

1-Introduction

Bacterial resistance to antibiotics is increasingly becoming a problem. Antibiotics work by affecting the cell wall of bacteria, distorting the cell surface, inhibiting bacterial protein synthesis, or preventing DNA formation. Some bacteria are able to adopt survival mechanisms against these agents, thus weakening our ability to treat some infectious diseases.

Most data published in the literature on antimicrobial resistance is heavily influenced by limited surveys and case reports. A collection of population-based data provides a more representative picture of drug resistance patterns.

The Antibiotic Sensitivity Surveillance System was started in 1998 to track the emergence of antibiotic resistant organisms. The goal of the program is to estimate the proportion of selected bacteria in the state that are resistant to antibiotics.

2-Methods

2.1-Active surveillance

Over the past years, about 60 hospitals have been a part of the active surveillance system. They provide information to the surveillance system each month on a brief reporting form. Each hospital reports the total number isolates from selected species from their lab for each month. In addition, they also report the total number of drug resistant or drug intermediate resistant isolates for each of those organisms. Duplicates are not reported. Each report is entered into a Microsoft® Access database and from this, annual summary reports are generated for the participating hospitals.

This type of surveillance is cumbersome and therefore limited to a few microorganisms.

2.2-Louisiana antibiogram

In 2001, a NCCLS (National Committee for Clinical Laboratory Standards which became in 2005 the Clinical and Laboratory Standard Institute CLSI) subcommittee issued Guidelines to use in analyzing and presenting cumulative antimicrobial susceptibility test data. They established standardized means of data extraction for all drugs tested and outlined how the data should be presented:

- Percent susceptibility for the first isolate from a patient within an analysis period (generally one year)
- Population tested (inpatient, ICU, or nursing home)
- Specimen source
- Number of isolates tested (minimum of 10 for each organism)
- Separate data for Gram-negative, Gram-positive, aerobic, and anaerobic organisms
- List drugs alphabetically, or by class
- Avoid selective reporting (cascading); secondary agents reported only if isolate is resistant to primary drug class

Most hospitals issue once a year an “Antibiogram”, which is a summary of the most important antibiotic resistance patterns for their hospital for the year. The Antibiogram is a table listing the microorganisms in the left-most column and antibiotics in the remaining columns. The percent of organisms found to be resistant to each antibiotic is recorded in the table’s cells. Some hospitals generate reports every three, six, or 12 months; issuing these frequent reports result in small numbers of isolates, and sometimes large variations in percentage from one quarter to the next. These variations are usually not sustained and do not mean much. Usually an annual report is sufficient

The antibiogram shows the spectrum of sensitivity/resistance among the most common microorganisms detected by the hospital laboratory. It provides useful information for the selection of an empiric antibiotic treatment when a presumptive diagnosis of infection with a specific bacteria is made. It is no longer useful once the specific bacteria has been identified and an antibiotic resistance established for the patient’s specific infection.

There are some limitations when using a hospital antibiogram:

1-Most hospital laboratories do not sort-out community acquired infections from hospital acquired. The antibiotic resistance patterns for both groups may be substantially different. Gram-negative rods tend to be more prevalent in hospital infections, and more resistant if they originate from a hospital source.

2-Some laboratories do not thoroughly eliminate duplicate cultures from the same patient, so that resistant strains that tend to be cultured more often artificially inflate the proportion of resistance.

If constructed carefully and interpreted with caution, a hospital Antibiogram is a useful tool.

The Statewide Louisiana Antibiogram

The Louisiana Antibiogram is not as useful as the individual hospital antibiogram for making empiric treatment decisions. However, it is useful to compare one individual hospital antibiogram to the rest of the state. Hospitals for which a specific antibiotic sensitivity is an outlier should investigate the reason for the discrepancy.

2.3-Analysis

The purpose of this analysis is to determine if there is a significant trend in the rates of antibiotic resistance for these microorganisms from 2000 to 2011.

For each organism of interest, using the annual rates, a test for trend was conducted using the Cochran-Armitage Trend test. The analyses were conducted using Winpepi [(Abramson, J.H. Winpepi (Pepi-for-Windows computer programs for epidemiologists.) Epidemiologic Perspectives & Innovations 2004, 1: 6]

Tables are presented with the first column for the number of isolates tested during the year, the second column with the number of resistant isolates and the third column with the percentage of resistant strains. At the bottom of the table the statistical tests presented are:

- The Cochran-Armitage test for linear trend (CoArm) with chi-square, degrees of freedom=1, and the p-value).
- The simple linear regression analysis equation with rate per 100 = a + (b x score): a value, b value/slope and the two tailed p-value, the next line shows b standard error and its confidence interval.

3-Results

3.1- *Staphylococcus aureus* resistance to Methicillin (oxacillin)

Staphylococcus aureus is a Gram-positive catalase positive coccus typically seen in clusters on Gram stain. *Staphylococcus aureus* is the most important human pathogen of the Staphylococcal group. Its golden yellow pigment gives the species its name, though some isolates are non-pigmented. *S. aureus* is widespread in the population; about 30% are carriers, particularly in the nasal cavity, but also in the perineum, anal area and finger tips, among other areas. The most common infections include carbuncles, furuncles, cellulitis and wound infections. Food poisoning, toxic shock syndrome, acute endocarditis, septic arthritis, meningitis, osteomyelitis, pneumonia and septicemia are also seen. It is often isolated from nosocomial infections (10% to 20% of nosocomial infections), especially bacteremias, skin infections and surgical site infections.

Table 1: Percent MRSA – Louisiana, 2000-2011

	<i>S. aureus</i> /Oxacillin (Methicillin)		
	Total	Res	% Res
2000	3,798	1,391	36.6%
2001	1,064	645	60.7%
2002	4,831	3,076	63.7%
2003	20,090	12,025	59.9%
2004	7,032	3,830	54.5%
2005	8,776	6,047	68.9%
2006	18,528	12,594	68.0%
2007	17,582	11,480	65.3%
2008	16,231	10,790	66.5%
2009	17,642	11,328	64.2%
2010	11,190	6,589	58.9%
2011	14,489	7,899	54.5%
CoArm	X2 46.27	df=1	p=000
SLReq	a 0.008	b 0.544	p 0.25
	SE 7.2	CI: -4.3	CI:21.8

Methicillin Resistant *Staphylococcus aureus* (MRSA) is a growing problem both in the hospital and in the community. Resistance to methicillin is due to altered penicillin binding proteins.

Penicillin resistance to *S. aureus* is primarily due to the organism's ability to produce β -lactamase, which is capable of breaking down the penicillin ring thus, making it ineffective.

Methicillin results from the addition of large radicals around the penicillin ring to provide protection against penicillinase. Methicillin is effective on *S.aureus* resistant to penicillin.

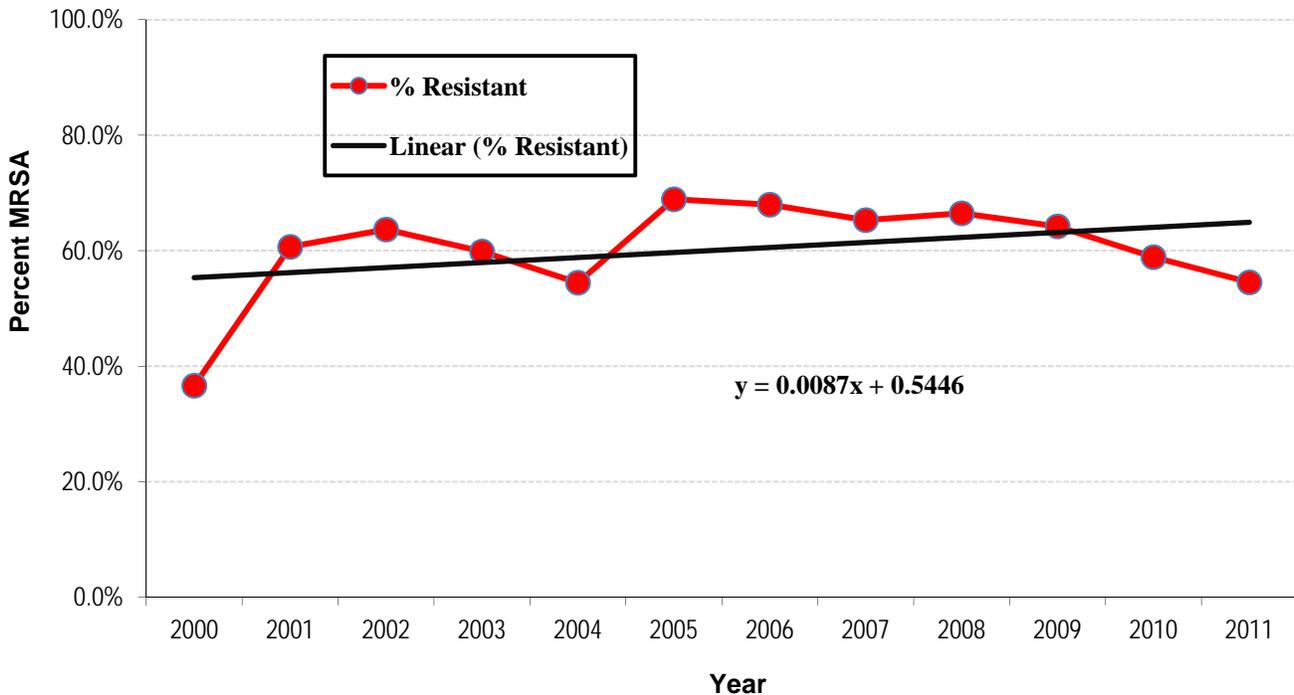
S.aureus was subsequently able to modify the site to which methicillin attaches (Penicillin Binding Protein) and thus became resistant to methicillin.

Acquisition of MRSA infections is a common concern among both patients and staff in acute and long-term care facilities.

The rates of methicillin-resistant *S. aureus* have increased from 2000 to 2008 from 38% to over 67% and seem to be stabilizing in more recent years.

MRSA infections that are reported here have not been differentiated into community associated (CA) MRSA (or SCC mec Type IV), and hospital associated (HA) MRSA (or SCC mec Type II/III). Most Type IV MRSA remains sensitive to TMP-SMX, clindamycin and fluoroquinolones, though some of these antibiotics may not be effective in vivo. Type II/III organisms tend to be sensitive only to vancomycin and newer agents like linezolid.

Figure 1: Percent MRSA – Louisiana, 2000-2011



3.2- Other Antibiotics to which Methicillin Resistant *S.aureus* (MRSA) is resistant

MRSA first appeared in hospitals, mostly as a nosocomial infection. MRSA was first recognized in 1961; one year after introduction of methicillin, resistant strains started to appear. The first documented MRSA outbreak in the U.S. was described at a Boston hospital in 1968. During the 1970s to the 1990s, most MRSA infections occurred in persons who had contact with hospitals or other Health Care Facilities (HCF) hence the term Healthcare-acquired or associated MRSA (HA-MRSA). In the 1990s and 2000s, MRSA infections became more frequent among previously healthy individuals with no association with HCF. The acquisition of infections seems to have been from the community, hence the term Community-acquired MRSA or CA-MRSA.

HA-MRSA causes mostly sporadic cases with the exception of a few strains causing epidemics in hospitals (EMRSA). Most MRSA were simple colonizers. HA-MRSA were not more virulent than other *S. aureus*; there was no difference in animal lethality, production of enzymes or production of toxins associated with invasiveness. However, this strain was resistant to most antibiotics except vancomycin and a few newer antibiotics.

CA-MRSA started to spread in the late 1990s and 2000s and soon was overtaking HA-MRSA. CA-MRSA is known to be more virulent, causing frequent skin and soft tissue infections as well as invasive infections (septicemia and pneumonias). Experiments showed that CA-MRSA produces toxins more frequently than its counterpart. CA-MRSA became the dominant MRSA clone in the United States.

MRSA resistance results from four mec genes (named I to IV), consisting in chromosomal elements of 30 to 50-kilobase coding penicillin-binding proteins. The *mecA* gene encodes a PBP with low affinity for β -lactam antibiotics. The *mecA* gene complex is carried on specific integrative genetic element (staphylococcal cassette chromosome - SCC). This cassette includes: *mec* complex + cassette

recombinase which integrate and excise the SCCmec element on staphylococcal chromosomes. Molecular strain typing is done by Pulse Field Gel Electrophoresis (PFGE), arbitrarily primed PCR, randomly amplified polymorphic DNA, plasmid fingerprinting and multilocus sequence typing (MLST). The difference between CA-MRSA isolates and HA-MRSA isolates is the type of SCCmec. The SCCmec is a cluster of chromosomes in which the *mecA* gene is carried. Typical CA-MRSA has SCCmec type IV while typical HA_MRSA carries SCCmec types I and II. Types I and II are larger genes, which may be carrying resistance for trimethoprim-sulfa, clindamycin, and some other antibiotics.

