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Extended Spectrum Beta-lactamases: Epidemiology and Infection Control Issues

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7/15/2002

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Objectives

1) What are Extended Spectrum Beta-Lactamases (ESBLs)?
2) Epidemiology - Europe, USA,
3) Canadian ESBL isolates
4) Rationale for controlling antibiotic resistance in these isolates
5) Infection Control measures and their effectiveness

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What are ESBLs?

- Plasmid-encoded enzymes which hydrolyze newer cephalosporins and aztreonam, but with little effect on the cephamycins. Their action is blocked by clavulanic acid.
- Strains may appear to be susceptible in vitro to the third generation cephalosporins making them difficult to detect
- No one-size-fits-all screening test for ESBLs

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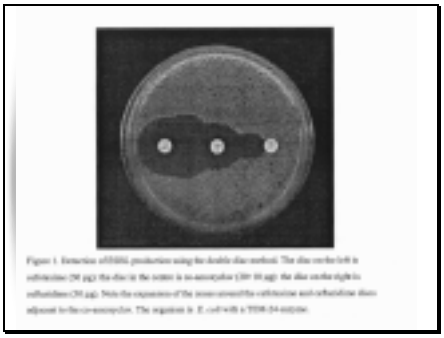

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Just to make it more confusing!

- **Most commonly seen in E.coli and Klebsiella but can be found in other gram negative organisms**
- **Different types of ESBLs and bacteria may produce more than one**
- **Can be difficult to sort out when combined with other types of beta-lactamase resistance (e.g. AmpC beta-lactamases)**

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Laboratory capacity to detect resistance

Ability to detect ESBLs is limited:

- **ESBLs may not exhibit third generation cephalosporin resistance**
- **screening methods are not reliable:**
- **automated systems not reliable**

compliance varies widely

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NCCLS Criteria

- **Screening: reduced susceptibility to the recommended screening agents**
- **Confirmatory testing: based on tests with combinations of the screening agents and the beta-lactamase inhibitor, clavulanate.**

  Done only after screening

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Epidemiology

World-wide

- **SENTRY Program (ICAAC 2001)**
  - **10% of isolates had positive ESBL test**
  - ***Ecoli* 0.2 - 8.5% to *K.pneumoniae* 0 to 34%.**
- **Rice: (ICAAC 1999)**
  - **455 consecutive cases of *K.pneumoniae* bacteremia from 6 continents**
  - **19% had ESBL phenotype (2-67%)**
  - **3.5% community, 43.5% ICU, 26% non-ICU**

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Epidemiology

United States

- **Jacoby (Annu Rev Med 47:169-170 1996):**

  5% *K.pneumoniae* ESBLs
- **Coudron (J Clin Microbiol 1997;35:2593-2597)**

  9% of Enterobacteriaceae had ESBLs
- **Jones (Diagn Microbiol Infect Dis 1998)20:215-228**

  CAZ resistance E.coli 10.3% Klebsiella 24%

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CHEC ESBL Study

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CHEC ESBL study

Phase One: a one year study to:

- **determine extent and nature of ESBL-producing *E.coli* and *Klebsiella***
- **establish a national collection of these isolates**
- **characterize the isolates by plasmid profiling, DNA fingerprinting, isoelectric focusing and PCR genotyping**
- **determine the antibiotic susceptibilities of confirmed ESBL isolates**

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The Study Design

- **All clinical isolates of *E.coli* and *Klebsiella* suspected to be ESBLs submitted**
- **Demographic data, clinical service, clinical site information obtained**
- **Isolates were then confirmed as ESBLs using phenotypic and genotypic methods**

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Number of *Confirmed* ESBLs

	NCCLS (%)
E. coli (n=389)	81 (21)
Kleb. (n=122)	41 (34)
Total (n=511)	122 (24)

*511 isolates submitted out of 29,323 *E.coli* and 5,156 Klebsiella tested

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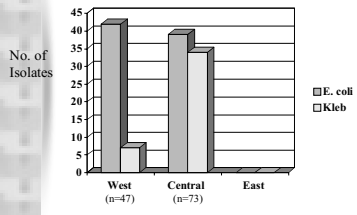
ESBL Canadian Distribution



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Vitek Drug Resistance

	ESBL		Non-ESBL	
	E	K	E	K
Ciprofloxacin	53	5	29	11
Levofloxacin	50	5	28	11
Nitrofurantoin	8	15	4	18
Gentamicin	52	68	21	11
Amikacin	7	0	0.6	0
Tobramycin	42	46	18	8
Trimeth-Sulfa	72	56	36	13

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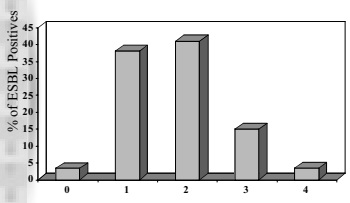
IEF Analysis of ESBL Isolates



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Summary of Laboratory Information

- **ESBLs have been identified in West and Central regions**
- **ESBL generally more resistant to other classes of antimicrobials**
- **numerous ESBL gene classes observed**
- **fingerprints vary considerably and may not be useful in some cases**
- **observed spread of plasmids across country in a few cases**

