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1-Introduction

1.1-Bacterial resistance to antibiotics is a major threat to human health

Bacterial resistance to antibiotics is becoming a major threat to human health. Bacteria become resistant to antibiotics through mutation or acquisition of genes from other bacteria. Antibiotics work by affecting the cell wall, distorting the cell surface, inhibiting bacterial protein synthesis, or preventing DNA formation. Some bacteria have been able to adopt ways to become resistant to the actions of antibiotics; some have even become resistant to several classes of antibiotics. Resistance often emerges first in hospitals because of selective pressure.

As antibiotic resistance was developing, medical science made progresses in treating illnesses that were fatal in older times. Therefore, there is now an increasing number of vulnerable patients with limited ability to fight infections (e.g. patients undergoing chemotherapy for cancer, dialysis for renal failure, and surgery, especially organ transplantation).

1.2-Tracking resistance patterns is a major action in the fight against antibiotic resistance

Most of the data published in the scientific literature on bacterial resistance is heavily influenced by limited surveys, case series and individual case reports. The data presented often comes from research institutions, tertiary care hospitals and other sources that are not representative of the “bacterial universe”. These sources are biased toward reporting the unusual and more severe patterns. A report based on population-based data sets provides a more representative picture of drug resistance patterns.

The Louisiana Antibiotic Resistance 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

In the early period of resistance monitoring, an active surveillance system was implemented. A select group of hospitals were called each month to provide information on a brief reporting form. The reports included (1) the number isolates from selected species from their lab for each month, (2) the number of drug resistant or drug intermediate resistant isolates for each one of those micro-organisms. Duplicates were not to be counted. Each report was entered into a Microsoft[®] Access database and from this annual summary, reports were generated for the participating hospitals. This type of surveillance was cumbersome, therefore limited to a few microorganisms. It was abandoned for the antibiogram collection approach.

2.2-Antibiogram collection

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 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 variations are not significant.

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 patients, 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 2012, and to present the resistance data for the most recent period from 2011 and 2012.

2.3.1-Trend: For micro-organisms of interest, a trend table is 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. Statistical tests presented are:

- The Cochran-Armitage test for linear trend (CoArm) with χ^2 -square, degrees of freedom=1, and p-value (Abramson, J.H. Winpepi (Pepi-for-Windows[®]): computer programs for epidemiologists. Epidemiologic Perspectives & Innovations 2004, 1: 6)
- The simple linear regression analysis equation with rate per 100 = $ax + b$, a representing the slope of the linear trend line.

2.3.2-Recent data on resistance: Recent data on resistance show resistance for the two most recent years (2011 and 2012 combined) with the total number of isolates tested, the average resistance in percentage and the range of resistance percentages observed (lowest and highest resistance observed in any hospital antibiogram).

3-Trends

3.1- Methicillin Susceptible *Staphylococcus aureus* (MSSA)

Staphylococcus aureus (SA), is a Gram-positive catalase-positive cocci 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.

Resistance due to penicillinase (an enzyme of the β -lactamase group) produced by *S.aureus*, developed as soon as penicillin was introduced for clinical use. This enzyme allows staphylococci to cleave the β -lactam ring of penicillin and neutralize its effectiveness. Nowadays, most *S.aureus* isolates are resistant to penicillin. The aminopenicillins (ampicillin, amoxicillin), carboxypenicillins (carbenicillin, ticarcillin), and ureidopenicillins (mezlocillin, piperacillin) are susceptible to neutralization by penicillinase-producing *S.aureus*. The preferred antibiotics for the treatment of MSSA 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:

- Amoxicillin-clavulanate
- Clindamycin if D test negative
- Doxycycline or minocycline plus Rifampin
- Moxifloxacin
- Trimethoprim-Sulfamethoxazole (TMP-SMX) plus rifampin
- Vancomycin, linezolid or daptomycin

Practically any infection caused by *Staphylococcus aureus* is presumed to be resistant to methicillin unless an antibiogram proves methicillin sensitivity.

Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
Methicillin Sensitive <i>Staph aureus</i> (MSSA)	Penicillin	Penicillin G	530	86%	83%	96%
	Penicillin Amino	Ampicillin	103	89%	89%	89%
	Penicillin R β -lactamase	Dicloxacillin	103	0%	0%	0%
	Cephalosporin I	Cefazolin	629	1%	0%	2%
	Penicillin & β -lactam Inhib	Clavulanic-Amoxicillin	285	1%	1%	1%
	Lincosamides	Clindamycin	1676	20%	7%	33%
	Rifamycin	Rifampin	1206	1%	0%	2%
	Cyclines	Tetracycline	1774	5%	2%	11%
	Cyclines	Doxycycline	103	5%	5%	5%
	Macrolides	Erythromycin	1877	47%	32%	72%
	Quinolone	Ciprofloxacin	1297	19%	8%	31%
	Quinolone	Moxifloxacin	743	20%	14%	29%
	Aminoglycosides	Gentamicin	1582	2%	0%	6%
	Sulfonamide	Trimethoprim-sulfa	1529	0%	0%	2%
	Glycopolypeptide	Vancomycin	1877	0%	0%	1%
	Lipopeptide	Daptomycin	344	0%	0%	2%
Oxazolidinone	Linezolid	990	0%	0%	2%	
Streptogramin	Quinu/Dalfopristin	452	0%	0%	0%	

3.2- *Staphylococcus aureus* resistance to methicillin (oxacillin)

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.

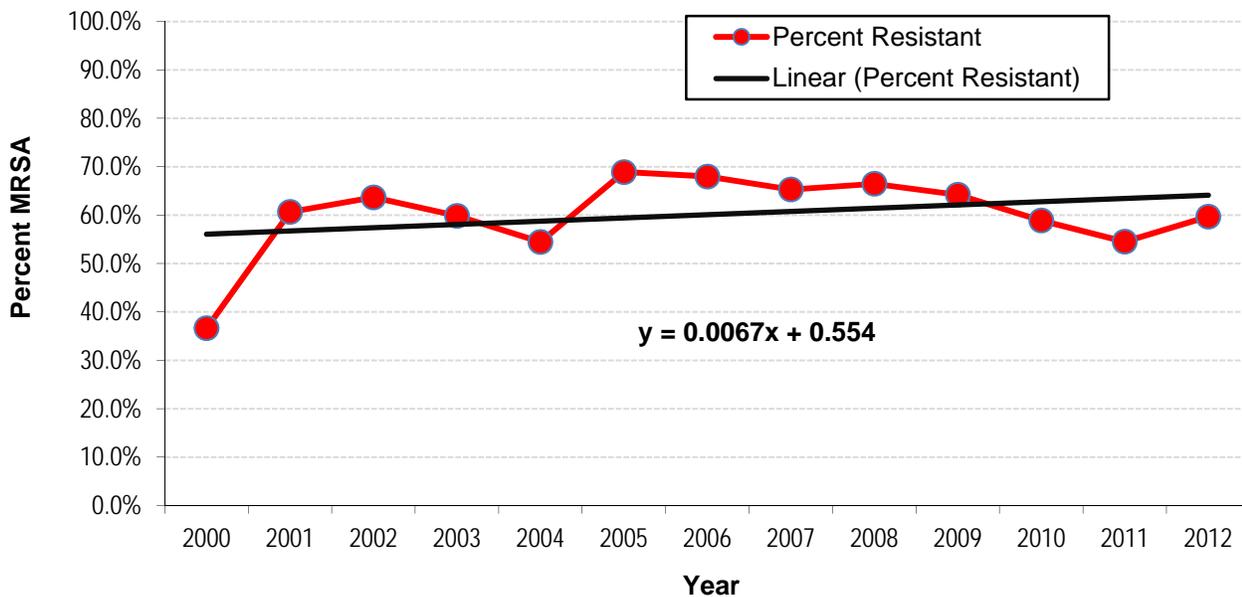
	<i>S. aureus</i> / Oxacillin (Methicillin)		
	Res	Total	% Res
2000	1,391	3,798	36.6%
2001	645	1,064	60.7%
2002	3,076	4,831	63.7%
2003	12,025	20,090	59.9%
2004	3,830	7,032	54.5%
2005	6,047	8,776	68.9%
2006	12,594	18,528	68.0%
2007	11,480	17,582	65.3%
2008	10,790	16,231	66.5%
2009	11,328	17,642	64.2%
2010	6,589	11,190	58.9%
2011	8,310	15,085	55.1%
2012	7,091	11,871	59.7%
CoArm	χ^2 15.88	df 1	p 0.00

S.aureus methicillin resistance resulted from a different mechanism. To overcome simple penicillin resistance, *S.aureus* was able to modify the site to which methicillin attaches (Penicillin Binding Protein), and thus became resistant to methicillin.

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

Acquisition of MRSA infections was a common concern among both patients and staff in acute and long-term care facilities, and now has become a concern for the general population.

The rates of methicillin-resistant *S. aureus* have increased from 2000 to 2005 from 38% to over 67%, and seem to be stabilizing around 60% ever since.



3.3-History of MRSA: Health care-associated (HA-MRSA) and community-associated MRSA (CA-MRSA).

MRSA infections that are reported in this report have not been differentiated into community-associated (CA) MRSA (or SCC mec Type IV or V PVL positive), 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.

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 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 SA: 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 taking over HA-MRSA. CA-MRSA is known to be more virulent, causing frequent skin and soft tissue infections as well as inva-

sive 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 USA.

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 SCC*mec* element on staphylococcal chromosome. 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 SCC*mec*. The SCC*mec* is a cluster of chromosomes in which the *mecA* gene is carried. Typical CA-MRSA has SCC*mec* type IV while typical HA_MRSA carries SCC*mec* types I and II. 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-associated MRSA 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.

3.4- Other Antibiotics to which MRSA is resistant

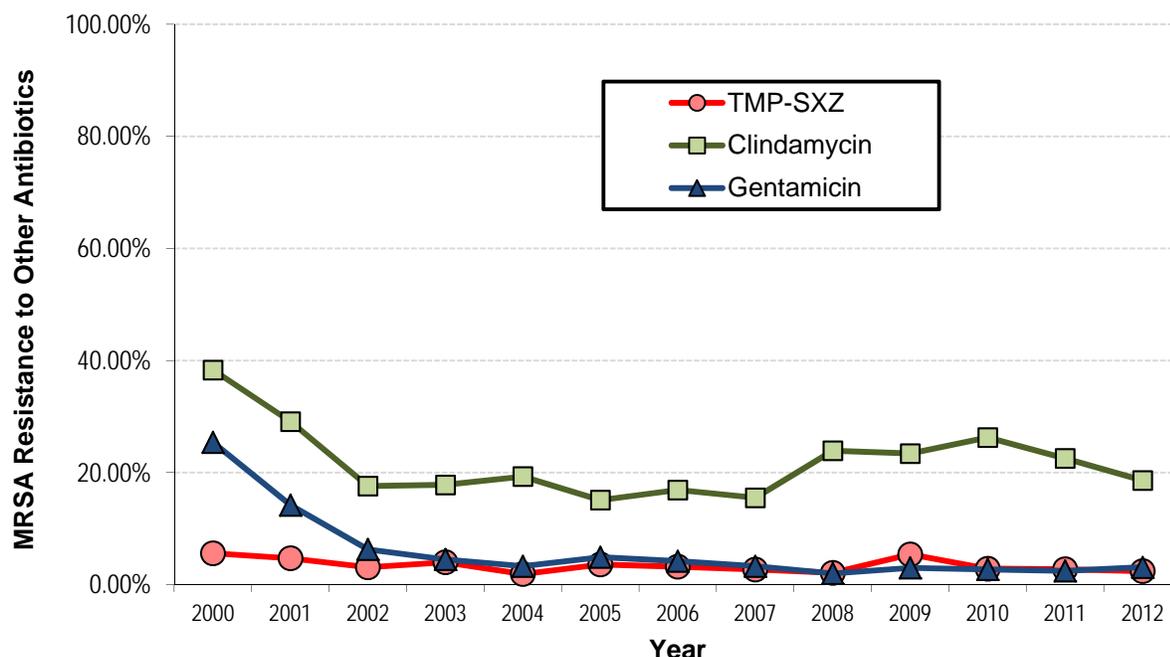
Many cutaneous abscesses respond to drainage alone, and most of the remaining Type IV MRSA infections can be treated with trimethoprim-sulfamethoxazole or a tetracycline, such as doxycycline or minocycline. For serious infections, other antibiotics may be required for treatment. Options include vancomycin,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

Quinolones, such as levofloxacin, or moxifloxacin, are effective orally and generally provide adequate coverage for CA-MRSA. Unfortunately, resistance is emerging among both MSSA and MRSA isolates; data suggest that overuse of quinolones 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.