The PFGE classification is widely used. It includes USA 100 and 200 (old CA-MRSA), and strains 300 to 1100. The USA 300 strain has spread into healthcare settings to become the dominant strain. In 2005, 22% community onset-MRSA were diagnosed in HCF and 16% hospital-onset invasive MRSA were caused by USA 300 (Klevens RM, Morrison MA, Nadle J, et al. Invasive methicillin-resistant *Staphylococcus aureus* infections in the United States. JAMA 2007; 298: 1763-1771).

The distinction between these two types of MRSA is becoming increasingly blurry. CA-MRSA, particularly USA 300 is emerging as the dominant MRSA strain in the community and in health care settings; hence the importance of monitoring the sensitivity of MRSA.

Many cutaneous abscesses respond to drainage alone, and most of the remaining Type IV MRSA infections can be treated with trimethoprim-sulfamethoxazole or a tetracycline, such as doxycycline or minocycline. For serious infections, other antibiotics may be required for treatment. Options include vancomycin, fluoroquinolones, daptomycin, quinupristin-dalfopristin, newer-generation carbapenems, and linezolid.

Fluoroquinolones, such as levofloxacin, moxifloxacin, and gatifloxacin, are effective orally and generally provide adequate coverage for CA-MRSA. Unfortunately, resistance is emerging among both MSSA (Methicillin-sensitive *S.aureus*) and MRSA isolates; data suggest that overuse of fluoroquinolones promotes emergence of MRSA strains in the community. Linezolid, an oxazolidinone, is useful for severe refractory MRSA infections and can also be administered orally. In some severely ill patients, linezolid therapy has proved to be more effective than vancomycin, but resistance is emerging and the drug should be reserved for serious infections.

The possibility of inducible clindamycin resistance has discouraged some physicians from prescribing clindamycin. The inducible macrolide-lincosamide-streptogramin B phenotype is related to the *erm* gene. Strains with inducible resistance will test clindamycin-susceptible in vitro, but are erythromycin-resistant. If inducible resistance is present, there is a potential for treatment failure with clindamycin, despite the culture and sensitivity report indicating susceptibility. Some laboratories issue a report stating that macrolide resistance may be a marker for inducible lincosamide resistance. If the clinician is considering clindamycin, an erythromycin-clindamycin “D-zone” test is prudent. To perform a D-test, clindamycin and erythromycin disks are placed close together on a culture plate. If inducible lincosamide resistance is present, the zone of inhibition around the clindamycin disk is flattened on the side toward the erythromycin disk. This results in a zone of inhibition resembling a capital letter D instead of an O.

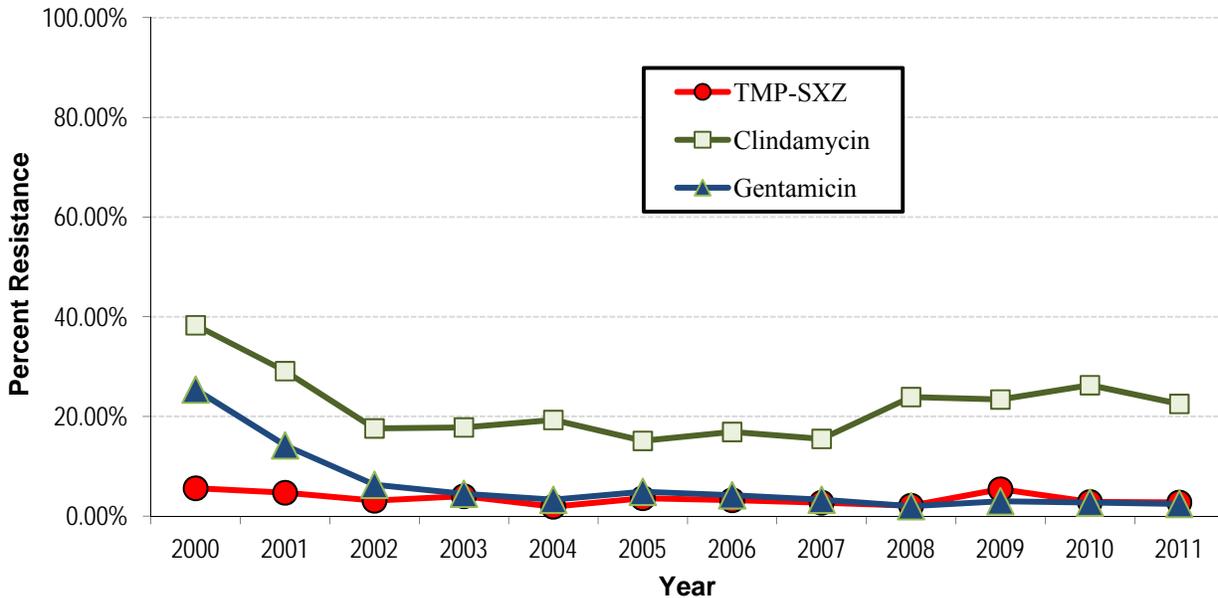
Table 2: Percent Resistant MRSA to Listed Drugs – Louisiana, 2000-2011

ABG	MRSA											
	Azithromycine			Ciprofloxacin			Clindamycine					
	Total	Res	% Res	Total	Res	% Res	Total	Res	% Res			
2000	116	106	91.0%	401	335	83.5%	401	153	38.3%			
2001	346	321	92.7%	811	596	73.5%	800	233	29.1%			
2002	233	214	91.9%	617	393	63.7%	797	140	17.6%			
2003	95	89	93.8%	2,707	1,091	40.3%	3,275	584	17.8%			
2004	478	446	93.4%	3,210	1,271	39.6%	3,808	734	19.3%			
2005	78	78	100.0%	2,987	1,275	42.7%	4,413	667	15.1%			
2006	198	184	93.0%	5,958	2,498	41.9%	6,902	1,166	16.9%			
2007	471	449	95.2%	2,598	1,138	43.8%	3,829	593	15.5%			
2008	431	383	88.8%	4,124	1,983	48.1%	4,930	1,180	23.9%			
2009	430	336	78.1%	2,383	1,221	51.2%	2,953	691	23.4%			
2010	379	355	93.6%	2,455	1,317	53.6%	5,814	1,527	26.3%			
2011	402	355	88.3%	2,955	1,714	58.0%	6,077	1,369	22.5%			
CoArm	X2 18.14	df1	p 0.00	X2 28.8	df1	p 0.00	X2 90.45	df1	p 0.00			
SLReq	a 95.02	b -5.13	p 0.23	a 64.61	b 17.3	p 0.15	a 25.22	b -4.8	p 0.4			
	SE 4.27	CI: -12.9	CI 2.61	SE 11.0	CI: -37.4	CI: 2.7	SE 5.7	CI: -15.1	CI: 5.6			

ABG	Gentamycin			Rifampin			Trimethoprim/Sulfa			Linezolid		
	Total	Res	% Res	Total	Res	% Res	Total	Res	% Res	Total	Res	% Res
2000	401	102	25.4%	401	20	5.0%	598	33	5.6%			
2001	811	115	14.2%	739	27	3.7%	902	42	4.7%			
2002	617	39	6.3%	539	5	1.0%	797	24	3.1%	155	0	0.0%
2003	2,750	125	4.5%	550	8	1.4%	3,355	134	4.0%	340	0	0.0%
2004	3,788	125	3.3%	2,438	40	1.6%	3,608	68	1.9%	1,867	0	0.0%
2005	4,830	239	4.9%	692	7	1.0%	5,518	198	3.6%	393	0	0.0%
2006	7,281	308	4.2%	3,067	50	1.6%	7,753	251	3.2%	1,556	0	0.0%
2007	4,358	146	3.3%	3,579	57	1.6%	5,058	135	2.7%	3,092	0	0.0%
2008	7,629	153	2.0%	6,634	97	1.5%	8,154	173	2.1%	6,233	0	0.0%
2009	3,843	116	3.0%	3,355	56	1.7%	3,540	189	5.4%	2,892	0	0.0%
2010	6,366	173	2.7%	5,031	117	2.3%	6,461	184	2.8%	4,553	11	0.2%
2011	4,149	102	2.5%	5,439	78	1.4%	5,964	164	2.7%	3,767	6	0.2%
CoArm	X2 347.7	df1	p 0.00	X2 4.1	df1	p 0.04	X2 7.4	df1	p 0.006	X2 17.2	df1	p 0.00
SLReq	a 15.3	b -1.38	p 0.008	a 3.0	b -0.2	p	a 4.3	b -0.13	p 0.2	a -0.06	b 0.02	p 0.04
	SE 0.41	CI: -2.12	CI: -0.63	SE 0.09	CI 0.3	CI .006	SE 0.01	CI: -0.3	CI: 0.04	SE 0.01	CI 0.01	CI 0.03

In Louisiana TMP-SMX retains a relatively high sensitivity for some MRSA, illustrating the pattern seen in community acquired organisms. Vancomycin remains effective and is still the first-line drug in the treatment of life-threatening infections caused by MRSA or *S.aureus* of unknown sensitivity. MRSA strains are consistently sensitive to vancomycin and linezolid. They are resistant to macrolides (75% to 100%), fluoroquinolones (60% to 80%), and clindamycin (20% to 40%). They are less resistant to aminoglycosides (5% to 6% in recent years) and trimethoprim-sulfamethoxazole (2% to 5%).

Figure 2: MRSA Percent Resistance to Other Antibiotics – Louisiana, 2000-2011



3.3- Methicillin Susceptible *Staphylococcus aureus* (MSSA)

Resistance due to penicillinase produced by *S.aureus* developed as soon as penicillin was introduced for clinical use. Consequently, most *S.aureus* isolates are resistant to penicillin. The aminopenicillins (ampicillin, amoxicillin), carboxypenicillins (carbenicillin, ticarcillin), and ureidopenicillins (mezlocillin, piperacillin) are not effective against penicillinase (β lactamase) producing *S.aureus*. The preferred antibiotics for the treatment of methicillin sensitive *S.aureus* are penicillinase-resistant penicillins. These antibiotics include nafcillin, oxacillin, methicillin, cloxacillin, and dicloxacillin.

Alternative drugs used in the treatment of methicillin sensitive *S.aureus* include:

- Trimethoprim-Sulfamethoxazole (TMP-SMX) plus Rifampin
- Doxycycline or Minocycline plus Rifampin
- Clindamycin if D test negative
- Vancomycin, Linezolid or Daptomycin

3.4- Coagulase negative *Staphylococci* are habitual inhabitants of the skin with very low pathogenic potential. The group includes *S. epidermidis* and *S. saprophyticus*. They are commonly isolated as contaminants, especially in blood cultures, hence the requirements of two blood cultures to define a coagulase-negative staphylococcal blood stream infection. They may cause nosocomial infections in patients with severe underlying medical problems or indwelling prosthetic devices (due to its polysaccharide capsule, causing adherence to devices). The great majority of coagulase negative Staphylococcal nosocomial infections are septicemias in immunocompromised neonates (*S. epidermidis*), followed by conjunctivitis, urinary tract (*S. saprophyticus*) and skin infections. The treatment of coagulase-negative Staphylococci depends on the organism and the type of infection. Treatment must ultimately be decided based on susceptibility testing of the isolate.

Coagulase-negative staphylococci from nosocomial infections, particularly *S. epidermidis* and *S. haemolyticus*, are usually resistant to multiple antibiotics, with more than 80% resistant to methicillin.