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Epidemiology

- **122 confirmed ESBLs**
- **66.4% (81) *E.coli* and 33.6% (41) were *K.pneumoniae***
- **ESBL E.coli 57% Female, 43% male**
- **ESBL Kleb 66% Female, 34% male**

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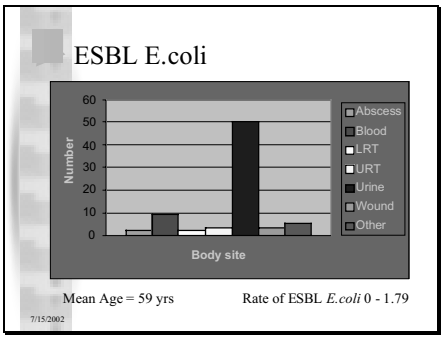

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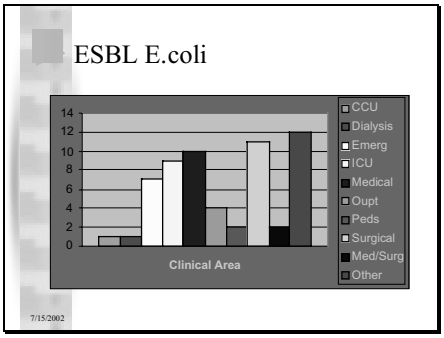

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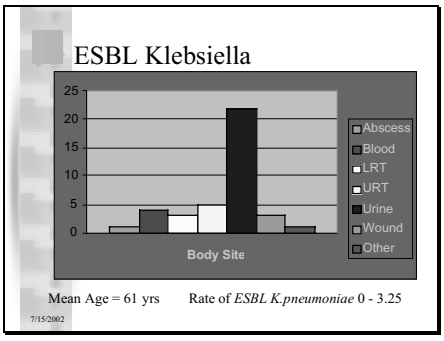

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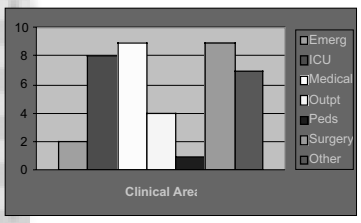
ESBL Klebsiella



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Should we use infection control precautions for ESBLs?

The jury is still out!

BUT outbreaks may be costly

- **Meyer K** (Ann Intern Med 1993;119;353-358)
  155 PTS with CAZ R Klebsiella: costs included personnel time, increased barrier precautions, increased laboratory screening, changes in antibiotic formulary

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They may be associated with increased morbidity/mortality

- **Schiappa (**JID 1996;174:529-36)
  Case control analysis 31 pts with CAZ R *K.pneumoniae* or *E.coli* bacteremia. NSD in LOS after bacteremia, but higher risk of dying in case group if inappropriate tx received.
- **Paterson et al** (ICAAC 1999)
  K.pneumoniae bacteremia in 12 transplant units. 28% were ESBLs. NSD in mortality, but more breakthrough bacteremias. Median LOS longer
- **Qavi (IDSA 1999)**
  NY case-control study ESBL + Klebsiella had greater likelihood of sepsis-related mortality

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Do isolation/precautions make a difference?

- Paterson et al. 70% of units had cross-transmission. These units did not isolate pts
- Rice. In 6/7 hospitals with evidence genotypic spread - pts not isolated

  3/5 hospitals with no spread isolated pts after detection

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Isolation...

- Nordmann.

  Increased isolation and barriers decreased ESBL rate from 16 to 10%
- Soulier (J Hosp Infect 95;31:89-97)

  SICU gut colonization ESBL: 70% pre-intervention, 40% post-intervention. Intervention = handwashing, single-use equipment, waste control, increased barriers. No change in antibiotic protocols.
- Paterson DL (CID 2001;33:126-128)

  interventions included emphasis on hand hygiene and gut decolonization with quinolones

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Role of Precautions….

- Miller et al. (ICAAC 2001)

  both Infection control and abx control measures were used but time-line analysis showed that infetion control most likely responsible for decreasing ESBLs which were polyclonal in origin?

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Long-Term Care as a Reservoir?

- **Wiener J et al (JAMA Feb 1999)**
  Over 2 yr pd, 31/55 ESBL + pts were from LTC; most harboured same beta-lactamase. Stool cultures from one LTC revealed 18/39 residents carried E.coli strain with same plasmid
- **Rahal (JAMA 1998;280-1253-1257)**
  27% of R Klebsiella arose in LTC
- **Schiappa (JID 116;174:529-36)**
  1/2 Of ESBL bacteremias arose in LTC

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Summary

- **Ability to detect ESBL in Canadian laboratories varies**
- **Many laboratories do not screen and/or confirm for ESBLs**
- **Prevalence remains largely unknown in many institutions but ESBLs not a large problem in Canada**
- **Evidence suggests increased morbidity from ESBLs due to inappropriate antibiotics**
- **Most hospitals have no formal infection control policies on ESBLs. Infection control useful in outbreak situations?**

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