	MRSA								
	Azithromycin			Levofloxacin			Clindamycin*		
	Res	Total	% Res	Res	Total	% Res	Res	Total	% Res
2000	106	116	91.0%	335	401	83.5%	153	401	38.3%
2001	321	346	92.7%	404	591	68.4%	233	800	29.1%
2002	214	233	91.9%	359	797	45.0%	140	797	17.6%
2003	89	95	93.8%	454	1,224	37.1%	584	3,275	17.8%
2004	446	478	93.4%	649	1,943	33.4%	734	3,808	19.3%
2005	78	78	100.0%	809	1,882	43.0%	667	4,413	15.1%
2006	184	198	93.0%	1,127	2,730	41.3%	1,166	6,902	16.9%
2007	449	471	95.2%	1,302	2,924	44.5%	593	3,829	15.5%
2008	383	431	88.8%	3,044	6,594	46.2%	1,180	4,930	23.9%
2009	336	430	78.1%	1,571	3,233	48.6%	691	2,953	23.4%
2010	355	379	93.6%	2,319	3,843	60.3%	1,527	5,814	26.3%
2011	355	402	88.3%	2,013	3,632	55.4%	1,369	6,077	22.5%
2012	210	242	86.8%	2,380	4,100	58.0%	1,084	5,820	18.6%

*Reports made do not specify if D test was made.

	Gentamycin			Rifampin*			Trimethoprim/Sulfa			Linezolid		
	Res	Total	% Res	Res	Total	% Res	Res	Total	% Res	Res	Total	% Res
2000	102	401	25.4%	20	401	5.0%	33	598	5.6%			
2001	115	811	14.2%	27	739	3.7%	42	902	4.7%			
2002	39	617	6.3%	5	539	1.0%	24	797	3.1%	0	155	0.0%
2003	125	2,750	4.5%	8	550	1.4%	134	3,355	4.0%	0	340	0.0%
2004	125	3,788	3.3%	40	2,438	1.6%	68	3,608	1.9%	0	1,867	0.0%
2005	239	4,830	4.9%	7	692	1.0%	198	5,518	3.6%	0	393	0.0%
2006	308	7,281	4.2%	50	3,067	1.6%	251	7,753	3.2%	0	1,556	0.0%
2007	146	4,358	3.3%	57	3,579	1.6%	135	5,058	2.7%	0	3,092	0.0%
2008	153	7,629	2.0%	97	6,634	1.5%	173	8,154	2.1%	0	6,233	0.0%
2009	116	3,843	3.0%	56	3,355	1.7%	189	3,540	5.4%	0	2,892	0.0%
2010	173	6,366	2.7%	117	5,031	2.3%	184	6,461	2.8%	10.78	4,553	0.2%
2011	102	4,149	2.5%	78	5,439	1.4%	164	5,964	2.7%	6	3,767	0.2%
2012	143	4,615	3.1%	62	3,709	1.7%	159	6,721	2.4%	5	3,869	0.1%

*Always to be used in conjunction with another antibiotic

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, linezolid and daptomycin. 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%).

Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
Methicillin Resistant <i>S. aureus</i> (MRSA)	Penicillin R b-lactamase	Oxacillin	171	99%	99%	99%
	Monobactam	Aztreonam	176	88%	88%	88%
	Lincosamides	Clindamycin	6655	22%	0%	88%
	Rifamycin	Rifampin	6032	2%	0%	14%
	Cyclines	Tetracycline	5675	5%	0%	17%
	Cyclines	Doxycycline	103	3%	3%	3%
	Glycylcycline	Tigecycline	1044	0%	0%	0%
	Macrolides	Azithromycin	402	88%	81%	95%
	Quinolone	Levofloxacin	7732	57%	46%	74%
	Quinolone	Ofloxacin	114	42%	42%	42%
	Quinolone	Moxifloxacin	806	23%	19%	40%
	Aminoglycosides	Gentamicin	4713	3%	0%	10%
	Sulfonamide	Trimethoprim-sulfa	6557	3%	0%	10%
	Aminoglycosides	Tobramycin	176	1%	1%	1%
	Glycopolypeptide	Vancomycin	7638	0%	0%	1%
	Lipopeptide	Daptomycin	1577	0%	0%	3%
Oxazolidinone	Linezolid	4331	0%	0%	6%	

3.5- Coagulase negative *Staphylococci* (CONS)

CONS 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. hemolyticus*, 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*. Antibiotics 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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Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
Staphylococcus Coagulase-negative	Penicillin	Penicillin G	1068	91%	43%	99%
	Penicillin Amino	Ampicillin	97	86%	83%	92%
	Penicillin R b-lactamase	Dicloxacillin	27	33%	33%	33%
	Penicillin & b-lactam Inhib	Clavulanic-Amoxicillin	797	65%	0%	78%
	Penicillin & b-lactam Inhib	Piperacillin/Tazobactam	455	0%	0%	0%
	Cephalosporin 4	Cefepime	70	46%	46%	46%
	Monobactam	Aztreonam	90	80%	80%	80%
	Carbapenem	Imipenem	455	63%	46%	69%
	Lincosamides	Clindamycin	4020	49%	0%	81%
	Rifamycin	Rifampin	4507	5%	0%	19%
	Macrolides	Azithromycin	120	65%	54%	69%
	Cyclines	Doxycycline	339	20%	4%	71%
	Cyclines	Tetracycline	4816	20%	0%	37%
	Glycylcycline	Tigecycline	3166	17%	0%	46%
	Quinolone	Ciprofloxacin	3290	55%	21%	69%
	Quinolone	Ofloxacin	70	60%	60%	60%
	Quinolone	Moxifloxacin	1533	34%	9%	49%
	Aminoglycosides	Gentamicin	5880	18%	0%	79%
	Sulfonamide	Trimethoprim-sulfa	5415	43%	17%	76%
	Glycopolypeptide	Vancomycin	7638	0%	0%	1%
	Lipopeptide	Daptomycin	1907	5%	0%	8%
	Oxazolidinone	Linezolid	3074	2%	0%	15%
	Streptogramin	Quinu/Dalfopristin	2039	2%	0%	14%

3.6- *Streptococcus pneumoniae*

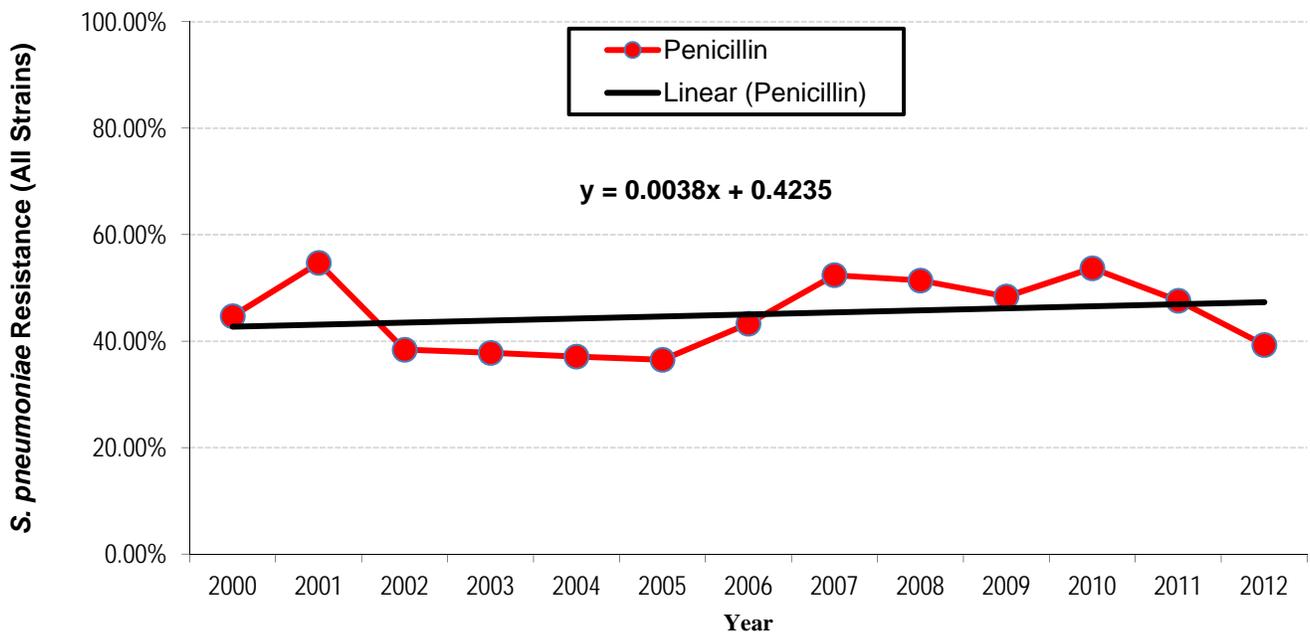
	<i>S. pneumoniae</i> /Penicillin		
	Res	Total	% Res
2000	108	242	44.7%
2001	60	110	54.7%
2002	154	400	38.4%
2003	317	839	37.8%
2004	153	414	37.1%
2005	232	635	36.5%
2006	322	744	43.3%
2007	727	1388	52.4%
2008	498	970	51.4%
2009	317	655	48.4%
2010	410	764	53.7%
2011	529	1112	47.6%
2012	529	1345	39.3%
CoArm	X2 11.95	Df 1	P 0.001

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.

Many antibiograms do not specify the criteria used to differentiate between intermediate and full resistance and do not specify what is included in their tables. So the percent resistance should be assumed to be a compilation of intermediate and fully resistant.

Because sensitive and rapid diagnostic tests are not available, most pneumococcal infections are treated empirically at first. Penicillin has been the drug of choice, although penicillin re-

sistance 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 $\geq 2.0 \mu\text{g/ml}$). 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 NCCLS as follows: Susceptible isolates are inhibited by $0.06 \mu\text{g/mL}$ (i.e., minimal inhibitory concentration [MIC] $\leq 0.06 \mu\text{g/mL}$). Isolates with reduced susceptibility (also known as intermediate resistance) are inhibited by 0.1 to $1.0 \mu\text{g/mL}$, and resistant isolates are inhibited by $2.0 \mu\text{g/mL}$ 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 $1.0 \mu\text{g/mL}$) 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 $\mu\text{g/mL}$; intermediately resistant, MIC 4 g/mL , resistant, MIC $>8 \text{ g/mL}$) 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 1 g every 12 hours or cefotaxime, 1 g 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 1 to 2 g 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, that vancomycin is recommended along with the β -lactam antibiotic - the vancomycin because of reliable 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.

Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
Methicillin Resistant <i>S. epidermidis</i> Coagulase-negative (MRSE)	Lincosamides	Clindamycin	169	51%	42%	53%
	Rifamycin	Rifampin	169	3%	0%	4%
	Cyclines	Tetracycline	169	21%	13%	23%
	Glycylcycline	Tigecycline	46	0%	0%	0%
	Macrolides	Erythromycin	77	76%	72%	83%
	Quinolone	Ciprofloxacin	169	65%	61%	70%
	Quinolone	Moxifloxacin	169	35%	30%	38%
	Aminoglycosides	Gentamicin	169	16%	7%	22%
	Sulfonamide	Trimethoprim-sulfa	169	59%	39%	65%
	Glycopolypeptide	Vancomycin	170	0%	0%	0%
	Lipopeptide	Daptomycin	169	0%	0%	0%
	Oxazolidinone	Linezolid	169	1%	0%	3%

3.6- Streptococci group A

	Streptococci Group A					
	Penicillin			Erythromycin		
	Res	Exam	%Res	Res	Exam	%Res
2008	0	588	0.0%	71	588	12.1%
2009	0	632	0.0%	94	632	14.9%
2010	0	608	0.0%	79	608	13.0%
2011	0	645	0.0%	90	645	14.0%
2012	0	529	0.0%	90	529	17.0%
CoArm				X2 3.42	df 1	p 0.064

Streptococcus pyogenes, the Group A Strep,

are β -hemolytic and are found in the naso-pharynx 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, ceftibuten, cefdinir, cefpodoxime and azithromycin are effective in eradication of group A streptococci from the pharynx when administered for five days or less.

Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
Streptococcus group A	Penicillin	Penicillin G	645	0%	0%	0%
	Cephalosporin 3	Cefotaxime	645	0%	0%	0%
	Lincosamides	Clindamycin	645	10%	10%	10%
	Macrolides	Erythromycin	645	14%	14%	14%
	Glycopolypeptide	Vancomycin	645	0%	0%	0%

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).

	Streptococci Group B											
	Penicillin			Erythromycin			Tetracycline			Clindamycin		
	Res	Exam	%Res	Res	Exam	%Res	Res	Exam	%Res	Res	Exam	%Res
2000	1	102	1.2%	19	175	11.0%	54	62	87.0%	62	8	7.7%
2001	1	83	1.2%	1	83	1.2%	7	9	78.0%	9	1	9.1%
2002	11	1,047	1.0%	95	1,221	7.8%	1,011	1,130	89.5%	331	42	7.9%
2003	25	3,448	0.7%	996	2,585	38.5%	2,078	2,439	85.2%	2758	485	5.7%
2004	10	854	1.1%	208	563	36.9%	207	218	95.0%	677	160	4.2%
2005	6	935	0.7%	336	824	40.8%	732	873	83.8%	902	155	5.8%
2006	5	2,331	0.2%	1,071	2,143	50.0%	1,677	1,960	85.5%	2122	535	4.0%
2007	55	3,302	1.7%	400	798	50.2%	476	581	81.9%	2929	818	3.6%
2008	2	1,458	0.1%	1,572	2,089	75.3%	1,694	2,032	83.4%	3141	1,295	2.4%
2009	3	2,157	0.1%	1,983	2,709	73.2%	2,249	2,628	85.6%	2999	1,973	1.5%
2010	4	3,360	0.1%	2,376	2,864	83.0%	2,396	2,749	87.1%	3299	1,538	2.1%
2011	5	856	0.6%	447	814	54.9%	568	686	82.8%	1216	539	2.3%
2012	4	732	0.5%	133	257	51.8%	247	318	77.7%	358	173	2.1%

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%.

Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
<i>Streptococcus group B, agalactiae</i>	Penicillin	Penicillin G	961	0%	0%	2%
	Penicillin Amino	Ampicillin	1444	0%	0%	12%
	Cephalosporin 3	Ceftriaxone	447	5%	0%	10%
	Monobactam	Aztreonam	109	50%	50%	50%
	Lincosamides	Clindamycin	1216	44%	0%	80%
	Cyclines	Tetracycline	791	82%	75%	88%
	Cyclines	Doxycycline	127	25%	25%	25%
	Glycylcycline	Tigecycline	717	0%	0%	0%
	Macrolides	Erythromycin	814	55%	50%	75%
	Glycopolypeptide	Vancomycin	1398	0%	0%	2%
	Quinolone	Levofloxacin	1444	1%	0%	8%
	Macrolides	Azithromycin	30	86%	86%	86%
	Lipopeptide	Daptomycin	158	0%	0%	0%
	Oxazolidinone	Linezolid	1020	0%	0%	6%
	Streptogramin	Quinu/Dalfopristin	548	2%	0%	2%

3.8-*Streptococcus viridans* group

Streptococcus viridans is a group of streptococci which possesses no Lancefield antigens. They are most abundant in the mouth. *S. mutans*, is the etiologic agent of dental caries. They may cause other mouth or gingival infections, and if they are introduced into the bloodstream, may cause endocarditis. They are the most common causes of subacute bacterial endocarditis.

Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
<i>Streptococcus viridans</i> group	Penicillin	Penicillin G	37	41%	41%	41%
	Glycopolypeptide	Vancomycin	72	0%	0%	0%
	Cephalosporin 3	Cefotaxime	37	5%	5%	5%
	Lincosamides	Clindamycin	72	15%	12%	18%
	Macrolides	Erythromycin	37	62%	62%	62%
	Oxazolidinone	Linezolid	35	0%	0%	0%

3.9- Enterococci and Vancomycin Resistant Enterococci

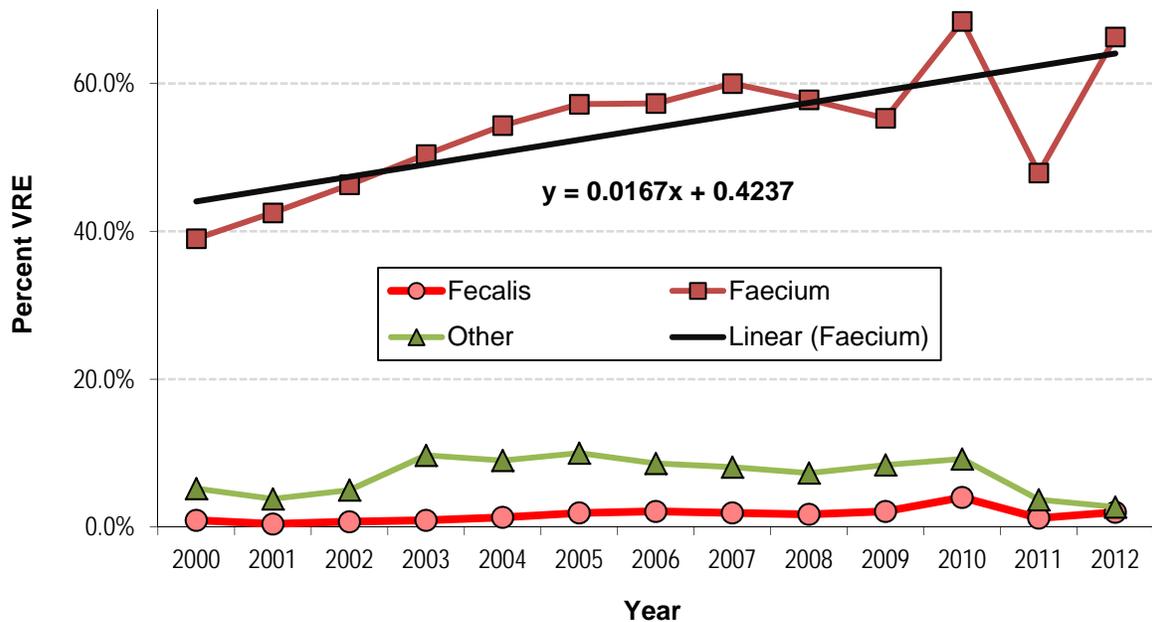
Enterococci, formerly of the Streptococci are now part of the *Enterococcus* genus. These organisms grow under harsh conditions and are differentiated from the non-enterococcal group D streptococci in part by their ability to grow in 6.5% sodium chloride. Enterococci constitute a sizable portion of the normal flora of the gut. When there is disruption of mucosal or epithelial barriers, they can produce infection, including UTIs, endocarditis and intra-abdominal 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.

Enterococci 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 them. 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 which is 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 and, 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 bi-functional phosphor-transferase /acetyl-transferase enzyme that inactivates gentamicin and all other currently available aminoglycosides except streptomycin. Such organisms are not killed synergistically by combinations of gentamicin plus cell-wall-active antibiotics.

	E.Fecalis/Vancomycin			E.Faecium/Vancomycin			E. spp/Vancomycin		
	Res	Exam	% Res	Res	Exam	% Res	Res	Exam	% Res
2000	56	6,187	0.9%	240	615	39.0%	63	1,223	5.2%
2001	33	7,381	0.4%	327	769	42.5%	42	1,118	3.8%
2002	59	7,867	0.7%	378	817	46.3%	54	1,079	5.0%
2003	72	8,024	0.9%	414	821	50.4%	139	1,428	9.7%
2004	85	6,414	1.3%	376	693	54.3%	112	1,239	9.0%
2005	72	3,737	1.9%	289	505	57.2%	104	1,040	10.0%
2006	73	3,491	2.1%	276	482	57.3%	111	1,295	8.6%
2007	88	4,581	1.9%	446	743	60.0%	118	1,458	8.1%
2008	112	6,455	1.7%	524	907	57.8%	93	1,276	7.3%
2009	147	6,898	2.1%	538	973	55.3%	107	1,278	8.4%
2010	422	10,585	4.0%	1,256	1,837	68.4%	127	1,381	9.2%
2011	123	10,505	1.2%	641	1,339	47.9%	43	1,153	3.7%
2012	192	9,828	2.0%	762	1,149	66.3%	31	1,137	2.7%

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).



Overall rates of Vancomycin Resistant Enterococcus showed a significant increase over the years.

3.10- *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%.

3.11-*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, fluoroquinolones, telithromycin and doxycycline. Alternative treatment includes carbapenems and cefepime.

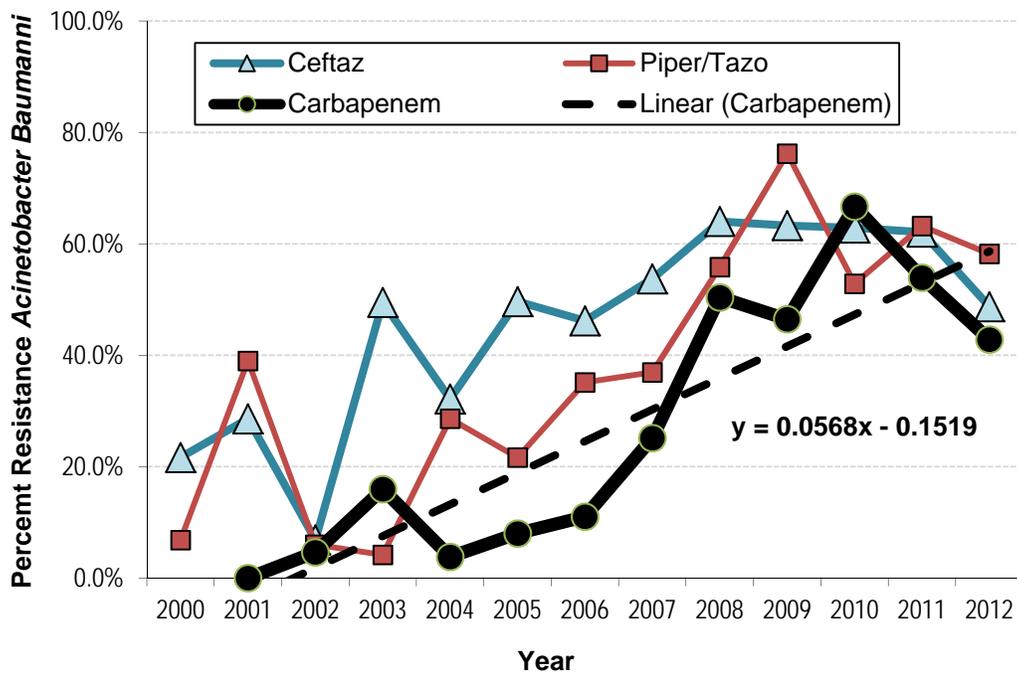
	<i>Haemophilus influenzae</i>											
	Ceftriaxone			TMP-SXZ			Azythromycin			Levofloxacin		
	Res	Exam	Res %	Res	Exam	Res %	Res	Exam	Res %	Res	Exam	Res %
2000	0	129	0.0%	25	94	26.7%				0	121	0.0%
2001	0	14	0.0%	21	87	24.1%				0	95	0.0%
2002	0	115	0.0%	27	127	21.6%				0	18	0.0%
2003	1	187	0.4%	25	186	13.4%				0	46	0.0%
2004	3	85	3.8%	27	85	31.6%						
2005	0	43	0.0%	10	43	23.1%	1	13	8.0%	0	43	0.0%
2006	0	38	0.0%	2	38	5.0%	4	28	14.0%	1	76	1.3%
2007	6	293	2.1%	80	320	25.2%	16	65	25.0%	1	126	0.8%
2008	0	138	0.0%	65	224	28.8%	19	46	41.0%	0	240	0.0%
2009	0	154	0.0%	71	294	24.0%	24	75	32.0%	0	214	0.0%
2010	0	108	0.0%	56	196	28.5%	28	88	32.0%	0	56	0.0%
2011	0	205	0.0%	65	237	27.4%	12	62	19.4%	0	30	0.0%
2012	0	174	0.0%	68	253	26.9%	27	92	29.3%	0	39	0.0%

3.12- *Acinetobacter baumannii*

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.