The methicillin-resistance gene (*mecA*) is identical in *S. aureus* and *S. epidermidis*. Antimicrobials to which most coagulase-negative staphylococci are susceptible in vitro include vancomycin, minocycline, linezolid, the combination streptogramin, quinupristin/dalfopristin, and daptomycin

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3.5- *Streptococcus pneumoniae*

Table 3: Percent *S. pneumoniae* Resistant to Penicillin – Louisiana, 2000-2011

ABG	<i>S. pneumo</i> /Penicillin		
	Total	Res	% R
2000	242	108	44.7%
2001	110	60	54.7%
2002	400	154	38.4%
2003	839	317	37.8%
2004	414	153	37.1%
2005	635	232	36.5%
2006	744	322	43.3%
2007	1388	727	52.4%
2008	970	498	51.4%
2009	655	317	48.4%
2010	764	410	53.7%
2011	558	255	45.7%
CoArm	X2 51.3	df 1	p 0.00
SLReq	a 40.9	b 0.7	p 0.25
	SE 0.56 CI: -0.33 CI: 1.68		

Streptococcus pneumoniae (Pneumococcus) is the most common cause of community acquired pneumonia both in children and adults. It causes about half of all otitis media cases and it is a frequent cause of meningitis and sepsis. Mortality resulting from pneumococcal infections is high; pneumococcal pneumonia ranks among the 10 leading causes of death in many countries, with a case fatality rate of 5% for pneumonia, 20% for bacteremia and 30% for meningitis.

Because sensitive and rapid diagnostic tests are not available, most pneumococcal infections are treated empirically at first. Penicillin has been the drug of choice, though penicillin resistance had been slowly spreading throughout the world. Resistance to penicillin is associated with a decreased affinity of the antibiotic for penicillin-binding proteins present in the bacterial cell wall. Penicillin resistance is thought to be due to horizontal transfer of genes of altered penicillin-binding proteins with lowered affinity to penicillin and other β -lactams. Pneumococci have become resistant by acquiring genetic material from other bacteria with which they

coexist in close proximity - presumably viridans streptococci in the nasopharynx. At least 30% of the pneumococcal strains in the U.S. show intermediate resistance to penicillin (MIC 0.1–2.0 μ g/ml). Except for meningitis patients, these are readily treatable with increased doses of penicillin.

Of more concern is the appearance of pneumococcal isolates that are regarded as highly resistant to penicillin (MIC \geq 2.0 μ g/ml). It is suggested that the extended consumption of oral cephalosporins contributes to pneumococcal resistance to penicillin. If these strains are circulating, it might be more reliable to treat severe pneumococcal infections with vancomycin. However, the rate of resistance to other commonly used antibiotics such as erythromycin, tetracycline and trimethoprim-sulfamethoxazole is much greater in penicillin-resistant strains than in penicillin-sensitive strains

The susceptibility of *S. pneumoniae* to penicillin is currently defined by the National Committee for Clinical Laboratory Standards as follows: susceptible isolates are inhibited by 0.06 μ g/mL (i.e., minimal inhibitory concentration [MIC] \leq 0.06 μ g/mL); isolates with reduced susceptibility (also known as intermediate resistance) are inhibited by 0.1 to 1.0 μ g/mL, and resistant isolates are inhibited by 2.0 μ g/mL or more. This definition was derived based on achievable concentrations of penicillin in CSF during treatment of children for meningitis. From a clinical point of view, the meaning of the MIC depends on the infection being treated. A strain with reduced susceptibility (e.g., MIC of 1.0 μ g/mL) behaves as a susceptible organism when it causes pneumonia, but may not when it causes otitis, and does not when it causes meningitis. The recently revised definition of amoxicillin resistance (susceptible,

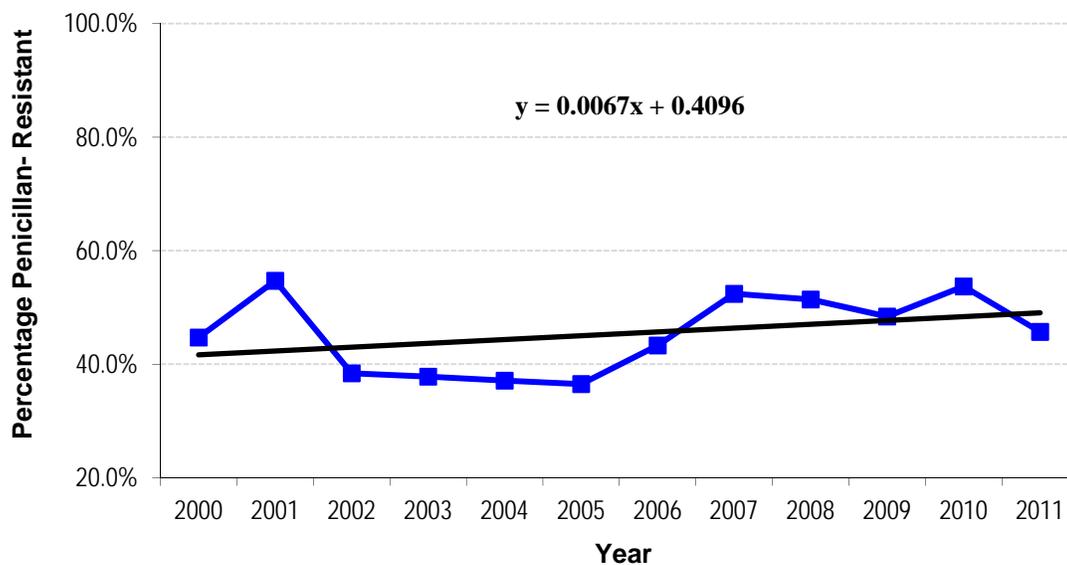
MIC <4µg/mL; intermediately resistant, MIC 4 g/mL, resistant, MIC >8 g/mL) is based on serum levels, assuming that no physician would knowingly treat meningitis with this oral medication.

Treatment of severe infections:

-Pneumonia: Because high-level resistance is very uncommon, ceftriaxone 1g every 12 hours or cefotaxime, 1g every 6 hours, is appropriate for resistant organisms. These considerations have led the Infectious Disease Society of America to recommend, for empiric therapy of community-acquired pneumonia, a third generation cephalosporin or a β-lactam/β-lactamase inhibitor plus a macrolide or quinolone, or a quinolone as sole therapy. Although vancomycin is likely to treat pneumococcal infection effectively, the impetus to not use this drug is strong because of the fear of emergence of resistant organisms and its lack of efficacy against other organisms that commonly cause pneumonia. Studies of the new ketolides suggest that one of these drugs might also be effective and would provide coverage for other agents that are likely to cause pneumonia, as well.

-Meningitis: Pneumococcal meningitis has been treated with 12 to 24 million units of penicillin every 24 hours or 1g to 2g of ceftriaxone every 12 hours. Either regimen is effective against antibiotic-susceptible *S. pneumoniae* and may be effective against intermediately resistant ones; pharmacokinetic considerations and achievable CSF levels favor the third-generation cephalosporins cefotaxime or ceftriaxone. During treatment of resistant strains, β-lactam antibiotics are likely not to achieve therapeutic levels in CSF. This explains why, until susceptibility results are reported, vancomycin is recommended along with the β-lactam antibiotic, the vancomycin because of its more certain antimicrobial efficacy and the β-lactam because it crosses the blood-brain barrier more reliably, and the organism may be susceptible. In patients who have major penicillin and cephalosporin allergies, vancomycin and/or imipenem can be used; unless the history suggests life-threatening reactions to penicillin, ceftriaxone or cefotaxime are preferred.

Figure 3: Percentage of *S. pneumoniae* Resistant to Penicillin – Louisiana, 2000-2011



3.6- Streptococci group A

Table 4: Percent *S. pyogenes*, Resistant to Penicillin and Erythromycin – Louisiana, 2000-2011

ABG	Streptococci Group A					
	Penicillin			Erythromycin		
	Exam	Res	%Res	Exam	Res	%Res
2008	588	0	0.0%	588	71	12.1%
2009	632	0	0.0%	632	94	14.9%
2010	608	0	0.0%	608	79	13.0%
2011	645	0	0.0%	645	90	14.0%

Streptococcus pyogenes, the Group A Strep, are β -hemolytic and are found in the nasopharynx of healthy carriers. They may cause pharyngitis, the most common clinical expression. The drug of choice in the treatment of streptococcal infection is penicillin, because of its efficacy in the prevention of rheumatic fever, safety, narrow spectrum, and

low cost. Oral cephalosporins are highly effective in the treatment of streptococcal pharyngitis. First-generation oral cephalosporins are acceptable alternatives in the penicillin-allergic patient whose allergy is not of the immediate type.

In penicillin-allergic patients, erythromycin is the therapy of choice. The newer macrolides (azithromycin, clarithromycin) appear to be effective. There have been reports of resistance to macrolides and azalide antibiotics from several countries.

There has also been considerable recent interest in abbreviated courses of antimicrobial therapy. It has been reported that clarithromycin, cefuroxime, cefixime, cefibuten, cefdinir, cefpodoxime, and azithromycin are effective in eradication of group A streptococci from the pharynx when administered for five days or less.

3.7-Streptococcus group B

Streptococcus agalactiae, the Group B Strep are partially β -hemolytic and can colonize the female genital tract which can lead to infection in the newborn. It is a cause of urinary tract infections (UTI) and IV line infections, especially in diabetics or the elderly. It is also a rare cause of subacute bacterial endocarditis (SBE).

Group B streptococci remain uniformly susceptible to penicillins and cephalosporins in vitro, and penicillin G is the drug of choice once the diagnosis is established. They are also susceptible to ampicillin, vancomycin, and teicoplanin. Meropenem and imipenem also have good in vitro activity. Increasing resistance to erythromycin (48%) and clindamycin (70%) restrict their use as empiric treatment for invasive infection or for intrapartum prophylaxis. Tetracycline resistance has increased to nearly 95%.

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Table 5: Percent Group B Streptococci, Resistant to Penicillin, Erythromycin and Tetracycline - Louisiana, 2000-2011

	Streptococci Group B								
	Penicillin			Erythromycin			Tetracycline		
	Exam	Res	%Res	Exam	Res	%Res	Exam	Res	%Res
2000	102	1	1.2%	175	19	11.0%	62	54	87.0%
2001	83	1	1.2%	83	1	1.2%	9	7	78.0%
2002	1,047	11	1.0%	1,221	95	7.8%	1,130	1011	89.5%
2003	3,448	25	0.7%	2,585	996	38.5%	2,439	2078	85.2%
2004	854	10	1.1%	563	208	36.9%	218	207	95.0%
2005	935	6	0.7%	824	336	40.8%	873	732	83.8%
2006	2,331	5	0.2%	2,143	1071	50.0%	1,960	1677	85.5%
2007	3,302	55	1.7%	798	400	50.2%	581	476	81.9%
2008	1,458	2	0.1%	2,089	1572	75.3%	2,032	1694	83.4%
2009	2,157	3	0.1%	2,709	1983	73.2%	2,628	2249	85.6%
2010	3,360	4	0.1%	2,864	2376	83.0%	2,749	2396	87.1%
2011	856	5	0.6%	2,872	2382	82.9%	2,757	2403	87.1%
CoArm	X2 16	df 1	p 0.00	X2 3883	df 1	p 0.00	X2 0.03	df 1	p 0.87
SLReq	a 1.3	b -0.08	p 0.060	a -4.6	b 7.8	p 0.00	a 85.5	b 0.04	p 0.92
	SE 0.04	CI: -0.15	CI: -0.01	SE 0.7	CI: 6.6	CI: 9	SE 0.37	CI: -0.62	CI: 0.7

3.8- Enterococci and Vancomycin Resistant Enterococci

Enterococci, formerly of the Streptococci are now part of the *Enterococcus* genus. These organisms grow under harsh conditions and are differentiated from the non-enterococcal group D streptococci in part by their ability to grow in 6.5% sodium chloride. Enterococci constitute a sizable portion of the normal flora of the gut. When there is disruption of mucosal or epithelial barriers, they can produce infection, including UTIs, endocarditis and intraabdominal abscesses. *E. faecalis* is more common than *E. faecium* as a pathogen. Enterococci are difficult to treat because of extensive resistance to antibiotics used against Gram-positive cocci. They are intrinsically resistant to a large number of antibiotics, but can also easily acquire new mechanisms of resistance.

They are naturally fairly resistant to all β -lactam antibiotics because of the low affinity of their penicillin binding proteins. With the exception of cefoperazone, cephalosporins are not effective on enterococci. They can also develop a more complete resistance to penicillin and ampicillin. Enterococci show a remarkable ability to acquire new mechanisms of resistance. As a result, susceptibility patterns vary considerably according to temporal and geographic variation. Aminoglycosides have difficulty penetrating through the outer envelope of the enterococci, but are used synergistically with penicillin or ampicillin in treatment. Enterococci have developed resistance to vancomycin (VRE) through a genetic mechanism also transferable within species and possibly to other species.

