacteriaceae that includes Enterobacter spp., Escherichia coli, Proteus spp. and Serratia spp.

- They are non-motile, rod-shaped, usually encapsulated organisms that are ubiquitous in nature, found both in the general environment and on mucosal surfaces of mammals.
- Species differentiation is based on various biochemical reactions.
- Medically important species are Klebsiella pneumoniae and to a lesser degree Klebsiella oxytoca
  - The vast majority of Klebsiella infections are nosocomial and are typically opportunistic.
  - As enteric organisms, Klebsiella spp. are involved in urinary tract infections, peritonitis, cholangitis and intra-abdominal infections. However, because of their ability to colonise the upper respiratory tract and the skin of critically ill patients, they also cause pneumonia and catheter-related bacteraemia.
  - The risk of colonisation and subsequent infection by Klebsiella spp. is related to previous exposure to antimicrobials, length of hospital stay and the presence of invasive lines, factors common to most nosocomial pathogens.
  - Klebsiella spp. display a particular proclivity for acquiring plasmids.
  - As a result, they are the likeliest of all the Enterobacteriaceae to possess extended-spectrum betalactamases, which are overwhelmingly plasmid-borne.
  - Extended-spectrum beta-lactamases are able to hydrolyse third generation cephalosporins (e.g. cefotaxime, ceftazidime, ceftriaxone) and aztreonam.
  - Extended-spectrum beta-lactamases-producing Klebsiella spp. were first identified in the 1980s and their prevalence is increasing, most likely due to the indiscriminate use of third generation cephalosporins.
  - the presence of resistance to ceftazidime that is reversed by the addition of clavulanic acid is suggestive of an extended-spectrum beta-lactamase.
  - Plasmids carrying extended-spectrum beta-lactamases display relatively high stability and persistence of colonisation. Extended-spectrum beta-lactamase-producing strains can be observed years after exposure to ceftazidime and other cephalosporins. In addition, these plasmids frequently contain genes encoding resistance to aminoglycosides and co-trimoxazole.
  - Although imipenem-resistant Klebsiellae have been documented, such strains are fortunately still rare

influence of ESBL on resistance

Antibiotics	ESBL negative (% resistant)	ESBL positive (% resistant)
Gentamicin	8	76
Amikacin	3	52
Ciprofloxacin	3	31
All the above	0	5

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resistance

general

colonisation

& infection