<i>Acinetobacter</i>									
	Ceftazidime			Piperacillin/Tazobactam			Carbapenem		
	Res	Total	% Res	Res	Total	% Res	Res	Total	% Res
2000	19	88	21.7%	3	44	6.8%			
2001	21	75	28.6%	84	215	39.0%	0	11	0.0%
2002	4	59	6.8%	3	50	6.0%	2	44	4.6%
2003	343	692	49.5%	2	49	4.2%	67	419	16.0%
2004	42	131	32.2%	158	554	28.6%	7	173	3.8%
2005	93	187	49.6%	42	194	21.6%	2	30	8.0%
2006	152	329	46.2%	66	187	35.1%	8	75	11.0%
2007	347	646	53.7%	101	274	36.9%	148	589	25.1%
2008	701	1,095	64.0%	130	233	55.8%	655	1,300	50.4%
2009	389	614	63.3%	412	541	76.2%	421	906	46.5%
2010	455	724	62.9%	245	464	52.8%	738	1,107	66.7%
2011	595	958	62.1%	188	297	63.2%	556	1,031	53.9%
2012	358	735	48.7%	95	163	58.2%	414	967	42.8%



<i>Acinetobacter baumannii</i>	Penicillin Amino	Ampicillin	35	96%	96%	96%
	Penicillin & β -lactam Inhib	Clavulanic-Amoxicillin	35	96%	96%	96%
	Penicillin & β -lactam Inhib	Clavulanic-Ticarcillin	282	47%	20%	76%
	Penicillin & β -lactam Inhib	Piperacillin/Tazobactam	163	58%	41%	84%
	Penicillin & β -lactam Inhib	Sulbactam-Ampicillin	842	42%	0%	67%
	Cephalosporin 3	Cefotaxime	180	60%	20%	68%
	Cephalosporin 3	Ceftazidime	1030	62%	0%	85%
	Cephalosporin 3	Ceftriaxone	552	78%	20%	97%
	Cephalosporin 4	Cefepime	570	66%	0%	84%
	Carbapenem	Imipenem	779	61%	21%	78%
	Carbapenem	Meropenem	348	43%	9%	76%
	Cyclines	Tetracycline	189	57%	20%	67%
	Glycylcycline	Tigecycline	148	54%	45%	66%
	Quinolone	Ciprofloxacin	1189	61%	19%	87%
	Quinolone	Levofloxacin	968	64%	12%	87%
	Quinolone	Moxifloxacin	16	81%	81%	81%
	Aminoglycosides	Amikacin	927	31%	0%	55%
	Aminoglycosides	Gentamicin	1268	50%	0%	75%
	Aminoglycosides	Tobramycin	1030	50%	0%	77%
	Sulfonamide	Trimethoprim-sulfa	760	52%	5%	81%

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

3.13- Enterobacteriaceae

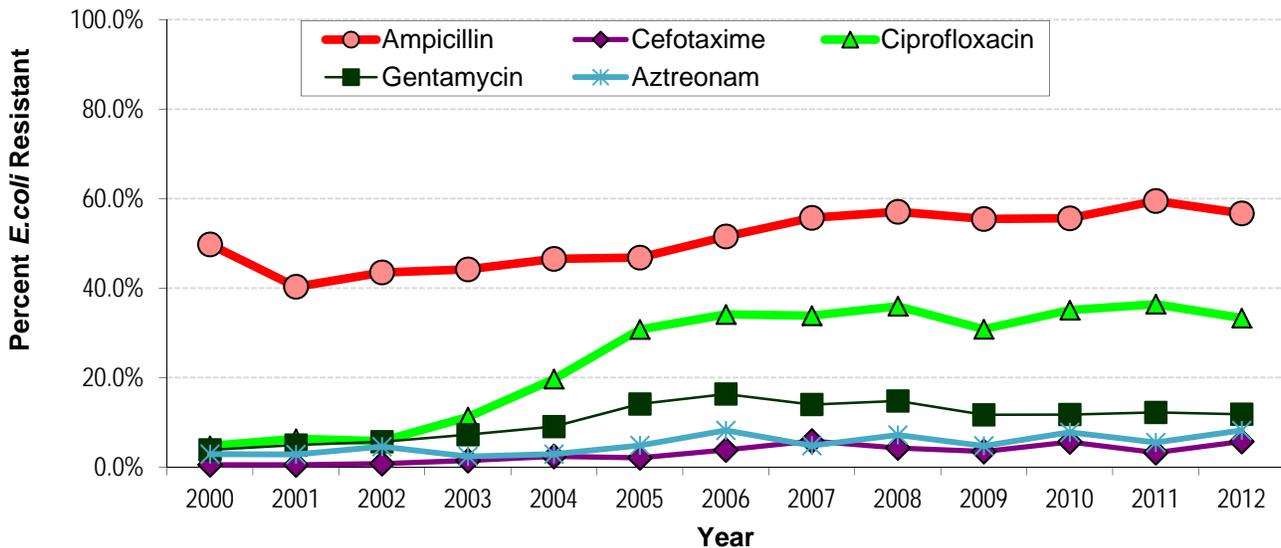
Enterobacteriaceae is a large group of gram negative organisms which are widely distributed in the soil and are normal colonizers of the intestinal tract of humans and animals. They are an important cause of infection when found outside the gastrointestinal tract. They account for 30% of all nosocomial 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*, *Shigella* and *Enterobacter* are the most important pathogens.

3.13.1- *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-toxigenic, entero-invasive and entero-hemorrhagic *E. coli*).

	<i>E. coli</i>								
	Ampicillin			Cefotaxime			Ciprofloxacin		
	Res	Exam	%R	Res	Exam	%R	Res	Exam	%R
2000	3,205	6,441	49.8%	20	4,015	0.5%	176	3,731	4.7%
2001	1,116	2,770	40.3%	12	2,511	0.5%	152	2,402	6.3%
2002	4,015	9,235	43.5%	57	7,580	0.8%	303	5,232	5.8%
2003	13,900	31,459	44.2%	136	9,370	1.4%	2,732	24,430	11.2%
2004	7,588	16,310	46.5%	134	5,687	2.4%	2,549	12,961	19.7%
2005	4,853	10,364	46.8%	47	2,300	2.1%	3,256	10,587	30.8%
2006	10,411	20,207	51.5%	278	7,277	3.8%	5,732	16,804	34.1%
2007	13,910	24,970	55.7%	553	9,514	5.8%	6,651	19,660	33.8%
2008	18,414	32,275	57.1%	477	11,156	4.3%	8,690	24,179	35.9%
2009	20,920	37,724	55.5%	421	12,127	3.5%	8,723	28,317	30.8%
2010	13,455	23,757	56.6%	303	5,399	5.6%	5,720	16,303	35.1%
2011	15,099	25,375	59.5%	317	9,874	3.2%	11,929	32,765	36.4%
2012	19,439	34,270	56.7%	400	7,017	5.7%	12,845	38,620	33.3%

	Gentamycin			Aztreonam			Nitrofurantoin		
	Res	Exam	%R	Res	Exam	%R	Res	Exam	%R
2000	268	6,996	3.8%	117	4,059	2.9%	187	6,243	3.0%
2001	136	2,770	4.9%	54	1,935	2.8%	24	1,207	2.0%
2002	522	9,235	5.6%	173	3,782	4.6%	118	7,766	1.5%
2003	2,367	32,685	7.2%	293	12,297	2.4%	507	21,499	2.4%
2004	1,507	16,644	9.1%	191	6,658	2.9%	333	11,340	2.9%
2005	2,240	15,894	14.1%	382	7,902	4.8%	345	9,744	3.5%
2006	4,395	26,941	16.3%	1,110	13,550	8.2%	1,296	16,856	7.7%
2007	3,550	25,406	14.0%	850	17,794	4.8%	947	19,784	4.8%
2008	5,020	33,981	14.8%	2,023	28,236	7.2%	1,537	31,894	4.8%
2009	4,407	37,724	11.7%	1,309	27,687	4.7%	1,008	21,774	4.6%
2010	2,834	24,163	11.7%	1,091	14,056	7.8%	971	20,182	4.8%
2011	4,331	35,428	12.2%	1,221	22,317	5.5%	1,787	30,579	5.8%
2012	4,952	41,905	11.8%	2,465	30,073	8.2%	1,927	24,795	7.8%



Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
<i>E.coli</i>	Penicillin Amino	Ampicillin	28599	59%	11%	80%
	Penicillin Carboxy	Ticarcillin	690	15%	15%	15%
	Penicillin Ureido	Piperacillin	2869	56%	54%	60%
	Penicillin & β -lactam Inhib	Clavulanic-Ticarcillin	5292	15%	0%	22%
	Penicillin & β -lactam Inhib	Piperacillin/Tazobactam	24025	5%	0%	14%
	Penicillin & β -lactam Inhib	Sulbactam-Ampicillin	20781	46%	0%	64%
	Carbapenem	Carbapenem	2257	1%	0%	1%
	Carbapenem	Ertapenem	16966	0%	0%	9%
	Carbapenem	Imipenem	36277	0%	0%	5%
	Carbapenem	Meropenem	10307	0%	0%	12%
	Monobactam	Aztreonam	24242	6%	0%	12%
	Cephalosporin 1	Cephalothin	3213	52%	0%	62%
	Cephalosporin 2	Cefotetan	632	2%	1%	9%
	Cephalosporin 2	Cefoxitin	18203	12%	0%	18%
	Cephalosporin 3	Cefotaxime	9874	3%	0%	13%
	Cephalosporin 3	Ceftazidime	28463	5%	0%	89%
	Cephalosporin 3	Ceftriaxone	36298	6%	0%	89%
	Cephalosporin 4	Cefepime	28354	4%	0%	89%
	Cyclines	Tetracycline	12106	30%	0%	40%
	Cyclines	Doxycycline	1682	25%	17%	30%
	Glycylcycline	Tigecycline	13518	0%	0%	1%
	Aminoglycosides	Amikacin	33113	0%	0%	9%
	Aminoglycosides	Gentamicin	38652	12%	0%	30%
	Aminoglycosides	Tobramycin	34015	12%	0%	35%
	Quinolone	Nitrofurantoin	33150	6%	1%	25%
	Quinolone	Ciprofloxacin	34873	36%	10%	65%
	Quinolone	Levofloxacin	32603	38%	9%	65%
	Quinolone	Moxifloxacin	3826	32%	12%	44%
	Sulfonamide	Trimethoprim-sulfa	34760	35%	0%	60%

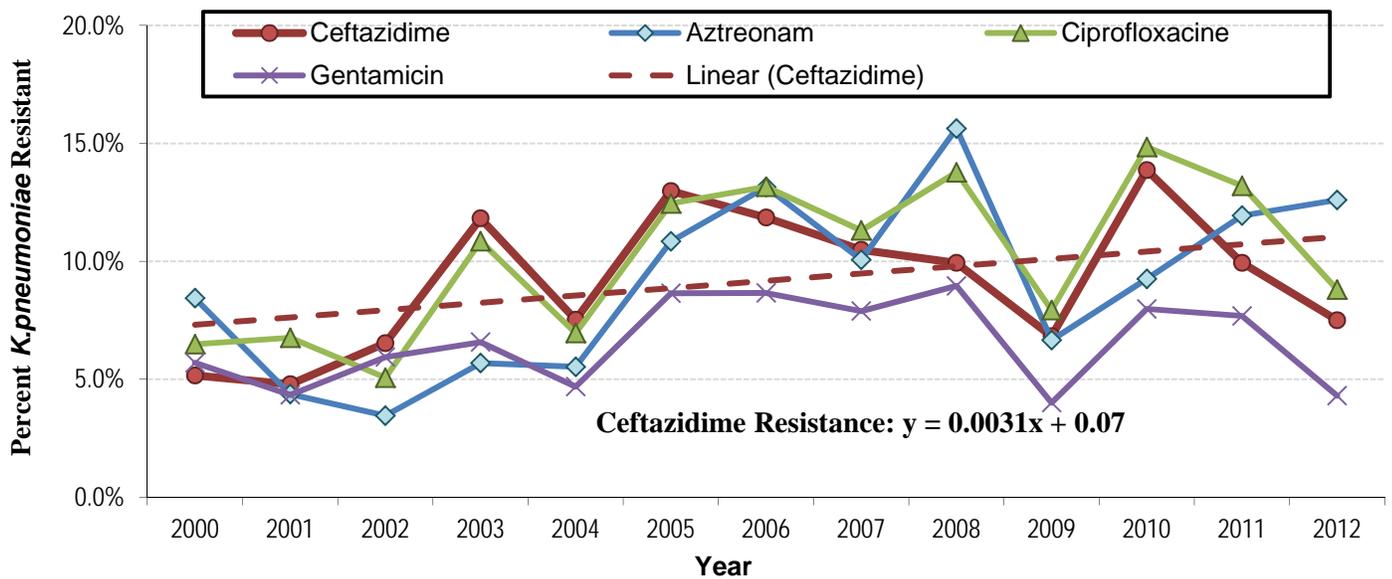
- Ampicillin resistance is found in many *E.coli* strains due to their production of extended spectrum beta lactamase (ESBL). Sensitivity to ampicillin has steadily increased to 55% overall in Louisiana. Resistance to cephalosporins is also increasing:
 - *E.coli* has become very resistant to ciprofloxacin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

3.13.2-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.