Combinations of penicillin plus aminoglycosides produce bactericidal killing of enterococci. Unfortunately, enterococci can develop high-level resistance to streptomycin via chromosomal mutation. Strains of enterococci with high level resistance to streptomycin are not necessarily highly resistant to gentamicin and other aminoglycosides; in recent years, penicillin (or ampicillin) plus gentamicin has become the standard of therapy for enterococcal endocarditis, meningitis, and other serious infections requiring bactericidal therapy. Unfortunately, the 1980s and 1990s have seen a marked worldwide increase in strains of enterococci with genes that encode a bifunctional phosphor-transferase /acetyl-transferase enzyme that inactivates gentamicin and all other currently available aminoglycosides ex-

cept streptomycin. Such organisms are not killed synergistically by combinations of gentamicin plus cell-wall-active antibiotics.

Table 6: Percent Enterococci, Resistant to Vancomycin - Louisiana, 2000-2011

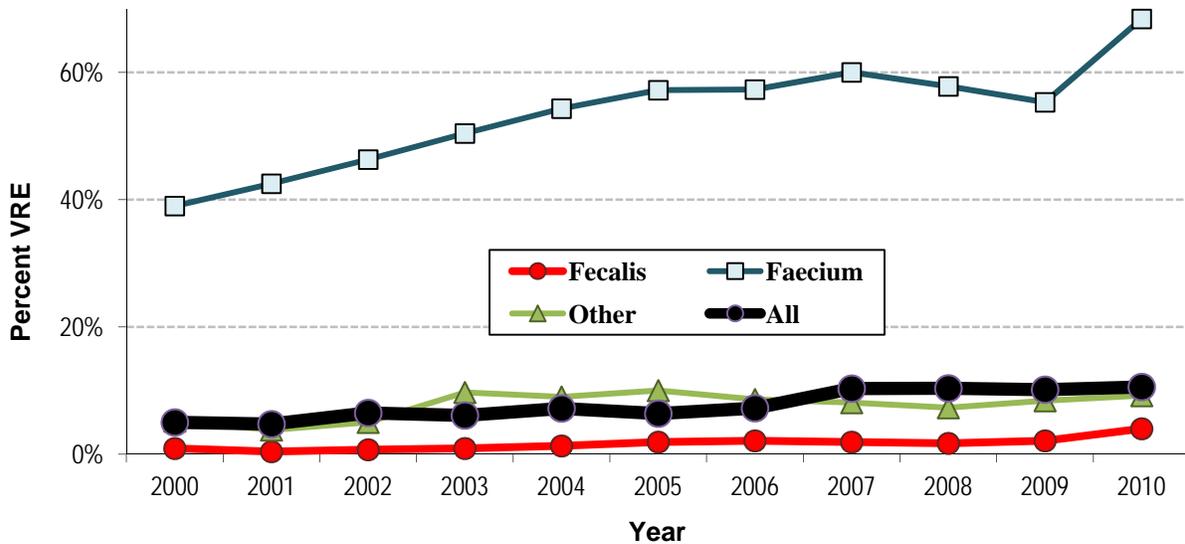
ALS	<i>E.fecalis</i> /Vancomycin				<i>E.faecium</i> /Vancomycin				<i>E. spp</i> /Vancomycin			
	Exam	Res	Int	% Res	Exam	Res	Int	% Res	Exam	Res	Inter	% Res
2000	6,187	56	6	0.9%	615	240	5	39.0%	1,223	63	1	5.2%
2001	7,381	33	14	0.4%	769	327	3	42.5%	1,118	42	0	3.8%
2002	7,867	59	18	0.7%	817	378	7	46.3%	1,079	54	1	5.0%
2003	8,024	72	14	0.9%	821	414	4	50.4%	1,428	139	1	9.7%
2004	6,414	85	19	1.3%	693	376	6	54.3%	1,239	112	2	9.0%
2005	3,737	72	13	1.9%	505	289	7	57.2%	1,040	104	1	10.0%
2006	3,491	73	15	2.1%	482	276	12	57.3%	1,295	111	0	8.6%
2007	4,581	88	6	1.9%	743	446	22	60.0%	1,458	118	0	8.1%
2008	6,455	112	3	1.7%	907	524	24	57.8%	1,276	93	1	7.3%
2009	6,898	147	8	2.1%	973	538	20	55.3%	1,278	107	3	8.4%
2010	10,585	422	2	4.0%	1,837	1256	15	68.4%	1,381	127	0	9.2%
2011												
CoArm	X2 399	df 1		p 0.000	X2 246	df 1		p 0.000	X2 24	df 1		p 0.000
SLReq	a 0.12	b 0.25		p 0.001	a 39.6	b 2.3		p 0.000	a 5.3	b 0.4		p 0.05
	SE 0.05	CI 0.2		CI 0.3	SE 0.3	CI 1.7		CI 2.9	SE 0.2	CI 0.06		CI 0.7

	Enterococci/Vancomycin		
	Total	Res	% Res
2000	9,028	451	5.0%
2001	10,509	496	4.7%
2002	9,974	647	6.5%
2003	4,734	288	6.1%
2004	8,346	600	7.2%
2005	6,731	429	6.4%
2006	11,420	826	7.2%
2007	10,359	1068	10.3%
2008	15,865	1643	10.4%
2009	10,550	1070	10.1%
2010	8,886	1003	11.3%
2011	5434	696	12.8%
CoArm	X2 801.6	df 1	p 0.000
SLReq	a 3.57	b 0.71	p 0.00
	SE 0.71	CI: 0.58	CI: 0.84

The emergence of Vancomycin resistant strains of enterococci (VRE) in the past 20 years has led to increased risks of invasive VRE infections, with high lethality.

Vancomycin resistant enterococcus is ubiquitous in the hospital environment, often found as a contaminant on medical equipment. Most patients are simply colonized and not infected (a ratio of 10:1). Persons at highest risk for VRE infections are those hospitalized with severe underlying or immunosuppressive conditions. These people may be affected by one of two mechanisms: drug resistance developed post-exposure to the antibiotic, or via contact with the drug resistant pathogen (person-to-person or environmental).

Figure 4: Percentage of Vancomycin Resistant *Enterococcus*– Louisiana, 2000-2010



Overall rates of Vancomycin Resistant *Enterococcus* showed a significant increase over the years, from 5% to 10% between 2000 and 2010.

3.9- *Neisseria meningitidis*

Neisseria meningitidis is a colonizer of a few percent of the population and also an important cause of septicemia and pyogenic meningitis. Reduced susceptibility to rifampin is of concern since this antibiotic is often used for prophylaxis of close contacts. The number of *Neisseria meningitidis* tested for antibiotic sensitivity is very small (less than 20 per year). Sensitivity to cephalosporins and rifampin remain at 100%.

3.10- *Acinetobacter Baumannii*

Table 7: Percent *Acinetobacter*, Resistant to Carbapenem - Louisiana, 2000-2011

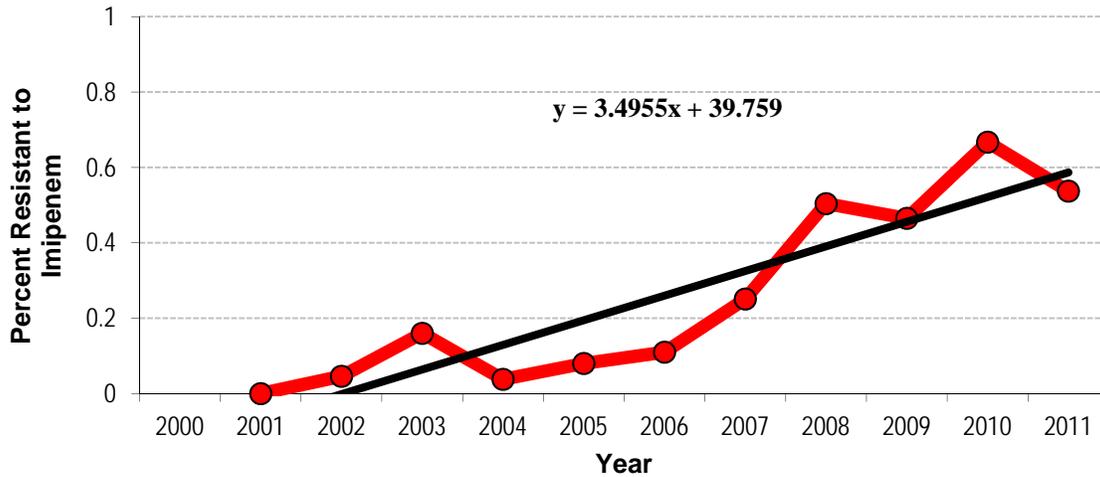
	Acinetobacter/Carbapenem		
	Total	Res	% Res
2000			
2001	11	0	0.0%
2002	44	2	4.6%
2003	419	67	16.0%
2004	173	7	3.8%
2005	30	2	8.0%
2006	75	8	11.0%
2007	589	148	25.1%
2008	1,300	655	50.4%
2009	906	421	46.5%
2010	1,107	738	66.7%
2011	970	521	53.7%
CoArm	X2 523.4	df 1	p 0.00
SLReq	a -13.41	b 6.5	p 0.00
	SE 1.0	CI: 4.6	CI: 8.4

Acinetobacter are small non-motile Gram-negative bacilli from the *Neisseriaceae* family. They have been designated *Mima*, *Herellea* and *Micrococcus* in the past. They are free-living organisms extremely common in food, water and on environmental surfaces. In humans they are common in sputum, urine, feces and vaginal secretions. About 25% of adults are colonized. They are becoming a more common cause of nosocomial infections, usually ventilator-associated pneumonia, line sepsis or burn wound sepsis.

Antibiotics of choice include ampicillin/sulbactam, piperacillin/tazobactam, imipenem, meropenem and cefepime. Alternative regimens use third generation cephalosporins, fluoroquinolones, tetracycline, aztreonam and colistin/polymyxin.

There is a huge increase in resistance to imipenem which went from 0% in 2001 to 67% in 2010.

Figure 5: Percentage of *Acinetobacter baumannii* Resistant to Imipenem - Louisiana, 2000-2011



3.11-Haemophilus influenzae

Haemophilus are Gram-negative bacilli specific to humans, normally colonizing the pharynx. They cause otitis media, sinusitis, conjunctivitis, bronchopneumonia, cellulitis and invasive disease such as meningitis and septic arthritis. *H. influenzae* is the most important pathogen and has strains that are ampicillin resistant. *H. influenzae* type b is responsible for haemophilus, the most invasive disease in humans.

Recommended therapies for both ampicillin-sensitive and ampicillin-resistant *Haemophilus* are second or third generation cephalosporins, flouroquinolones, telithromycin and doxycycline. Alternative treatment includes carbapenems and cefepime.

Table 8: Percent *H. influenzae*, Resistant to Listed Drugs - Louisiana, 2000-2011

	<i>Haemophilus influenzae</i>											
	Ceftriaxone			TMP-SXZ			Macrolides			Fquinolones		
	Exam	Res	Res %	Exam	Res	Res %	Exam	Res	Res %	Exam	Res	Res %
2000	129	0	0.0%	94	25	26.7%				121	0	0.0%
2001	14	0	0.0%	87	21	24.1%				95	0	0.0%
2002	115	0	0.0%	127	27	21.6%				18	0	0.0%
2003	187	1	0.4%	186	25	13.4%				34	0	0.0%
2004	85	3	3.8%	85	27	31.6%				84	0	0.0%
2005	43	0	0.0%	43	10	23.1%	13	1	8.0%	43	0	0.0%
2006	38	0	0.0%	38	2	5.0%	28	4	14.0%	38	1	3.0%
2007	293	6	2.1%	320	80	25.2%	65	16	25.0%	126	1	0.9%
2008	138	0	0.0%	224	65	28.8%	46	19	41.0%	102	0	0.0%
2009	154	0	0.0%	294	71	24.0%	75	24	32.0%	60	0	0.0%
2010	108	0	0.0%	196	56	28.5%	88	28	32.0%	56	0	0.0%
2011	205	0	0.0%	0	237	65.0%	62	12	19.4%	30	0	0.0%
CoArm SLReq				X2 3.78 df 1 p 0.052 a 21.3 b 0.27 p 0.728 SE 0.76 CI: -1.1 CI: 1.7				X2 21.3 df 1 p 0.052 a 3 b 0.01 p 0.9 SE 0.05 CI: -1.1 CI: 1.7				

3.12-Enterobacteriaceae

Enterobacteriaceae is a large group of Gram-negative organisms which are widely distributed in the soil and are normal colonizers of the intestinal tract of humans and animals. They are an important cause of infection when found outside the gastrointestinal tract. They account for 30% of all nosocomial infectious agents isolated (30% of septicemia isolates, 20% of surgical site infections, 55% of urinary tract isolates and 20% of pulmonary infections isolates). Among the enterobacteriaceae, *Escherichia coli*, *Klebsiella*, *Proteus*, *Salmonella*, and *Shigella* are the most important pathogens.

