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**Resistance of *P. aeruginosa*
to antibiotics in France:
epidemiological data in 2005**

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- **Opportunistic pathogen bacteria**
- Innocuous among immuno-competent
- **Important cause of hospital-acquired infections particularly among immuno-compromised patients** (patients in intensive care units, cystic fibrosis patients, neutropenic patients)

Prevalence (%) of *Pseudomonas aeruginosa* in hospital acquired infections

	EPIIC* study 24.04.1992	EPIIC*study France 24.04.1992	French prevalence study 2001
Total infections	28.7	29	11
Lower respiratory tract infections	29.8	36.8	21.6
Urinary tract infections	18.7	17.2	9.6
Wound, post- chirurgical infections	21.2	14.6	25.2
Bacteremia	9.7	6.7	-

•EPIIC = European Prevalence of Infection in Intensive Care

Pseudomonas aeruginosa and intrinsic resistance

Wild phenotype

- **Resistance to β -lactam-agents :**
 - **Aminopenicillin, first and second generation cephalosporins**
- **Resistance to aminoglycosides:**
 - **Kanamycin, neomycin**
- **Resistance to other antibiotics:**
 - **Phenicol, tetracyclines, trimethoprim,**
 - **first generation quinolones**

Susceptibility (%) to antibiotics of *Pseudomonas aeruginosa* according to studies

	Réussir** 2002	COL-BVH* 2003	GERPB** 1998 1999		GERPA** 2004	
	N=2361	N = 58	N = 665	N = 701	France N = 450	Lille N = 30
TIC	65	52	55	58	62	43
TCC					61	43
PIP	83	73	71	73	79	63
TZP	82	82			80	60
CAZ	86	79	75	76	78	57
FEP					64	53
IPM	83	90	83	82	83	63
CIP	69	79	56	60	68	53
AN	84		69	64	86	76

* = bacteremia; ** = total infections; TIC = ticarcillin, TCC = ticarcillin - clavulanic acid, PIP = piperacillin, TZP = piperacillin - tazobactam; CAZ = ceftazidime, FEP = cefepime, IPM = imipenem, CIP = ciprofloxacin, AN = amikacin

Susceptibility of *P. aeruginosa* to antibiotics in France and distribution of resistance mechanisms to β -lactam- agents

- 450 strains of *P. aeruginosa* collected in April - May 2004 by 15 french laboratory hospitals
- 30 non-repetitive strains, isolated only from diagnostic samples (except for cystic fibrosis samples)

Susceptibility of *P. aeruginosa* according to main serogroup O

SEROGROUP		TIC	PIP	ATM	CAZ	IPM	AN	TM	CIP
Total serogroups		62	79	50	78	83	86	80	68
6	25%	70	88	54	83	85	91	89	79
11	16%	44	59	41	60	74	77	69	47
4	10%	50	67	33	67	78	91	46	43
1	10%	60	82	56	84	87	93	91	78
3	6%	72	90	52	86	90	90	100	83
10	6%	85	96	61	96	92	100	96	77
12	4%	11	33	11	61	61	39	28	28

TIC= ticarcillin, PIP = piperacillin, ATM = aztreonam, CAZ=ceftazidime, IPM=imipenem, AN=amikacin, TM = tobramycin, CIP = ciprofloxacin

Susceptibility of *P. aeruginosa* to ciprofloxacin (%) according to serogroup O « REUSSIR » network 1998

Strain	12	4	11	6	1	3	NT
N	403	360	880	1105	683	462	1219
%S	7 ^a	49 ^b	51 ^c	83	88	88	67

a. b. c % idem GERPB

a: Penicillinase ± Cephalosporinase; b: Efflux; c: Cephalosporinase

Susceptibility of *P. aeruginosa* to ciprofloxacin (%) according to samples « REUSSIR » network 1998

Strain	urine	pulmonary samples	blood culture	purulent collection	ears
N total	2900	219	300	2800	313
% S	57	61	66	71	94

Decreased susceptibility to IPM, CIP, AN and TM according to the phenotype TIC / PIP / CAZ

phenotype				main mechanism of resistance	susceptibility %			
TIC	PIP	CAZ	%		IPM	CIP	AN	TM
S	S	S	82	no mechanism	95	97	95	86
R/I	S	S/I	16	no enzyme	73	85	78	54
I	I/R	I	6	low level Case	75	71	50	32
R	R	R	4	high level Case	25	38	31	25
R	I	I	3	Case ± efflux	64	86	64	36
R	R	S	2	acquired Pase	70	20	20	0
R	R	I	5	Case ± acquired Pase	41	50	23	23

TIC= ticarcillin, PIP = piperacillin, ATM = aztreonam, CAZ=ceftazidime, IPM=imipenem, AN=amikacin, TM = tobramycin, CIP = ciprofloxacin,