	<i>Klebsiella pneumoniae</i>								
	Ampicillin			Ceftazidime			Aztreonam		
	Res	Exam	Res %	Res	Exam	Res %	Res	Exam	Res %
2000	1,531	1,721	89.0%	56	1,088	5.2%	93	1,097	8.4%
2001	541	578	93.7%	41	860	4.8%	32	737	4.4%
2002	2,209	2,245	98.4%	135	2,071	6.5%	34	984	3.5%
2003	6,496	6,652	97.7%	720	6,093	11.8%	186	3,281	5.7%
2004	3,438	3,557	96.7%	191	2,536	7.5%	122	2,212	5.5%
2005	2,259	2,316	97.6%	305	2,349	13.0%	279	2,571	10.8%
2006	4,269	4,473	95.4%	521	4,393	11.9%	433	3,290	13.1%
2007	4,764	4,824	98.7%	733	6,989	10.5%	606	6,016	10.1%
2008	4,327	4,631	93.4%	848	8,540	9.9%	1,188	7,598	15.6%
2009	378	385	98.1%	474	6,948	6.8%	1,001	15,036	6.7%
2010	389	479	81.2%	712	5,134	13.9%	187	2,019	9.3%
2011	323	341	94.7%	678	6,818	9.9%	724	6,062	11.9%
2012	0	0	0.0%	488	6,549	7.5%	923	7,310	12.6%

	Res	Cipro	Res %	Gentamicin			Carbapenems		
		Exam		Res	Exam	Res %	Res	Exam	Res %
2000	75	1,151	6.5%	112	1,969	5.7%	6	1,848	0.3%
2001	58	854	6.8%	47	1,087	4.3%	8	909	0.8%
2002	68	1,340	5.1%	148	2,500	5.9%	6	2,336	0.3%
2003	769	7,091	10.9%	615	9,353	6.6%	20	6,021	0.3%
2004	228	3,272	7.0%	200	4,273	4.7%	34	3,199	1.1%
2005	322	2,586	12.5%	349	4,039	8.6%	0	3,064	0.0%
2006	487	3,704	13.2%	560	6,467	8.7%	186	5,026	3.7%
2007	641	5,671	11.3%	627	7,952	7.9%	37	9,616	0.4%
2008	877	6,365	13.8%	881	9,840	9.0%	95	13,759	0.7%
2009	499	6,294	7.9%	344	8,591	4.0%	91	12,945	0.7%
2010	635	4,276	14.8%	493	6,175	8.0%	42	6,191	0.7%
2011	1,127	8,543	13.2%	691	8,995	7.7%	151	16,270	0.9%
2012	787	8,949	8.8%	400	9,226	4.3%	187	16,076	1.2%

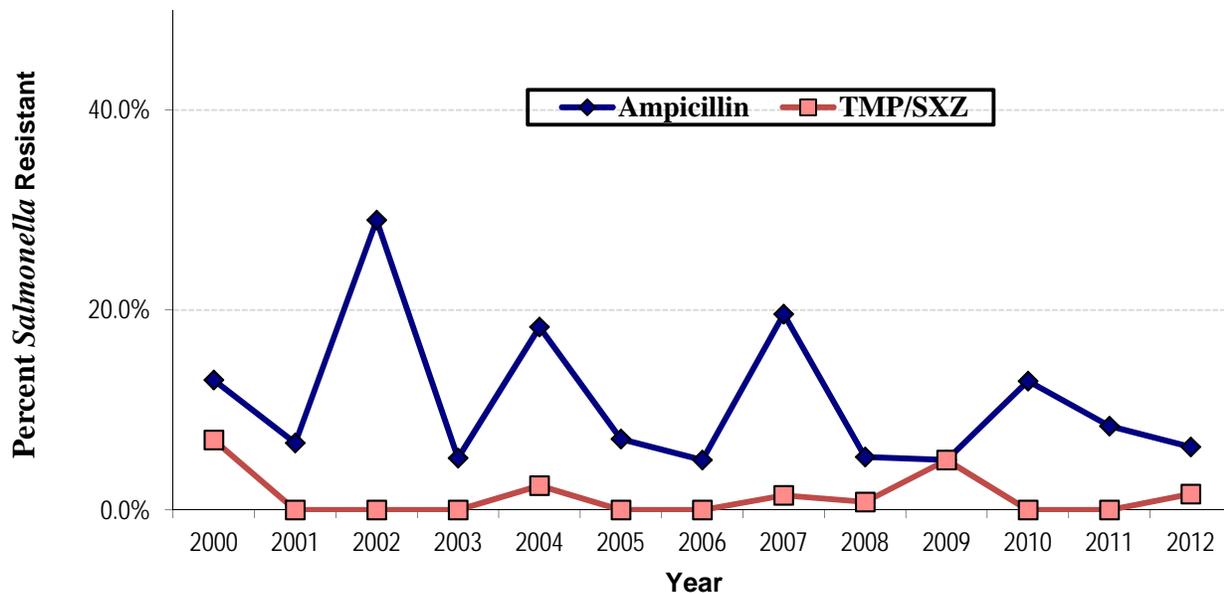


Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
<i>Klebsiella pneumoniae</i>	Penicillin Amino	Ampicillin	341	95%	94%	97%
	Penicillin & β -lactam Inhib	Clavulanic-Amoxicillin	2665	11%	2%	27%
	Penicillin & β -lactam Inhib	Clavulanic-Ticarcillin	1511	9%	2%	28%
	Penicillin & β -lactam Inhib	Piperacillin/Tazobactam	6399	6%	0%	25%
	Penicillin & β -lactam Inhib	Sulbactam-Ampicillin	6303	19%	8%	39%
	Cephalosporin 1	Cephalothin	497	16%	8%	33%
	Cephalosporin 2	Cefoxitin	4270	13%	3%	25%
	Cephalosporin 3	Ceftazidime	7344	10%	0%	30%
	Cephalosporin 3	Ceftriaxone	9420	11%	0%	33%
	Cephalosporin 4	Cefepime	7699	11%	0%	32%
	Carbapenem	Carbapenem	540	3%	0%	4%
	Carbapenem	Ertapenem	4708	1%	0%	4%
	Carbapenem	Imipenem	9487	1%	0%	6%
	Carbapenem	Meropenem	3034	1%	0%	7%
	Cyclines	Doxycycline	304	15%	14%	17%
	Glycylcycline	Tigecycline	3197	6%	0%	12%
	Quinolone	Nitrofurantoin	6613	58%	20%	78%
	Quinolone	Levofloxacin	8177	13%	0%	33%
	Quinolone	Moxifloxacin	1400	10%	0%	23%
	Aminoglycosides	Amikacin	8156	2%	0%	13%
Aminoglycosides	Gentamicin	9854	8%	0%	28%	
Aminoglycosides	Tobramycin	8648	10%	0%	25%	
Sulfonamide	Trimethoprim-sulfa	9312	22%	11%	32%	

3.13.3- *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.

	<i>Salmonella</i> spp											
	Ampicillin			TMP-SXZ			Cefotaxime			Ciprofloxacin		
	Res	Exam	Res %	Res	Exam	Res %	Res	Exam	Res %	Res	Exam	Res %
2000	2	16	13.0%	1	16	7.0%	0	16	0.0%			
2001	1	15	6.7%	0	12	0.0%	0	15	0.0%			
2002	2	7	29.0%	0	7	0.0%	0	12	0.0%	0	7	0.0%
2003	1	19	5.2%	0	19	0.0%	0	7	0.0%	0	18	0.0%
2004	7	38	18.3%	1	41	2.4%	0	7	0.0%	0	40	0.0%
2005	2	27	7.1%	0	27	0.0%	0	6	0.0%	0	27	0.0%
2006	6	113	5.0%	0	118	0.0%	0	118	0.0%	1	118	0.8%
2007	29	146	19.6%	2	142	1.5%	0	4	0.0%	0	142	0.0%
2008	7	127	5.3%	1	127	0.8%	0	22	0.0%	0	112	0.0%
2009	2	41	5.0%	2	41	5.0%	0	41	0.0%	0	41	0.0%
2010	18	136	12.9%	0	146	0.0%	0	61	0.0%	0	136	0.0%
2011	13	154	8.4%	0	154	0.0%	0	75	0.0%	0	154	0.0%
2012	8	128	6.3%	2	128	1.6%	0	83	0.0%	1	108	0.9%



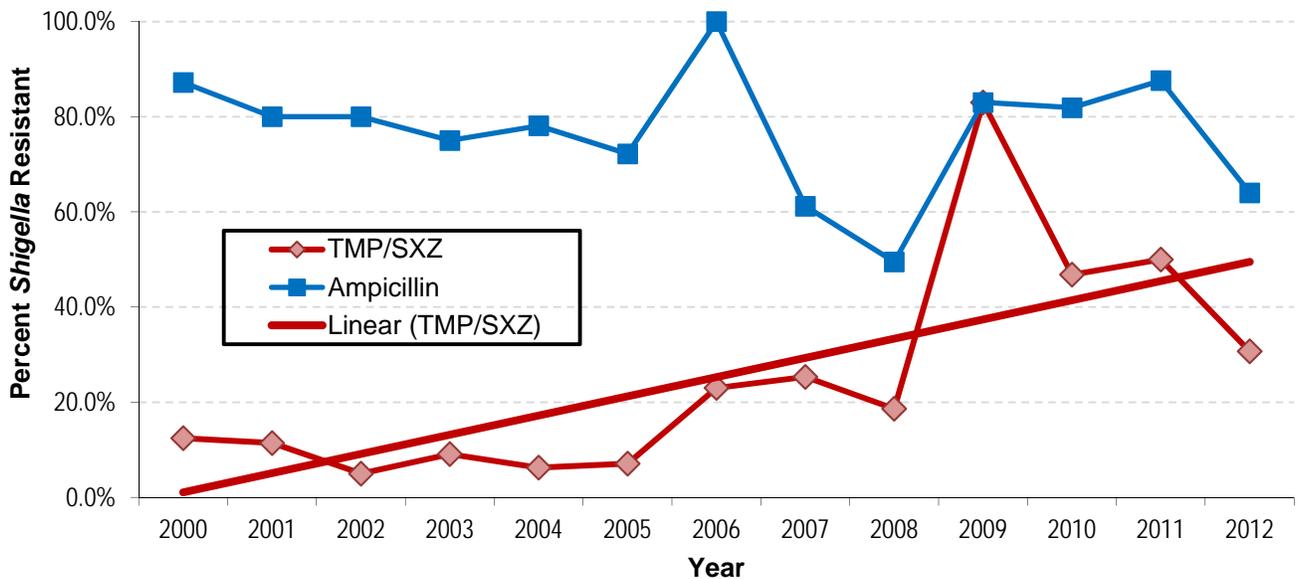
In most cases of simple enterocolitis due to *Salmonella*, no treatment is necessary. For severe enterocolitis and invasive disease (typhoid fever, paratyphoid fever) treatment is recommended. *Salmonella* resistance to ampicillin vary from 5% to 20% with no significant increase (Cochrane-Armitage test 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.

Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
<i>Salmonella</i>	Penicillin Amino	Ampicillin	154	8%	0%	13%
	Cephalosporin 3	Cefotaxime	75	0%	0%	0%
	Quinolone	Ciprofloxacin	154	0%	0%	0%
	Sulfonamide	Trimethoprim-sulfa	154	0%	0%	0%

3.13.4-- *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 day-care centers, homosexual men, and in overcrowded or unsanitary conditions.

<i>Shigella</i> spp												
Ampicillin			TMP-SXZ			Cephalosporin 3			Ciprofloxacin			
Res	Exam	Res %	Res	Exam	Res %	Res	Exam	Res %	Res	Exam	Res %	
2000	41	47	87.2%	6	47	12.4%	0	12	0.0%			
2001	4	5	80.0%	4	35	11.4%	0	10	0.0%	0	5	
2002	8	10	80.0%	2	41	5.0%	0	9	0.0%	0	1	0.0%
2003	9	12	75.0%	3	33	9.1%	0	7	0.0%	0	1	0.0%
2004	25	32	78.1%	2	32	6.3%	0	25	0.0%	0	31	0.0%
2005	26	36	72.2%	2	31	7.1%	0	1	0.0%	0	1	0.0%
2006	110	110	100.0%	25	110	23.0%	0	110	0.0%	1	110	0.9%
2007	97	158	61.2%	40	158	25.3%	0	52	0.0%	0	158	0.0%
2008	50	101	49.5%	19	102	18.6%	0	19	0.0%	0	104	0.0%
2009	5	6	83.0%	5	6	83.0%	0	15	0.0%	0	6	0.0%
2010	77	94	81.9%	44	94	46.8%	0	0	0.0%	0	94	0.0%
2011	113	129	87.6%	69	138	50.0%	0	75	0.0%	0	129	0.0%
2012	48	75	64.0%	23	75	30.7%	0	75	0.0%	0	75	0.0%
CoArm	χ^2 2.06	df 1	p 0.151	χ^2 68.87	df 1	p 0.00						



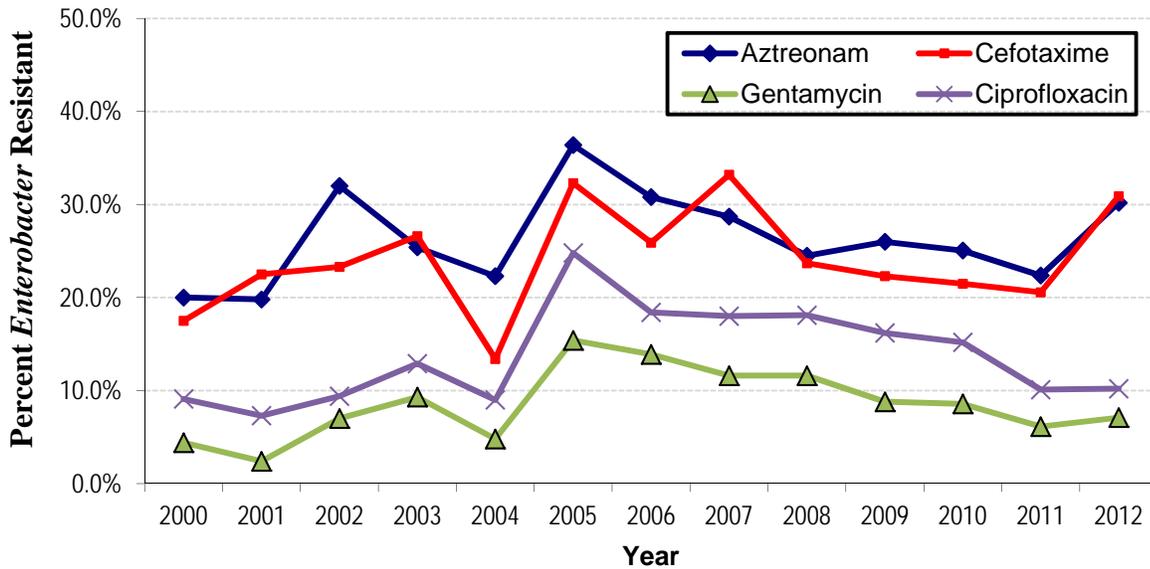
Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
<i>Shigella</i>	Penicillin Amino	Ampicillin	75	99%	99%	99%
	Cephalosporin 3	Cefotaxime	75	0%	0%	0%
	Quinolone	Ciprofloxacin	129	0%	0%	0%
	Sulfonamide	Trimethoprim-sulfa	129	11%	11%	11%

3.13.5-*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.

	<i>Enterobacter cloacae</i>								
	Aztreonam			Cefotaxime			Gentamicin		
	Res	Exam	Res %	Res	Exam	Res %	Res	Exam	Res %
2000	74	372	20.0%	66	378	17.5%	28	628	4.4%
2001	23	115	19.8%	31	140	22.5%	5	203	2.4%
2002	75	235	32.0%	117	504	23.3%	42	595	7.0%
2003	236	930	25.4%	223	840	26.6%	203	2,173	9.3%
2004	116	522	22.3%	35	261	13.4%	39	822	4.8%
2005	219	603	36.4%	33	101	32.3%	110	716	15.4%
2006	256	832	30.8%	72	278	25.9%	176	1,265	13.9%
2007	431	1,505	28.7%	300	901	33.2%	255	2,199	11.6%
2008	428	1,744	24.5%	130	551	23.7%	269	2,312	11.6%
2009	352	1,354	26.0%	153	685	22.3%	171	1,939	8.8%
2010	107	427	25.1%	44	205	21.5%	103	1,202	8.6%
2011	136	607	22.4%	111	540	20.6%	86	1,397	6.1%
2012	425	1,405	30.2%	89	288	30.9%	128	1,806	7.1%

	Carbapenems			Ciprofloxacin			TMP/SXZ		
	Res	Exam	Res %	Res	Exam	Res %	Res	Exam	Res %
2000	4	847	0.5%	37	348	10.6%	56	607	9.1%
2001	3	272	1.1%	20	169	11.6%	15	203	7.3%
2002	4	881	0.5%	26	402	6.4%	62	655	9.4%
2003	12	2,263	0.5%	243	1,748	13.9%	172	1,331	12.9%
2004	12	1,286	0.9%	41	574	7.2%	62	686	9.0%
2005	10	1,052	1.0%	88	411	21.5%	146	587	24.8%
2006	44	1,719	2.6%	123	723	17.0%	192	1,042	18.4%
2007	71	3,312	2.1%	250	1,518	16.5%	369	2,053	18.0%
2008	103	4,223	2.4%	221	1,630	13.6%	394	2,178	18.1%
2009	80	3,727	2.1%	193	1,493	12.9%	299	1,848	16.2%
2010	56	2,532	2.2%	125	823	15.2%	225	1,202	18.7%
2011	50	3,784	1.3%	134	1,329	10.1%	182	1,397	13.1%
2012	81	4,435	1.8%	175	1,715	10.2%	267	1,806	14.8%



Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
<i>Enterobacter</i> spp: <i>aerogenes/cloacae</i> have similar resistance patterns	Penicillin & β -lactam Inhib	Clavulanic-Amoxicillin	20	95%	95%	95%
	Penicillin & β -lactam Inhib	Piperacillin/ Tazobactam	92	34%	34%	34%
	Carbapenem	Ertapenem	92	5%	5%	5%
	Carbapenem	Imipenem	134	1%	0%	1%
	Carbapenem	Meropenem	92	2%	2%	2%
	Cephalosporin 3	Cefotaxime	92	41%	41%	41%
	Cephalosporin 3	Ceftriaxone	134	31%	0%	42%
	Cephalosporin 4	Cefepime	134	8%	0%	10%
	Cyclines	Tetracycline	92	24%	24%	24%
	Glycylcycline	Tigecycline	92	12%	12%	12%
	Aminoglycosides	Amikacin	92	2%	2%	2%
	Aminoglycosides	Gentamicin	134	9%	0%	35%
	Aminoglycosides	Tobramycin	134	10%	0%	30%
	Quinolone	Ciprofloxacin	42	19%	5%	35%
	Sulfonamide	Trimethoprim-sulfa	112	13%	10%	25%

These "ICU bugs" cause significant morbidity and mortality; infection management is complicated by resistance to multiple antibiotics. *Enterobacter* species possess inducible β -lactamases, which are undetectable in vitro but are responsible for resistance during treatment.

E.cloacae is 96% to 99% resistant to amoxicillin, ampicillin, penicillin derivatives with clavulanates, and 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 an increase.

3.13.6- *Proteus mirabilis*

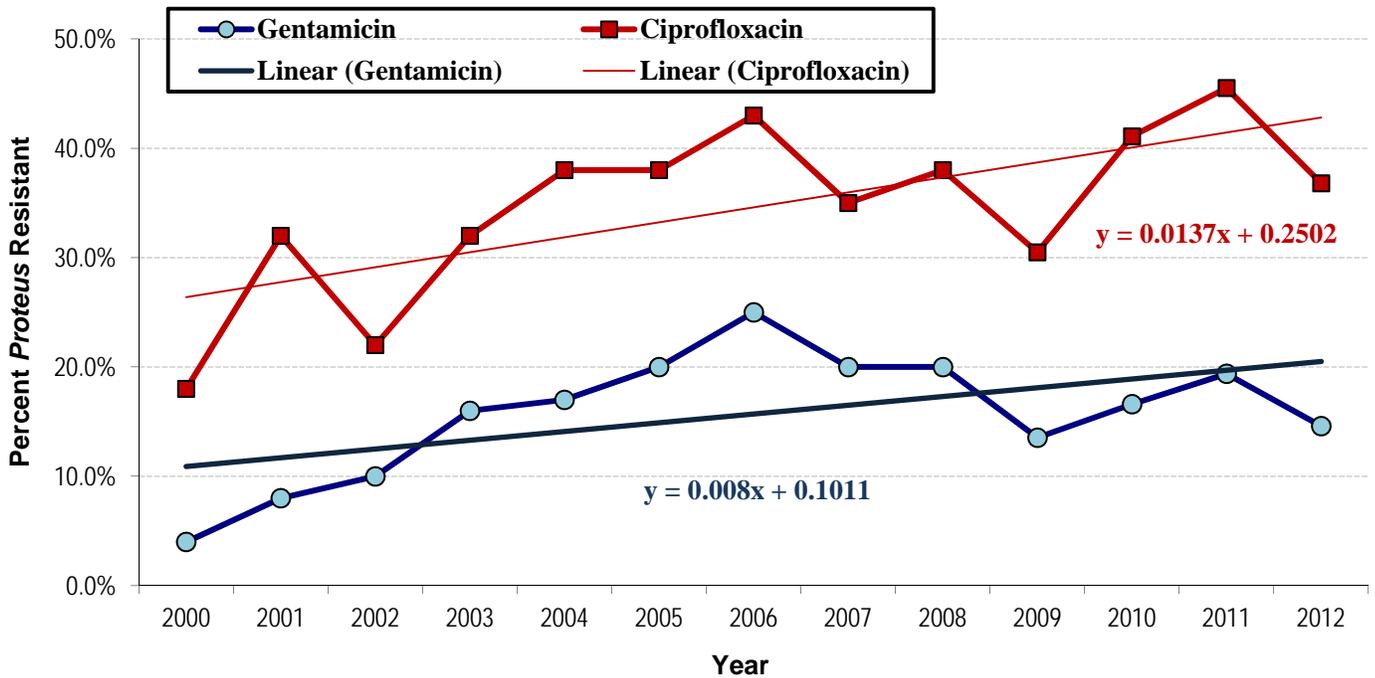
Proteus organisms are most commonly found in the human intestinal tract as part of normal human intestinal flora, along with *Escherichia coli* and *Klebsiella* species, of which *E coli* is the predominant resident. They are implicated as serious causes of infections in humans. *Proteus* are prone to colonize and infect the urinary tract. Iatrogenic hematologic dissemination can occur after urologic procedures. Patients with recurrent infections, those with structural abnormalities of the urinary tract, those who have had urethral instrumentation, and those whose infections were acquired in the hospital have an increased frequency of infection caused by *Proteus* and other organisms (eg, *Klebsiella*, *Enterobacter*, *Pseudomonas*, enterococci, staphylococci). *Proteus* are found in multiple environmental habitats, including long-term care facilities and hospitals.