3.12.1- *E.coli*

E.coli is a normal inhabitant of the human gastrointestinal tract. It produces disease when it is in other habitats such as the urinary tract, biliary tract, blood or meninges. A few isolates are not part of the human flora and when introduced in humans, cause gastroenteritis (entero-toxicogenic, entero-invasive and entero-hemorrhagic *E. coli*).

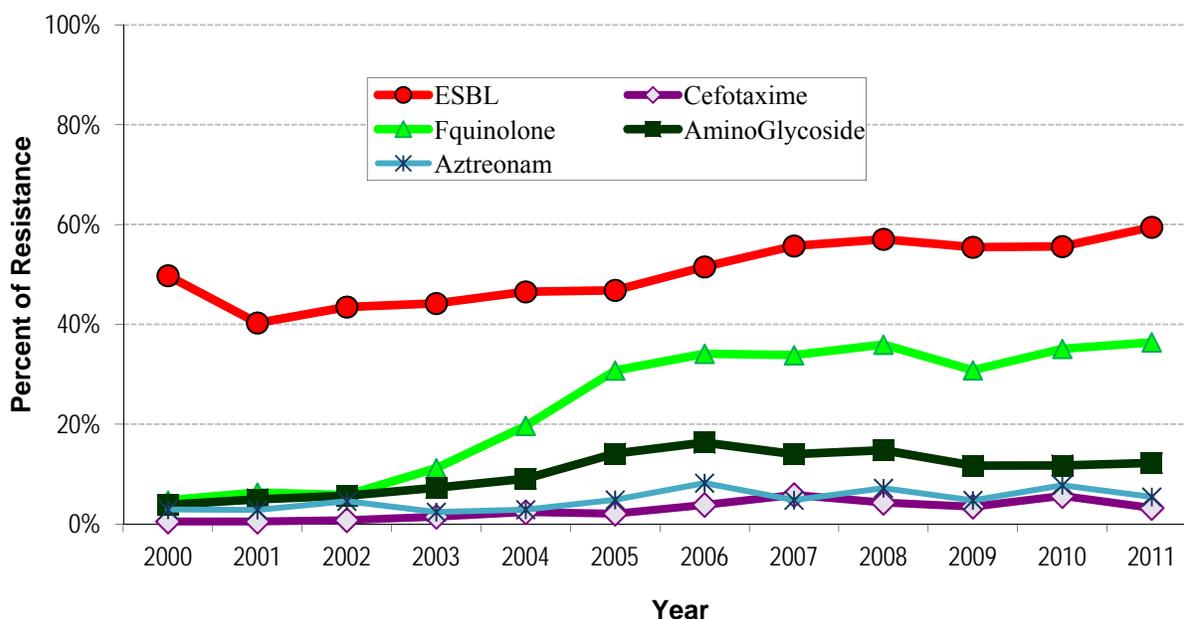
- Ampicillin resistance is found in many *E.coli* strains due to their production of extended spectrum beta lactamase (ESBL). Sensitivity to ampicillin has steadily increasing to 55% overall in Louisiana.
- Resistance to cephalosporines is also increasing
- *E.coli* became very resistant to ciprofloxacin in the early 2000s
- Resistance to aminoglycosides has also been increasing since 2004
- Although not as sharply, resistance to aztreonam is also increasing

Table 9: Percent *E.coli*, Resistant to Listed Drugs - Louisiana, 2000-2011

	<i>E coli</i>								
	Ampicillin			Cefotaxime			FluoQ		
	Exam	Res	%R	Exam	Res	%R	Exam	Res	%R
2000	6,441	3,205	49.8%	4,015	20	0.5%	3,731	176	4.7%
2001	2,770	1,116	40.3%	2,511	12	0.5%	2,402	152	6.3%
2002	9,235	4,015	43.5%	7,580	57	0.8%	5,232	303	5.8%
2003	31,459	13,900	44.2%	9,370	136	1.4%	24,430	2,732	11.2%
2004	16,310	7,588	46.5%	5,687	134	2.4%	12,961	2,549	19.7%
2005	10,364	4,853	46.8%	2,300	47	2.1%	10,587	3,256	30.8%
2006	20,207	10,411	51.5%	7,277	278	3.8%	16,804	5,732	34.1%
2007	24,970	13,910	55.7%	9,514	553	5.8%	19,660	6,651	33.8%
2008	32,275	18,414	57.1%	11,156	477	4.3%	24,179	8,690	35.9%
2009	37,724	20,920	55.5%	12,127	421	3.5%	28,317	8,723	30.8%
2010	23,757	13,455	56.6%	5,399	303	5.6%	16303	5720	35.1%
2011	25197	14984	59.5%	9874	316.62	3.2%	31601	11504	36.4%
CoArm	X2 1695	df 1	p 0.000	X2 502	df 1	p 0.000	X2 6228	df 1	p 0.000
SLReq	a 41	b 1.4	p 0.002	a -0.2	b 0.5	p 0.000	a 1.1	b 3.5	p 0.000
	SE 0.3	CI 0.8	CI 2.0	SE 0.1	CI 0.3	CI 0.6	SE 0.6	CI 2.5	CI 4.5

	AmGly			Aztreonam		
	Exam	Res	%R	Exam	Res	%R
2000	6,996	268	3.8%	4,059	117	2.9%
2001	2,770	136	4.9%	1,935	54	2.8%
2002	9,235	522	5.6%	3,782	173	4.6%
2003	32,685	2,367	7.2%	12,297	293	2.4%
2004	16,644	1,507	9.1%	6,658	191	2.9%
2005	15,894	2,240	14.1%	7,902	382	4.8%
2006	26,941	4,395	16.3%	13,550	1,110	8.2%
2007	25,406	3,550	14.0%	17,794	850	4.8%
2008	33,981	5,020	14.8%	28,236	2,023	7.2%
2009	37,724	4,407	11.7%	27,687	1,309	4.7%
2010	24,163	2,834	11.7%	14,056	1,091	7.8%
2011	35250	4305.8	12.21%	22139	1199.8	5.4%
CoArm	X2 1157	df 1	p 0.000	X2 239	df 1	p 0.00
SLReq	a 4.1	b 1.0	p 0.005	a 2.4	b 0.42	p 0.016
	SE 0.3	CI 0.5	CI 1.5	SE 0.13	CI: 0.14	CI: 0.61

Figure 6: Percentage of *E. coli* Resistance - Louisiana, 2000-2011



3.12.2-Klebsiella Pneumoniae

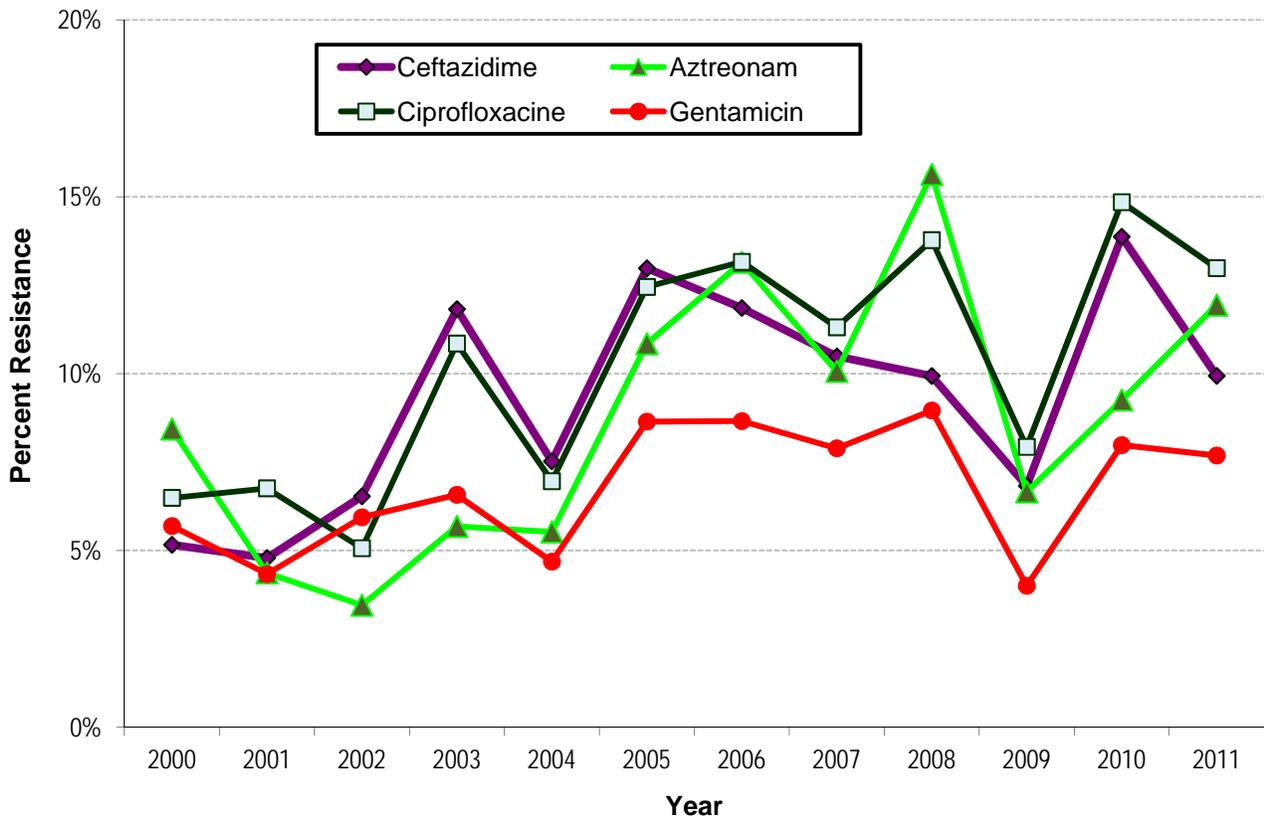
Klebsiella pneumoniae may cause community-acquired lobar pneumonia in patients with severe underlying medical conditions. More importantly, these organisms have a predisposition to cause nosocomial infections such as ventilator-associated pneumonia, meningitis, cellulitis and UTIs. It is the most common pathogen in ICUs.

Table 10: Percent *Klebsiella pneumoniae*, Resistant to Listed Drugs - Louisiana, 2000-2011

<i>Klebsiella pneumoniae</i>									
Ampicillin			Ceftazidime			Aztreonam			
	Exam	Res	Res %	Exam	Res	Res %	Exam	Res	Res %
2000	1,721	1,531	89.0%	1,088	56	5.2%	1,097	93	8.4%
2001	578	541	93.7%	860	41	4.8%	737	32	4.4%
2002	2,245	2,209	98.4%	2,071	135	6.5%	984	34	3.5%
2003	6,652	6,496	97.7%	6,093	720	11.8%	3,281	186	5.7%
2004	3,557	3,438	96.7%	2,536	191	7.5%	2,212	122	5.5%
2005	2,316	2,259	97.6%	2,349	305	13.0%	2,571	279	10.8%
2006	4,473	4,269	95.4%	4,393	521	11.9%	3,290	433	13.1%
2007	4,824	4,764	98.7%	6,989	733	10.5%	6,016	606	10.1%
2008	4,631	4,327	93.4%	8,540	848	9.9%	7,598	1,188	15.6%
2009	385	378	98.1%	6,948	474	6.8%	15,036	1,001	6.7%
2010	479	389	81.2%	5,134	712	13.9%	2,019	187	9.3%
2011	341	323	94.7%	6,763	672	9.9%	6,007	717	11.9%
CoArm	X2 5.6	df 1	p 0.02	X2 10.25	df 1	p 0.001	X2 57.26	df 1	p 0.00
SLReq	a 96.06	b -0.23	p 0.61	a 6.24	b 0.47	p 0.06	a 4.88	b 0.60	p =.05
	SE 0.44	CI: -1.03	CI: 0.56	SE 0.03	CI: 0.01	CI: 0.11	SE 0.03	CI: 0.02	CI: 0.14

Cipro			Gentamicin			Carbapenem			
	Exam	Res	Res %	Exam	Res	Res %	Exam	Res	Res %
2000	1,151	75	6.5%	1,969	112	5.7%	1,848	6	0.3%
2001	854	58	6.8%	1,087	47	4.3%	909	8	0.8%
2002	1,340	68	5.1%	2,500	148	5.9%	2,336	6	0.3%
2003	7,091	769	10.9%	9,353	615	6.6%	6,021	20	0.3%
2004	3,272	228	7.0%	4,273	200	4.7%	3,199	34	1.1%
2005	2,586	322	12.5%	4,039	349	8.6%	3,064	0	0.0%
2006	3,704	487	13.2%	6,467	560	8.7%	5,026	186	3.7%
2007	5,671	641	11.3%	7,952	627	7.9%	9,616	37	0.4%
2008	6,365	877	13.8%	9,840	881	9.0%	13,759	95	0.7%
2009	6,294	499	7.9%	8,591	344	4.0%	12,945	91	0.7%
2010	4,276	635	14.8%	6,175	493	8.0%	6,191	42	0.7%
2011	8,250	1,071	13.0%	8,940	687	7.7%	12,147	92	0.8%
CoArm	X2 101.2	df 1	p 0.00	X2 16.07	df 1	p 0.00	X2 0.15	df 1	p 0.70
SLReq	a 5.86	b 0.67	p 0.01	a 5.32	b 0.22	p 0.15	a 0.6	b 0.03	p 0.70
	SE 0.21	CI: 0.3	CI: 1.04	SE 0.14	CI: -0.04	CI: 0.48	SE 0.08	CI: -0.12	CI: 0.18

Figure 7: Percentage of *Klebsiella pneumoniae* Resistance - Louisiana, 2000-2011



3.12.3- Salmonella

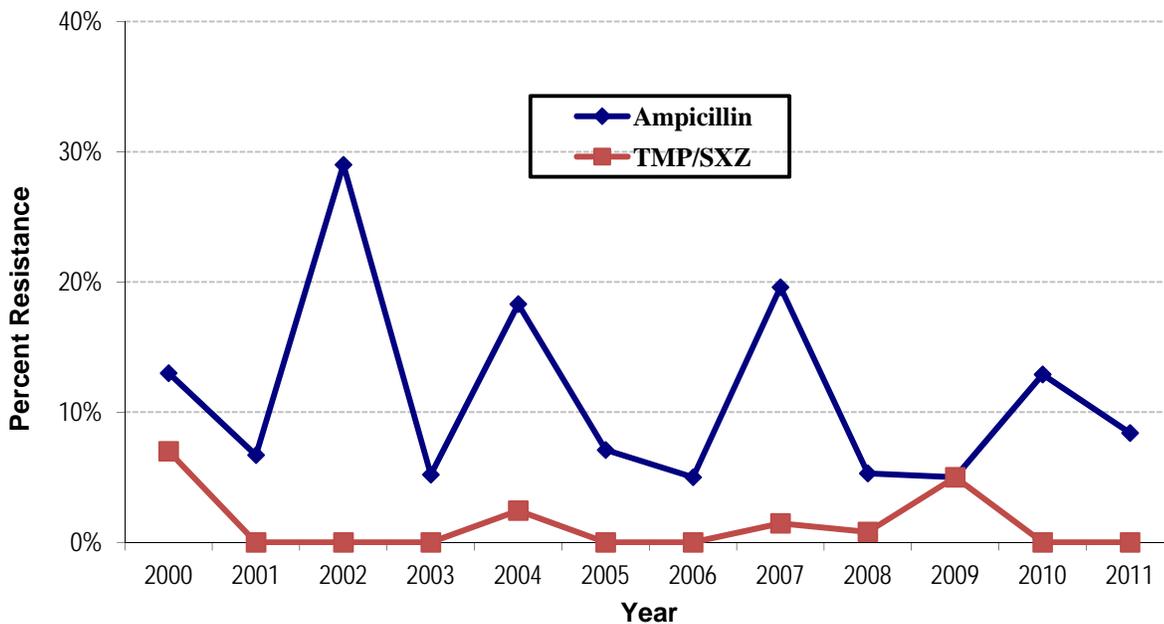
Salmonella is a group of organisms containing numerous serotypes, many of which are pathogenic for both animals and humans. The human pathogens are within the species *S. enterica*. Ingestion of contaminated food is the main mode of transmission with a few cases originating from contaminated water or from person-to-person transmission via the fecal-oral route. Gastroenteritis and enteric fever are the main clinical syndromes observed. *Salmonella* is periodically the source of foodborne outbreaks, usually arising from undercooked egg products, raw dairy or contaminated meat.

In most cases of simple enterocolitis due to *Salmonella*, no treatment is necessary. For severe enterocolitis and invasive disease (typhoid fever, paratyphoid fever) treatment is recommended. *Salmonella* resistance to ampicillin vary from 5% to 20% with no significant increase (Cochrane-Armitage test for linear trend: $\chi^2 = 0.00$, $df=1$, $p = 0.99$). *Salmonella* remain very sensitive to penicillin/ β lactamase inhibitors, carbapenems, aminoglycosides, quinolones and trimethoprim-sulfamethoxazole. Both fluoroquinolones and trimethoprim-sulfamethoxazole can prolong the carrier state.

Table 11: Percent *Salmonella spp.*, Resistant to Listed Drugs - Louisiana, 2000-2011

	Salmonella spp											
	Ampicillin			TMP-SXZ			Cefotaxime			Ciprofloxacin		
	Exam	Res	%R	Exam	Res	%R	Exam	Res	%R	Exam	Res	%R
2000	16	2	13.0%	16	1	7.0%	16	0	0.0%			
2001	15	1	6.7%	12	0	0.0%	15	0	0.0%			
2002	7	2	29.0%	7	0	0.0%	12	0	0.0%	7	0	0.0%
2003	19	1	5.2%	19	0	0.0%	7	0	0.0%	18	0	0.0%
2004	38	7	18.3%	41	1	2.4%	7	0	0.0%	40	0	0.0%
2005	27	2	7.1%	27	0	0.0%	6	0	0.0%	27	0	0.0%
2006	113	6	5.0%	118	0	0.0%	118	0	0.0%	118	1	0.8%
2007	146	29	19.6%	142	2	1.5%	4	0	0.0%	142	0	0.0%
2008	127	7	5.3%	127	1	0.8%	22	0	0.0%	112	0	0.0%
2009	41	2	5.0%	41	2	5.0%	41	0	0.0%	41	0	0.0%
2010	136	18	12.9%	146	0	0.0%	61	0	0.0%	136	0	0.0%
2011	154	13	8.4%	154	0	0.0%	75	0	0.0%	154	0	0.0%
CoArm	X2 .49 df 1 p .49											
SLReq	a 14.7 b -0.52 p 0.44											
	SE 0.64 CI: -1.67 CI: 0.64											

Figure 8: Percentage of *Salmonella spp* Resistance - Louisiana, 2000-2011



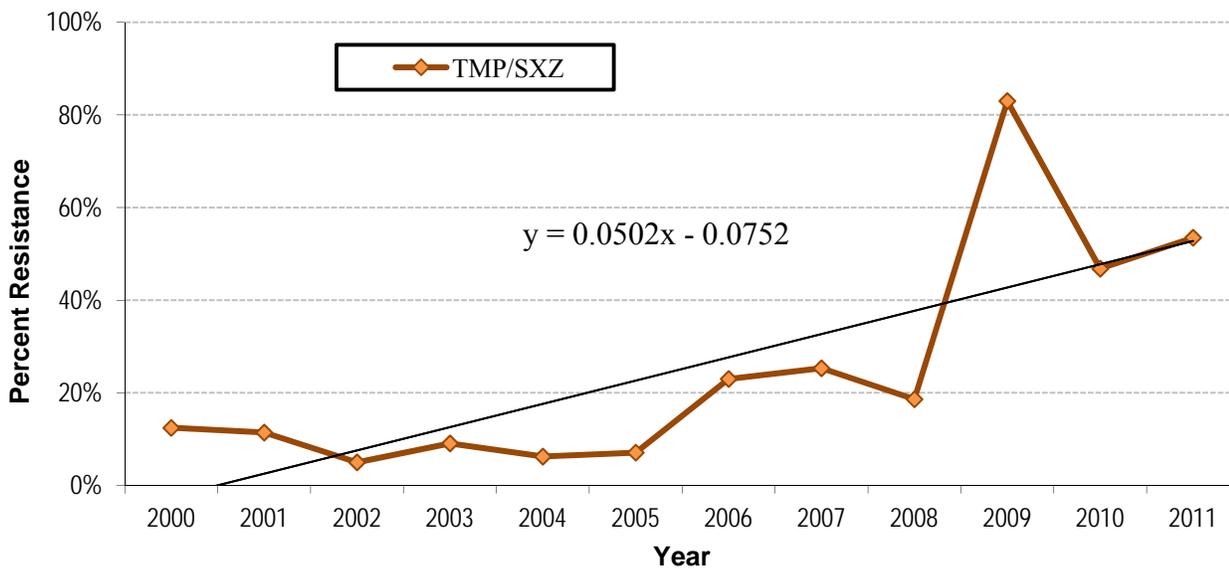
3.12.4--*Shigella*

Shigella are responsible for acute gastroenteritis and bacillary dysentery transmitted by the fecal-oral route. It is a frequent cause of community outbreaks, particularly among homosexual men and in overcrowded or unsanitary conditions.

Table 12: Percent *Shigellaa spp.*, Resistant to Listed Drugs - Louisiana, 2000-2011

ABG	Shigella spp											
	Ampicillin			TMP-SXZ			Cephalo 3			Ciprofloxacin		
	Exam	Res	Res %	Exam	Res	Res %	Exam	Res	Res %	Exam	Res	Res %
2000	47	41	87.2%	47	6	12.4%	12	0	0.0%			
2001	5	4	80.0%	35	4	11.4%	10	0	0.0%	5	0	
2002	10	8	80.0%	41	2	5.0%	9	0	0.0%	1	0	0.0%
2003	12	9	75.0%	33	3	9.1%	7	0	0.0%	1	0	0.0%
2004	32	25	78.1%	32	2	6.3%	25	0	0.0%	31	0	0.0%
2005	36	26	72.2%	31	2	7.1%	1	0	0.0%	1	0	0.0%
2006	110	110	100.0%	110	25	23.0%	110	0	0.0%	110	1	0.9%
2007	158	97	61.2%	158	40	25.3%	52	0	0.0%	158	0	0.0%
2008	101	50	49.5%	102	19	18.6%	19	0	0.0%	104	0	0.0%
2009	6	5	83.0%	6	5	83.0%	15	0	0.0%	6	0	0.0%
2010	94	77	81.9%	94	44	46.8%	0	0	0.0%	94	0	0.0%
2011	129	113	87.6%	129	69	53.5%	75	0	0.0%	129	0	0.0%
CoArm	X2 0.2 df 1 p 0.65			X2 83.6 df 1 p 0.00								
SLReq	a 80.42 b -0.37 p 0.75			a -7.56 b 5.02 p 0.005								

Figure 9: Percentage of *Shigella spp* Resistance to TMP-SXZ - Louisiana, 2000-2011



3.12.5-Enterobacter cloacae

Enterobacter species, particularly *Enterobacter cloacae* and *Enterobacter aerogenes*, are important nosocomial pathogens responsible for various infections, including bacteremia, lower respiratory tract infections, skin and soft-tissue infection urinary tract infections (UTI) endocarditis, intra-abdominal infections septic arthritis, osteomyelitis, and ophthalmic infections. *Enterobacter* species can also cause various community-acquired infections, including UTIs, skin and soft-tissue infections, and wound infections, among others.

These "ICU bugs" cause significant morbidity and mortality, and infection management is complicated

by resistance to multiple antibiotics. *Enterobacter* species possess inducible beta-lactamases, which are undetectable in vitro but are responsible for resistance during treatment.