Proteus mirabilis causes 90% of *Proteus* infections and can be considered a community-acquired infection. *Proteus vulgaris* and *Proteus penneri* are easily isolated from individuals in long-term care facilities and hospitals, and from patients with underlying diseases or compromised immune systems.

Proteus vulgaris is indole-positive and has more antibiotic resistance. *Proteus mirabilis*, which is indole-negative, is the most common species encountered in humans (90%).

	<i>Proteus mirabilis</i>								
	Ampicillin			Piperacillin-Tazobactam			Ceftriaxone (Cephalosp 3)		
	Res	Exam	%R	Res	Exam	%R	Res	Exam	%R
2000	102	1,341	7.6%	3	1,339	0.3%	14	973	1.5%
2001	93	566	16.5%	13	419	3.2%	9	459	1.9%
2002	585	2,511	23.3%	44	2,295	1.9%	3	1,362	0.2%
2003	2,323	7,798	29.8%	86	3,900	2.2%	50	4,496	1.1%
2004	1,582	4,711	33.6%	87	2,804	3.1%	49	2,493	2.0%
2005	902	2,741	32.9%	84	2,573	3.3%	14	1,967	0.7%
2006	1,780	4,982	35.7%	139	5,229	2.7%	161	3,827	4.2%
2007	1,737	6,183	28.1%	55	6,572	0.8%	121	6,057	2.0%
2008	2,547	7,891	32.3%	70	8,318	0.8%	464	7,716	6.0%
2009	1,311	4,792	27.4%	86	5,940	1.4%	198	4,326	4.6%
2010	600	2,564	23.4%	58	4,179	1.4%	247	3,896	6.4%
2011	2,070	6,369	32.5%	65	4,939	1.3%	777	6,661	11.7%
2012	1,270	3,967	32.0%	44	4,112	1.1%	622	5,575	11.2%

	Gentamicin			Nitrofurantoin			Ciprofloxacin			TMP/SXZ		
	Res	Exam	%R	Res	Exam	%R	Res	Exam	%R	Res	Exam	%R
2000	65	1,540	4.2%	1,212	1,348	89.9%	167	925	18.1%	72	1,491	4.8%
2001	56	702	7.9%	168	168	100.0%	164	516	31.7%	71	702	10.1%
2002	254	2,511	10.1%	1,458	1,467	99.4%	323	1,487	21.7%	524	2,737	19.1%
2003	1,194	7,637	15.6%	4,232	4,403	96.1%	2,020	6,307	32.0%	1,683	5,776	29.1%
2004	784	4,711	16.6%	2,449	2,516	97.3%	1,341	3,554	37.7%	1,292	3,893	33.2%
2005	557	2,774	20.1%	1,652	1,684	98.1%	589	1,567	37.6%	807	2,326	34.7%
2006	1,360	5,392	25.2%	3,262	3,735	87.3%	1,112	2,589	42.9%	1,907	4,675	40.8%
2007	1,341	6,857	19.6%	3,909	3,939	99.2%	1,742	4,959	35.1%	2,154	6,444	33.4%
2008	1,687	8,860	19.0%	4,932	4,989	98.9%	2,209	5,693	38.8%	3,166	8,162	38.8%
2009	815	6,025	13.5%	409	842	48.5%	1,314	4,309	30.5%	1,815	6,012	30.2%
2010	688	4,144	16.6%	89	94	94.4%	1,293	3,146	41.1%	1,545	4,243	36.4%
2011	1,326	6,827	19.4%	385	565	68.2%	3,007	6,650	45.2%	2,464	6,400	38.5%
2012	891	6,102	14.6%	20	25	80.0%	2,240	6,090	36.8%	231	532	43.4%



P. mirabilis remains susceptible to nearly many antimicrobials except cyclines. Resistance does not appear to be a significant clinical factor, but 10% to 30% of strains have acquired resistance to ampicillin and some cephalosporins. Acquisition of resistance to extended-spectrum alpha-lactamases remains uncommon in *Proteus*.

P. vulgaris and *P. penneri* show higher resistance to ampicillin and cephalosporins. Activation of an inducible chromosomal beta-lactamase (not found in *P. mirabilis*) occurs in up to 30% of these strains. Imipenem, fourth-generation cephalosporins, aminoglycosides, TMP/SMZ, and quinolones have excellent activity (90%-100%).

Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
<i>Proteus</i> spp: mirabilis mostly	Penicillin Amino	Ampicillin	332	34%	13%	62%
	Penicillin & β -lactam Inhib	Clavulanic-Amoxicillin	2937	6%	0%	40%
	Penicillin & β -lactam Inhib	Clavulanic-Ticaracillin	1265	0%	0%	2%
	Penicillin & β -lactam Inhib	Piperacillin/Tazobactam	5101	1%	0%	36%
	Penicillin & β -lactam Inhib	Sulbactam-Ampicillin	5356	19%	0%	48%
	Cephalosporin 1	Cefazolin	7411	22%	6%	70%
	Cephalosporin 2	Cefoxitin	3850	11%	0%	32%
	Cephalosporin 2	Cefuroxime	1756	5%	0%	14%
	Cephalosporin 3	Cefotaxime	2219	1%	0%	6%
	Cephalosporin 3	Ceftazidime	6116	6%	0%	82%
	Cephalosporin 3	Ceftriaxone	7355	13%	0%	76%
	Cephalosporin 4	Cefepime	5983	15%	0%	76%
	Monobactam	Aztreonam	4702	12%	0%	58%
	Carbapenem	Carbapenem	559	0%	0%	0%
	Carbapenem	Ertapenem	4000	0%	0%	5%
	Carbapenem	Imipenem	6304	9%	0%	30%
	Carbapenem	Meropenem	2552	1%	0%	3%
	Cyclines	Tetracycline	647	93%	55%	99%
	Glycylcycline	Tigecycline	662	91%	75%	99%
	Aminoglycosides	Amikacin	6626	1%	0%	11%
	Aminoglycosides	Gentamicin	7521	19%	0%	43%
	Aminoglycosides	Tobramycin	7047	15%	0%	42%
	Quinolone	Nitrofurantoin	565	68%	2%	99%
	Quinolone	Ciprofloxacin	7102	46%	0%	83%
	Quinolone	Levofloxacin	6665	43%	0%	81%
	Quinolone	Moxifloxacin	866	43%	25%	60%
Sulfonamide	Trimethoprim-sulfa	7094	39%	3%	81%	

3.13.7-*Serratia marcescens*

Members of this genus produce characteristic red pigment, prodigiosin. *S. marcescens*, was formerly known as *Bacillus prodigosus* 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%).

Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
<i>Serratia marcescens</i>	Penicillin Amino	Ampicillin	93	91%	80%	95%
	Penicillin Ureido	Piperacillin	157	11%	0%	16%
	Penicillin & β -lactam Inhib	Clavulanic-Ticarcillin	155	18%	0%	44%
	Penicillin & β -lactam Inhib	Piperacillin/Tazobactam	493	14%	0%	33%
	Penicillin & β -lactam Inhib	Sulbactam-Ampicillin	52	91%	87%	95%
	Cephalosporin 2	Cefoxitin	170	83%	78%	88%
	Cephalosporin 3	Ceftriaxone	802	7%	0%	22%
	Cephalosporin 3	Ceftazidime	661	11%	0%	27%
	Cephalosporin 4	Cefepime	629	2%	0%	7%
	Monobactam	Aztreonam	320	9%	0%	17%
	Carbapenem	Ertapenem	394	3%	0%	6%
	Carbapenem	Imipenem	713	2%	0%	20%
	Carbapenem	Meropenem	268	2%	0%	27%
	Cyclines	Tetracycline	15	87%	87%	87%
	Cyclines	Doxycycline	20	90%	90%	90%
	Glycylcycline	Tigecycline	171	3%	0%	8%
	Quinolone	Ciprofloxacin	586	21%	0%	56%
	Quinolone	Levofloxacin	581	15%	0%	49%
	Quinolone	Moxifloxacin	112	7%	0%	27%
	Aminoglycosides	Amikacin	626	2%	0%	10%
	Aminoglycosides	Gentamicin	833	6%	0%	25%
	Aminoglycosides	Tobramycin	664	17%	0%	43%
Sulfonamide	Trimethoprim-sulfa	826	12%	0%	39%	

3.13.8-*Citrobacter freundii*

Citrobacter 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 (90% to 10%), It shows little resistance to carbapenems (1%), amino-glycosides (5% or less) and quinolones (5%-15%).

Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
<i>Citrobacter</i> species	Ampicillin	Penicillin Amino	224	71%	17%	95%
	Piperacillin	Penicillin Ureido	94	45%	7%	75%
	Clavulanic/Amoxicillin	Penicillin & β -lactam Inhib	455	19%	0%	97%
	Clavulanic/Ticarcillin	Penicillin & β -lactam Inhib	700	13%	0%	27%
	Piperacillin/Tazobactam	Penicillin & β -lactam Inhib	1391	5%	0%	40%
	Sulbactam/Ampicillin	Penicillin & β -lactam Inhib	837	25%	0%	52%
	Cefazolin	Cephalosporin 1	876	6%	0%	80%
	Cefuroxime	Cephalosporin 2	201	34%	8%	64%
	Ceftriaxone	Cephalosporin 3	2025	11%	0%	54%
	Cefotaxime	Cephalosporin 3	482	16%	0%	50%
	Ceftazidime	Cephalosporin 3	1851	11%	0%	54%
	Cefepime	Cephalosporin 4	1823	1%	0%	5%
	Aztreonam	Monobactam	1324	14%	0%	57%
	Imipenem	Carbapenem	1330	0%	0%	5%
	Imipenem/Cilastatin	Carbapenem	102	0%	0%	0%
	Meropenem	Carbapenem	1052	1%	0%	8%
	Ertapenem	Carbapenem	1246	2%	0%	7%
	Tetracycline	Cyclines	971	16%	0%	33%
	Doxycycline	Cyclines	80	16%	15%	17%
	Tigecycline	Glycylcycline	292	6%	0%	19%
	Nitrofurantoin	Quinolone	1325	16%	0%	54%
	Ciprofloxacin	Quinolone	1996	11%	0%	46%
	Levofloxacin	Quinolone	1364	12%	0%	66%
	Moxifloxacin	Quinolone	739	12%	0%	50%
	Amikacin	Aminoglycosides	1967	1%	0%	6%
	Gentamicin	Aminoglycosides	2118	7%	0%	54%
	Tobramycin	Aminoglycosides	2003	6%	0%	25%
	Trimethoprim-sulfa	Sulfonamide	2046	16%	0%	60%

3.13.9-*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 infections and nosocomial infections.

It is resistant to ampicillin (95%), piperacillin (40%), penicillin/ β lactamase-inhibitors (90% to those with amoxicillin or ampicillin, 10%-20% to those with piperacillin or tazobactam), cyclines (50%) and quinolones (50%). Resistance to cephalosporins is variable (80% to 30%). It shows little resistance to carbapenems (2%), amino-glycosides (15% or less).

Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
<i>Morganella morganii</i>	Penicillin Amino	Ampicillin	122	95%	70%	98%
	Penicillin Ureido	Piperacillin	31	35%	35%	35%
	Penicillin & β -lactam Inhib	Clavulanic-Amoxicillin	78	83%	75%	89%
	Penicillin & β -lactam Inhib	Clavulanic-Ticarcillin	90	22%	15%	39%
	Penicillin & β -lactam Inhib	Piperacillin/Tazobactam	604	8%	0%	17%
	Cephalosporin 1	Cefazolin	180	91%	70%	98%
	Cephalosporin 2	Cefoxitin	411	42%	11%	70%
	Cephalosporin 3	Ceftriaxone	851	9%	0%	27%
	Cephalosporin 3	Ceftazidime	735	29%	6%	37%
	Cephalosporin 4	Cefepime	747	2%	0%	7%
	Monobactam	Aztreonam	429	12%	0%	26%
	Carbapenem	Ertapenem	565	1%	0%	2%
	Carbapenem	Imipenem	670	5%	0%	11%
	Carbapenem	Meropenem	345	1%	0%	1%
	Cyclines	Tetracycline	120	55%	31%	74%
	Glycylcycline	Tigecycline	87	38%	26%	70%
	Quinolone	Ciprofloxacin	573	52%	27%	81%
	Quinolone	Levofloxacin	523	47%	22%	70%
	Quinolone	Moxifloxacin	87	49%	44%	55%
	Aminoglycosides	Amikacin	735	0%	0%	6%
	Aminoglycosides	Gentamicin	876	25%	0%	50%
	Aminoglycosides	Tobramycin	789	11%	0%	50%
Sulfonamide	Trimethoprim-sulfa	614	47%	14%	77%	

3.13.10-*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 (75%), piperacillin (25%), penicillin/ β lactamase-inhibitors (95% to those with amoxicillin or ampicillin, 5%-10% to those with piperacillin or tazobactam), cyclines (90%) and quinolones (70%). Resistance to cephalosporins and amino-glycosides is variable. It shows little resistance to carbapenems (0-2%).

Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
<i>Providencia Stuartii</i>	Penicillin Amino	Ampicillin	17	76%	71%	80%
	Penicillin Ureido	Piperacillin	16	25%	17%	30%
	Penicillin & β -lactam Inhib	Piperacillin/Tazobactam	196	2%	0%	14%
	Cephalosporin 2	Cefoxitin	222	17%	3%	43%
	Cephalosporin 3	Ceftazidime	296	19%	0%	32%
	Cephalosporin 4	Cefepime	359	6%	0%	90%
	Monobactam	Aztreonam	219	2%	0%	10%
	Carbapenem	Ertapenem	298	0%	0%	1%
	Carbapenem	Imipenem	271	1%	0%	1%
	Carbapenem	Meropenem	40	0%	0%	0%
	Glycylcycline	Tigecycline	10	30%	30%	30%
	Quinolone	Ciprofloxacin	151	79%	50%	92%
	Quinolone	Levofloxacin	143	75%	47%	92%
	Quinolone	Moxifloxacin	28	82%	76%	91%
	Sulfonamide	Trimethoprim-sulfa	205	53%	25%	68%
	Aminoglycosides	Amikacin	304	0%	0%	1%
	Aminoglycosides	Gentamicin	37	59%	55%	71%
	Aminoglycosides	Tobramycin	37	62%	55%	86%

3.14- *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, the 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 neutropenic 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.

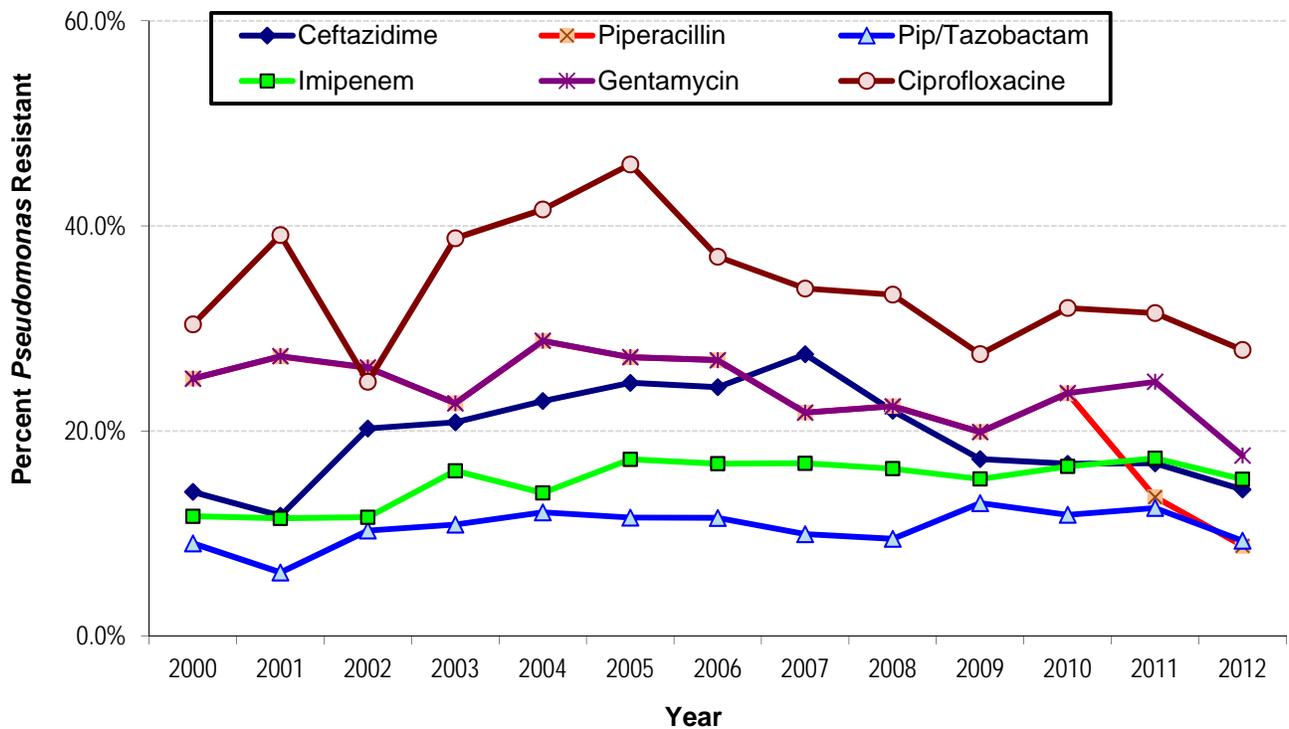
One of the most worrisome characteristics of *P. aeruginosa* is its low antibiotic susceptibility. This low susceptibility is attributable to a concerted action of multidrug efflux pumps with chromosomally-encoded antibiotic resistance genes (e.g. *mexAB*, *mexXY*) and the low permeability of the bacterial 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 de-

terminants. 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.

	<i>Pseudomonas Aeruginosa</i>								
	Ceftazidime			Piperacillin			Pipe/Tazobactam		
	Res	Exam	Res %	Res	Exam	Res %	Res	Exam	Res %
2000	260	1,852	14.1%	61	638	25.1%	135	1,491	9.0%
2001	158	1,350	11.7%	71	990	27.3%	64	1,025	6.2%
2002	535	2,643	20.2%	293	1,692	26.2%	291	2,823	10.3%
2003	1,700	8,152	20.8%	432	2,980	22.7%	685	6,302	10.9%
2004	780	3,402	22.9%	163	1,191	28.8%	400	3,314	12.1%
2005	679	2,748	24.7%	14	137	27.2%	430	3,717	11.6%
2006	1,262	5,201	24.3%	100	596	26.9%	692	6,001	11.5%
2007	2,088	7,597	27.5%	196	1,298	21.8%	711	7,151	9.9%
2008	2,105	9,580	22.0%	226	2,063	22.4%	1,011	10,658	9.5%
2009	1,188	6,882	17.3%	77	888	19.9%	950	7,322	13.0%
2010	840	4,999	16.8%	70	713	23.7%	623	5,267	11.8%
2011	1,248	7,423	16.8%	199	1,466	13.6%	775	6,203	12.5%
2012	938	6,555	14.3%	78	883	8.8%	451	4,860	9.3%
CoArm	X2 82.43	df 1	p 0.00	X2 9.73	df 1	p 0.002	X2 7.15	df 1	p 0.007

	Imipenem			Gentamicin			Ciprofloxacin		
	Res	Exam	Res %	Res	Exam	Res %	Res	Exam	Res %
2000	224	1,917	11.7%	500	1,990	25.1%	527	1,749	30.1%
2001	155	1,350	11.5%	405	1,486	27.3%	525	1,344	39.1%
2002	318	2,748	11.6%	795	3,041	26.2%	729	2,096	34.8%
2003	1,131	7,015	16.1%	2,506	11,030	22.7%	3,460	8,912	38.8%
2004	528	3,781	14.0%	1,491	5,183	28.8%	1,657	3,988	41.6%
2005	660	3,826	17.2%	1,175	4,322	27.2%	968	2,104	46.0%
2006	911	5,419	16.8%	1,795	6,669	26.9%	1,111	3,000	37.0%
2007	1,361	8,075	16.9%	1,772	8,125	21.8%	1,959	5,780	33.9%
2008	1,620	9,916	16.3%	2,179	9,714	22.4%	2,161	6,488	33.3%
2009	1,013	6,613	15.3%	1,526	7,664	19.9%	1,572	5,725	27.5%
2010	808	4,882	16.5%	1,281	5,411	23.7%	1,315	4,106	32.0%
2011	1,344	7,758	17.3%	2,018	8,141	24.8%	2,481	7,878	31.5%
2012	765	4,992	15.3%	1,310	7,462	17.6%	1,923	6,883	27.9%
CoArm	X2 37.62	df 1	p 0.00	X2 123.45	df 1	p 0.00	X2 307.95	df 1	p 0.00

Pseudomonas is resistant to ampicillin (99%) and ticarcillin (40%), less resistant to ureido penicillin (Mezlocillin, piperacillin 10%) resistant and most cephalosporins (the less resistance is to ceftazidime and cefepime). It shows some resistance to aminoglycosides (10% - 20%), quinolones (30%-50%), and carbapenems (20%). Double drug therapy is recommended for serious infection, consisting of an anti-pseudomonal penicillin (piperacillin/tazobactam, ticarcillin/clavulanate), meropenem or cefipime plus a fluoroquinolone or an aminoglycoside.



Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
<i>Pseudomonas aeruginosa</i>	Penicillin Amino	Ampicillin	108	99%	99%	99%
	Penicillin Ureido	Piperacillin	1466	14%	4%	32%
	Penicillin & β -lactam Inhib	Clavulanic-Ticarcillin	2210	24%	0%	50%
	Penicillin & β -lactam Inhib	Piperacillin/Tazobactam	6516	12%	0%	39%
	Cephalosporin 1	Cefazolin	234	99%	99%	99%
	Cephalosporin 3	Cefotaxime	1075	89%	77%	97%
	Cephalosporin 3	Ceftriaxone	1965	89%	62%	99%
	Cephalosporin 3	Ceftazidime	7850	17%	0%	57%
	Cephalosporin 4	Cefepime	7439	21%	0%	37%
	Monobactam	Aztreonam	4359	32%	0%	57%
	Carbapenem	Imipenem	8383	17%	0%	38%
	Carbapenem	Meropenem	3865	17%	0%	35%
	Glycylcycline	Tigecycline	234	97%	96%	98%
	Quinolone	Ciprofloxacin	8302	31%	0%	56%
	Quinolone	Levofloxacin	7113	38%	0%	68%
	Quinolone	Moxifloxacin	188	54%	50%	56%
	Aminoglycosides	Amikacin	8053	8%	0%	19%
	Aminoglycosides	Gentamicin	8766	24%	0%	42%
	Aminoglycosides	Tobramycin	8525	10%	0%	29%
	Sulfonamide	Trimethoprim-sulfa	606	99%	98%	99%

3.15- *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), and 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%-70% to those with piperacillin or tazobactam), most cephalosporins (50%-90%, ceftazidime 50%). It shows resistance to aminoglycosides (5%-15%), quinolones (20% - 30%) and carbapenems (90% to imipenem and 8% to carbapenem). Trimethoprim-sulfamethoxazole is very effective (less than 1% resistance).

Agent	Group	Antibiotic	Nbr Isol	Avg Res	Low Res	High Res
<i>Stenotrophomonas maltophilia</i>	Penicillin & β-lactam Inhib	Clavulanic-Ticarcillin	140	43%	27%	65%
	Cephalosporin 3	Ceftazidime	160	52%	33%	74%
	Quinolone	Levofloxacin	232	21%	8%	50%
	Sulfonamide	Trimethoprim-sulfa	358	6%	0%	17%