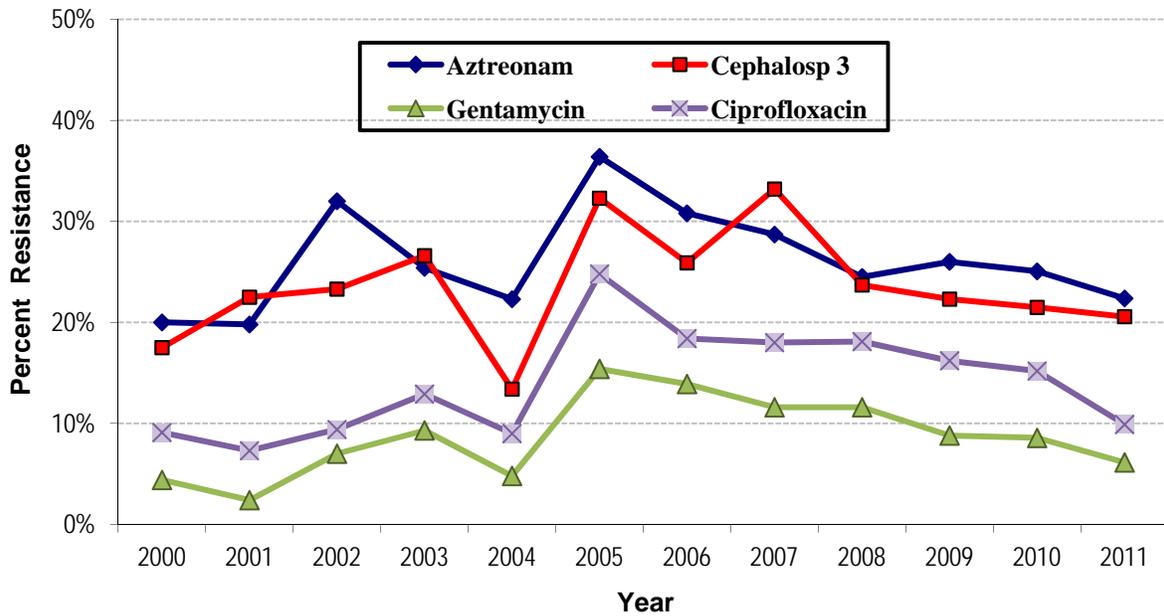
Table 13: Percent *Enterobacter spp.*, Resistant to Listed Drugs - Louisiana, 2000-2011

ABG	Enterobacter cloacae								
	Aztreonam			Cephalosporin 3rd G			Gentamicin		
	Exam	Res	%R	Exam	Res	%R	Exam	Res	%R
2000	372	74	20.0%	378	66	17.5%	628	28	4.4%
2001	115	23	19.8%	140	31	22.5%	203	5	2.4%
2002	235	75	32.0%	504	117	23.3%	595	42	7.0%
2003	930	236	25.4%	840	223	26.6%	2,173	203	9.3%
2004	522	116	22.3%	261	35	13.4%	822	39	4.8%
2005	603	219	36.4%	101	33	32.3%	716	110	15.4%
2006	832	256	30.8%	278	72	25.9%	1,265	176	13.9%
2007	1,505	431	28.7%	901	300	33.2%	2,199	255	11.6%
2008	1,744	428	24.5%	551	130	23.7%	2,312	269	11.6%
2009	1,354	352	26.0%	685	153	22.3%	1,939	171	8.8%
2010	427	107	25.1%	205	44	21.5%	1,202	103	8.6%
2011	607	136	22.4%	540	111	20.6%	1,397	86	6.1%
CoArm	X2 .23	df 1	p 0.63	X2 0.78	df 1	p 0.38	X2 2.75	df 1	p 0.097
SLReq	a 25.16	b 0.14	p 0.75	a 22.19	b 0.21	p0.68	a 6.03	b 0.41	p 0.23
	SE 0.44	CI: -0.65	CI: 0.94	SE 0.49	CI: -0.68	CI: 1.1	SE 0.32	CI: -0.17	CI: 0.99

	Ciprofloxacin			TMP/SXZ		
	Exam	Res	%R	Exam	Res	Res %
2000	348	37	10.6%	607	56	9.1%
2001	169	20	11.6%	203	15	7.3%
2002	402	26	6.4%	655	62	9.4%
2003	1,748	243	13.9%	1,331	172	12.9%
2004	574	41	7.2%	686	62	9.0%
2005	411	88	21.5%	587	146	24.8%
2006	723	123	17.0%	1,042	192	18.4%
2007	1,518	250	16.5%	2,053	369	18.0%
2008	1,630	221	13.6%	2,178	394	18.1%
2009	1,493	193	12.9%	1,848	299	16.2%
2010	823	125	15.2%	1,202	225	18.7%
2011	1,277	126	9.9%	1,397	182	13.1%
CoArm	X2 0.27	df 1	p 0.605	X2 34.5	df 1	p 0.00
SLReq	a 11.02	b 0.31	p0.41	a 9.23	b 0.83	p 0.06
	SE 0.36	CI: -0.34	CI: 0.96	SE 0.38	CI: 0.14	CI: 1.52

- *E.cloacae* is 96% to 99% resistant to amoxicillin, ampicillin, penicillin derivatives with clavulanic acids, about 30% resistant to macrolides and carbapenems.
- Resistance to aminoglycosides remains around 10% but with a significant increasing. Resistance to amikacin is low at around 1%.
- Resistance to quinolones is slightly higher at around 15% with a significant increasing trend.
- Resistance to Aztreonam is around 25% to 30% showing no increasing trend.
- Resistance to most cephalosporins third generation, around 20% to 30%; shows a significant trend towards increase.

Figure 10: Percentage of *Enterobacter spp* Resistance - Louisiana, 2000-2011



3.12.6-*Proteus mirabilis*

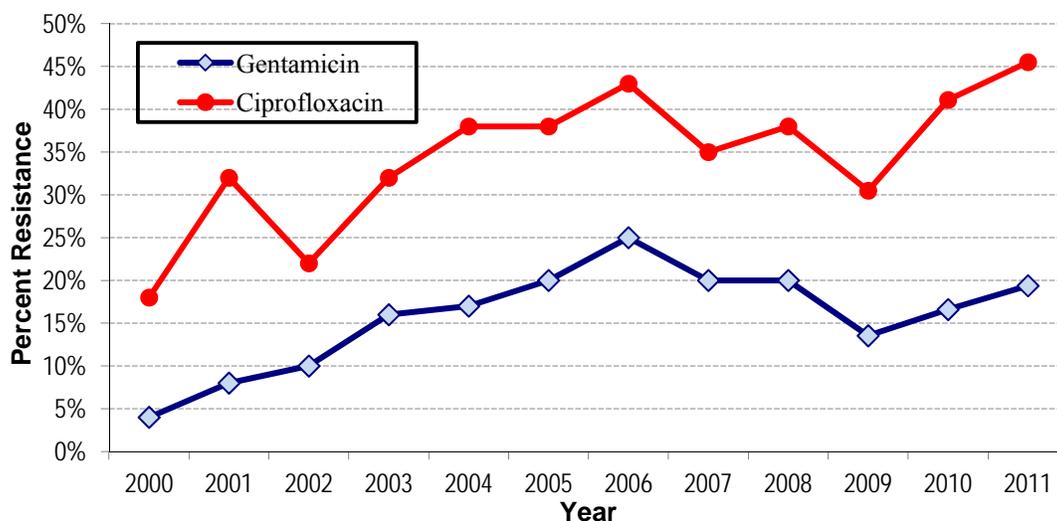
Proteus species are prone to colonize and infect the urinary tract. Iatrogenic hematologic dissemination can occur after urologic procedures. The most common diseases seen are urinary tract infections and surgical site infections. *Proteus vulgaris* is indole-positive and has more antibiotic resistance. *Proteus mirabilis*, which is indole-negative, is the most common species encountered.

Table 14: Percent *Proteus mirabilis*, Resistant to Listed Drugs - Louisiana, 2000-2011

ABG	Proteus mirabilis								
	Ampicillin			Clav-Ticarcillin			Cephalosporin 3rd G		
	Exam	Res	%R	Exam	Res	%R	Exam	Res	%R
2000	1,341	102	7.6%	1,261	7	0.5%	973	14	1.5%
2001	566	93	16.5%	606	7	1.1%	459	9	1.9%
2002	2,511	585	23.3%	1,063	26	2.4%	1,362	3	0.2%
2003	7,798	2,323	29.8%	2,135	26	1.2%	4,496	50	1.1%
2004	4,711	1,582	33.6%	1,380	10	0.7%	2,493	49	2.0%
2005	2,741	902	32.9%	682	2	0.3%	1,967	14	0.7%
2006	4,982	1,780	35.7%	1,489	123	8.3%	3,827	161	4.2%
2007	6,183	1,737	28.1%	2,653	165	6.2%	6,057	121	2.0%
2008	7,891	2,547	32.3%	2,217	16	0.7%	7,716	464	6.0%
2009	4,792	1,311	27.4%	2,584	21	0.8%	4,326	198	4.6%
2010	2,564	600	23.4%	875	2	0.2%	3,896	247	6.4%
2011	4,310	1,178	27.3%	1,266	4	0.3%	6,611	775	11.7%
CoArm	X2 16.2	df 1	p 0.00	X2 0.01	df 1	p 0.91	X2 845	df 1	p 0.00
SLReq	a 19.51	b 1.07	p 0.11	a 1.9	b -0.002	p 0.995	a -1.28	b 0.74	p 0.001
	SE 0.61	CI: -0.04	CI: 2.19	SE 0.23	CI: -0.41	CI: 0.41	SE 0.17	CI: 0.43	CI: 1.05

	Gentamicin			Ciprofloxacin			TMP/SXZ		
	Exam	Res	%R	Exam	Res	%R	Exam	Res	%R
2000	1,540	65	4.2%	925	167	18.1%	1,491	72	4.8%
2001	702	56	7.9%	516	164	31.7%	702	71	10.1%
2002	2,511	254	10.1%	1,487	323	21.7%	2,737	524	19.1%
2003	7,637	1,194	15.6%	6,307	2,020	32.0%	5,776	1,683	29.1%
2004	4,711	784	16.6%	3,554	1,341	37.7%	3,893	1,292	33.2%
2005	2,774	557	20.1%	1,567	589	37.6%	2,326	807	34.7%
2006	5,392	1,360	25.2%	2,589	1,112	42.9%	4,675	1,907	40.8%
2007	6,857	1,341	19.6%	4,959	1,742	35.1%	6,444	2,154	33.4%
2008	8,860	1,687	19.0%	5,693	2,209	38.8%	8,162	3,166	38.8%
2009	6,025	815	13.5%	4,309	1,314	30.5%	6,012	1,815	30.2%
2010	4,144	688	16.6%	3,146	1,293	41.1%	4,243	1,545	36.4%
2011	6,777	1,313	19.4%	6,375	2,901	45.5%	6,350	2,446	38.5%
CoArm	X2 116.3	df 1	p 0.00	X2 341.9	df 1	p 0.00	X2 639.4	df 1	p 0.00
SLReq	a 8.87	b 1.05	p 0.24	a 23.5	b 1.67	p 0.006	a 12.3	b 2.59	p 0.002
	SE 0.40	CI: 0.33	CI: 1.76	SE 0.49	CI: 0.79	CI: 2.56	SE 0.61	CI: 1.48	CI: 3.7

Figure 11: Percentage of *Proteus spp.* Resistance - Louisiana, 2000-2011



3.15.3-*Serratia marcescens*

Members of this genus produce characteristic red pigment, prodigiosin. *S. marcescens*, was formerly known as *Bacillus prodigiosus* because of its causing a bright red color on communion bread. It was also thought to be non-pathogenic and was used to study the dispersal of bacteria throughout the atmosphere (California coastal area 1950). In fact *Serratia marcescens* is the only pathogen in this genus and usually causes nosocomial infections.

In the hospital, *Serratia* species tend to colonize the respiratory and urinary tracts, rather than the gastrointestinal tract, in adults. *Serratia* infection is responsible for about 2% of nosocomial infections of the bloodstream, lower respiratory tract, urinary tract, surgical wounds, and skin and soft tissues in adult patients. Outbreaks of *S. marcescens* meningitis, wound infections, and arthritis have occurred in pediatric wards.

It is resistant to ampicillin (90%), piperacillin (30%), penicillin/ β -lactamase-inhibitors (95% to those with amoxicillin or ampicillin, 5% to those with piperacillin or tazobactam), cyclines (70-90%). It shows little resistance to cephalosporins (10% or less), amino-glycosides (10%) and quinolones (5-10%).

3.15.4-Citrobacter freundii

These bacteria can be found almost everywhere in soil, water, wastewater, etc. It can also be found in the human intestine. They are rarely the source of illnesses, except for infections of the urinary tract, and infant meningitis and sepsis.

C. freundii strains have inducible ampC genes encoding resistance to ampicillin and first-generation cephalosporins. In addition, isolates of *Citrobacter* may be resistant to multiple other antibiotics as a result of plasmid-encoded resistance genes.

It is resistant to ampicillin (80%), piperacillin (15%), penicillin/ β -lactamase-inhibitors (80% to those with amoxicillin or ampicillin, 15% to those with piperacillin or tazobactam), cyclines (20%). Resistance to cephalosporins is variable (10% to 90%). It shows little resistance to carbapenems (1%), amino-glycosides (5% or less) and quinolones (5% to 15%).

3.15.5-Morganella morganii

Morganella morganii is a commensal Gram-negative bacillus of the intestinal tract of humans and other mammals and reptiles. Few reports exist in the literature regarding infections caused by this organism.

It is an uncommon cause of community-acquired infection and nosocomial infections.

It is resistant to ampicillin (95%), piperacillin (40%), penicillin/ β -lactamase-inhibitors (90% to those with amoxicillin or ampicillin, 35% to those with piperacillin or tazobactam), cyclines (50%), and quinolones (50%). Resistance to cephalosporins is variable (30% to 80%). It shows little resistance to carbapenems (2%), and amino-glycosides (15% or less).

3.15.5-Providencia stuartii

Providencia stuartii is an opportunistic pathogen seen in patients with severe burns or long-term indwelling urinary catheters. In animals *P. stuartii* infections can cause neonatal diarrhea due to *P. stuartii* infection in dairy cows. In humans, *P. stuartii* can be isolated from urine (most common), stool and blood, as well as from sputum, skin and wound cultures. *P. stuartii* septicemia is primarily of urinary origin. It is the most common cause of purple urine bag syndrome.

It is resistant to ampicillin (95%), piperacillin (20%), penicillin/ β -lactamase-inhibitors (95% to those with amoxicillin or ampicillin, 10% to those with piperacillin or tazobactam), cyclines (90%), and quinolones (70%). Resistance to cephalosporins and amino-glycosides (10% to 40%) is variable (30% to 80%). It shows little resistance to carbapenems (2%)

3.16-Pseudomonas aeruginosa

Pseudomonas aeruginosa is a common bacterium which can cause infections in animals and humans. It is found in soil, water, and most man-made environments throughout the world. It thrives not only in normal atmospheres, but also with little oxygen, and has thus colonized many natural and artificial environments. It uses a wide range of organic material for food; in animals, this versatility enables the

organism to infect damaged tissues or people with reduced immunity.

It causes pneumonias (community acquired but predominantly health care associated), septicaemia, urinary tract infection, gastrointestinal infection (especially in premature infants and neutropaenic cancer patients), and skin and soft tissue infections. It is often associated to diffuse bronchopneumonia, skin lesions of ecthyma gangrenosum, urinary tract catheterisation, necrotising enterocolitis (NEC), haemorrhage and necrosis.

Those at greatest risk of infection are cystic fibrosis patients, neutropenic patients, burn victims and patients with wound infections.

Table 15: Percent *Pseudomonas aeruginosa*, Resistant to Listed Drugs - Louisiana, 2000-2011

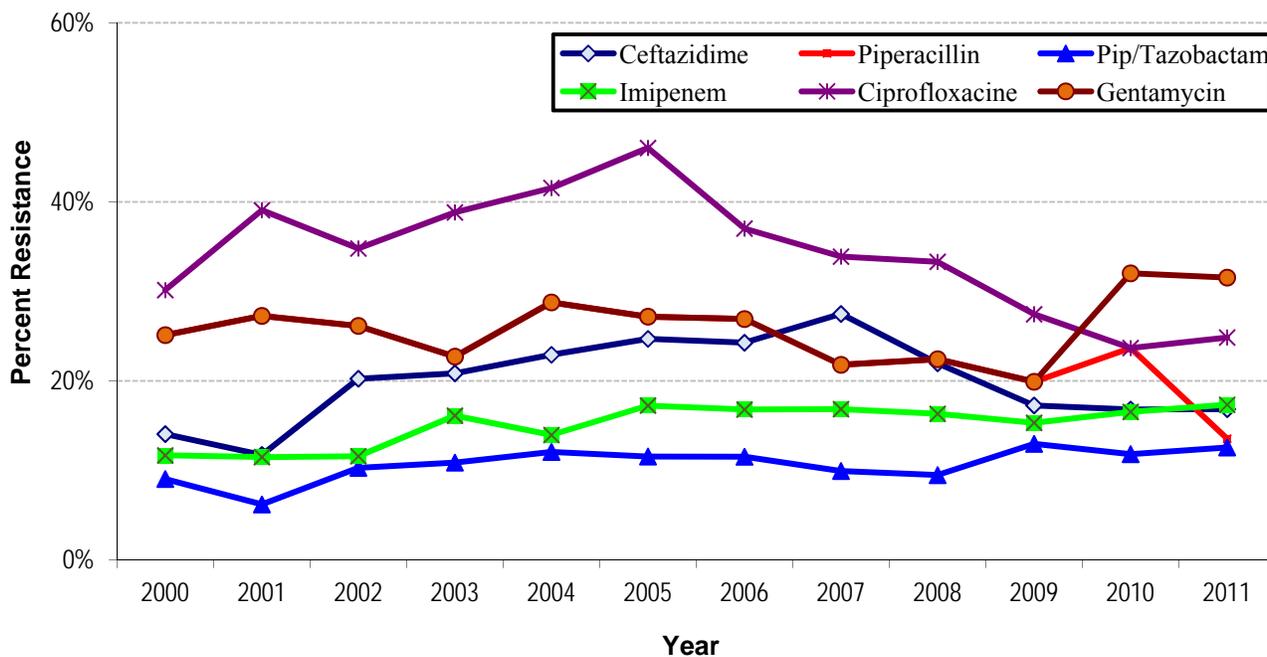
ABG	Pseudomonas								
	Ceftazidime			Piperacillin			Pipe/Tazobactam		
	Exam	Res	Res %	Exam	Res	Res %	Exam	Res	Res %
2000	1,852	260	14.1%	638	61	25.1%	1,491	135	9.0%
2001	1,350	158	11.7%	990	71	27.3%	1,025	64	6.2%
2002	2,643	535	20.2%	1,692	293	26.2%	2,823	291	10.3%
2003	8,152	1,700	20.8%	2,980	432	22.7%	6,302	685	10.9%
2004	3,402	780	22.9%	1,191	163	28.8%	3,314	400	12.1%
2005	2,748	679	24.7%	137	14	27.2%	3,717	430	11.6%
2006	5,201	1,262	24.3%	596	100	26.9%	6,001	692	11.5%
2007	7,597	2,088	27.5%	1,298	196	21.8%	7,151	711	9.9%
2008	9,580	2,105	22.0%	2,063	226	22.4%	10,658	1,011	9.5%
2009	6,882	1,188	17.3%	888	77	19.9%	7,322	950	13.0%
2010	4,999	840	16.8%	713	70	23.7%	5,267	623	11.8%
2011	7,377	1,243	16.8%	1,466	199	13.6%	6,157	773	12.6%
CoArm	X2 12.44	df 1	p 0.00	X2 3.08	df 1	p 0.079	X2 23.7	df 1	p 0.00
SLReq	a 18.23	b 0.26	p 0.53	a 12.27	b 0.002	p 0.995	a 8.57	b 0.33	p 0.03
	SE 0.4	CI: -0.47	CI: 0.99	SE 0.29	CI: -0.53	CI: 0.53	SE 0.13	CI: 0.10	CI: 0.56

	Imipenem			Gentamicin			Ciprofloxacin		
	Exam	Res	Res %	Exam	Res	Res %	Exam	Res	Res %
	2000	1,917	224	11.7%	1,990	500	25.1%	1,749	527
2001	1,350	155	11.5%	1,486	405	27.3%	1,344	525	39.1%
2002	2,748	318	11.6%	3,041	795	26.2%	2,096	729	34.8%
2003	7,015	1,131	16.1%	11,030	2,506	22.7%	8,912	3,460	38.8%
2004	3,781	528	14.0%	5,183	1,491	28.8%	3,988	1,657	41.6%
2005	3,826	660	17.2%	4,322	1,175	27.2%	2,104	968	46.0%
2006	5,419	911	16.8%	6,669	1,795	26.9%	3,000	1,111	37.0%
2007	8,075	1,361	16.9%	8,125	1,772	21.8%	5,780	1,959	33.9%
2008	9,916	1,620	16.3%	9,714	2,179	22.4%	6,488	2,161	33.3%
2009	6,613	1,013	15.3%	7,664	1,526	19.9%	5,725	1,572	27.5%
2010	4,882	808	16.5%	5,411	1,281	23.7%	4,106	1,315	32.0%
2011	7,712	1,338	17.3%	8,095	2,012	24.9%	7,631	2,407	31.5%
CoArm	X2 53.7	df 1	p 0.00	X2 32.17	df 1	p 0.00	X2 186.5	df 1	p 0.00
SLReq	a 11.85	b 0.5	p 0.003	a 27.04	b -0.36	p 0.11	a 39.07	b -0.56	p 0.22
	SE 0.13	CI: 0.27	CI: 0.73	SE 0.21	CI: -0.73	CI: 0.02	SE 0.43	CI: -1.33	CI: 0.22

One of the most worrisome characteristics of *P. aeruginosa* is its low antibiotic susceptibility. This low susceptibility is attributable to a concerted action of multidrug efflux pumps with chromosomally-encoded antibiotic resistance genes (e.g. *mexAB*, *mexXY*), and the low permeability of the bacterial cellular envelopes. In addition to this intrinsic resistance, *P. aeruginosa* easily develops acquired resistance either by mutation in chromosomally-encoded genes, or by the horizontal gene transfer of antibiotic resistance determinants. Development of multidrug resistance by *P. aeruginosa* isolates requires several different genetic events including acquisition of different mutations and/or horizontal transfer of antibiotic resistance genes. Hypermutation favors the selection of mutation-driven antibiotic resistance in *P. aeruginosa* strains producing chronic infections, whereas the clustering of several different antibiotic resistance genes in integrons favors the concerted acquisition of antibiotic resistance determinants. Some recent studies have shown that phenotypic resistance associated to biofilm formation or to the emergence of small-colony variants may be important in the response of *P. aeruginosa* populations to antibiotic treatment.

Pseudomonas is resistant to ampicillin (99%) and ticarcillin(40%), less resistant to ureido penicillin (Mezlocillin, piperacillin 10%) resistantand most cephalosporins (the less resistance is to cefepime - 20%). It shows resistance to aminoglycosides (10 - 20%), quinolones (20 – 30%), and carbapenems (20%). Double drug therapy is recommended for serious infection, consisting of an antipseudomonal penicillin (piperacillin/tazobactam, ticarcillin/clavulanate), meropenem or cefipime plus a fluoroquinolone or an aminoglycoside.

Figure 12: Percentage of *Proteus spp.* Resistance - Louisiana, 2000-2011



3.17-*Stenotrophomonas maltophilia*

Stenotrophomonas maltophilia is a Gram-negative rod which causes uncommon, but difficult to treat infections in humans. Initially classified as *Pseudomonas maltophilia*, *S. maltophilia* was also grouped in the genus *Xanthomonas* before eventually becoming the type species of the genus *Stenotrophomonas* in 1993.

S. maltophilia is ubiquitous in aqueous environments, soil and plants, including water, urine, or respiratory secretions. In immunocompromised patients, *S. maltophilia* can lead to nosocomial infections. *S. maltophilia* frequently colonizes breathing tubes such as endotracheal or tracheostomy tubes, the respiratory tract and indwelling urinary catheters. Infection is usually facilitated by the presence of prosthetic material (plastic or metal); the most effective treatment is removal of the prosthetic material (usually a central venous catheter or similar device). The growth of *S. maltophilia* in microbiological cultures of respiratory or urinary specimens is therefore sometimes difficult to interpret and not a proof of infection. If, however, it is grown from sites which would be normally sterile (e.g., blood), then it **usually** represents true infection.

In immunocompetent individuals, *S. maltophilia* is a relatively unusual cause of pneumonia, urinary tract infection, or blood stream infection; in immunocompromised patients, however, *S. maltophilia* is a growing source of latent pulmonary infections. *S. maltophilia* colonization rates in individuals with cystic fibrosis have been increasing.

S. maltophilia is naturally resistant to many broad-spectrum antibiotics and is thus often difficult to eradicate. *S. maltophilia* is resistant to ticarcillin (85%), penicillin/ β -lactamase-inhibitors (60% to 70% to those with piperacillin or tazobactam), most cephalosporins (50% to 90%, ceftazidime 50%). It shows resistance to aminoglycosides (5% to 15%), quinolones (20% to 30%) and carbapenems (90% to imipenem and 8% to carbapenem). Trimethoprim-sulfa-methoxazole is very effective (less than 1% resistance).