Distribution of acquired resistance mechanisms to β -lactam-agents

Resistance to IPM excluded	%
No mechanism	62
Acquired P_{ase} (PSE type, TEM2, OXA type)	3
BLSE (SHV, OXA type)	1
Acquired P_{ase} + C_{ase}	2
Case	9
Case + resistance non enzymatique	6
Non enzymatic resistance (efflux)	16
Other mechanisms	1
Resistance to IPM (essentially porine D2)	
porine D2 modification	16,6
Carbapenemase (VIM-type)	0,4

Epidemiological data 2001: « ARECLIN » network

« Association Régionale des Comités de Lutte contre les Infections Nosocomiales »

- **28 hospitals in Nord - Pas de Calais (teaching and general hospitals)**
- **18.500 beds**
- **Survey during 2 months/year since 1996 (more than 75.000 patient admissions during each survey)**
- **Survey 2001 = 1.129 non repetitive strains**

Epidemiological data 2001: « ARECLIN » network

Incidence of infected and/or colonised patients by *Pseudomonas aeruginosa*

Incidence / 1000 admissions	Incidence / 1000 hospitalisation days
10.5	1.3

Incidence (for 1000 HD) of *P. aeruginosa* according to medical speciality and infection site - ARECLIN

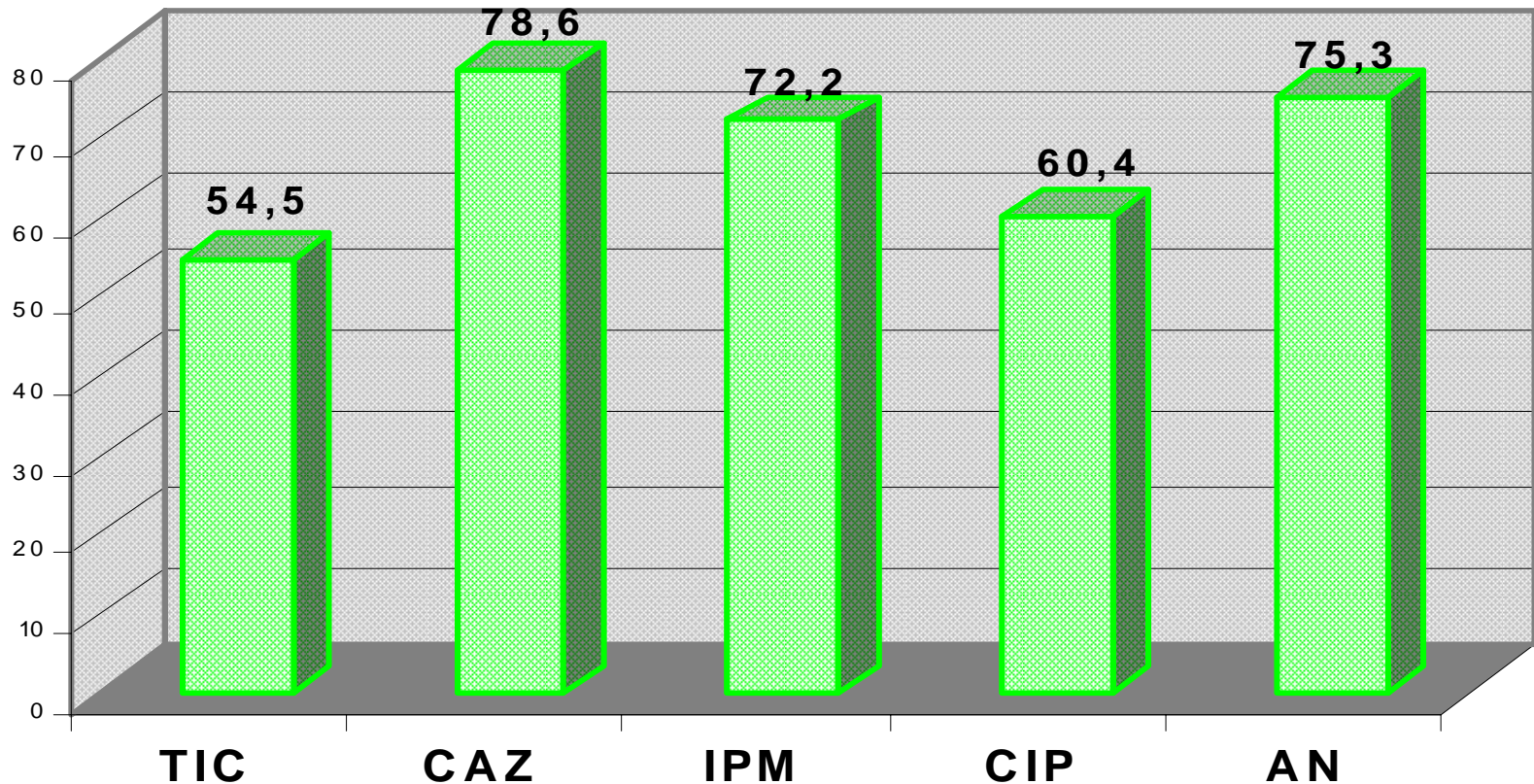
➤ Medical speciality

Intensive care	Medical unit	Surgical unit	Pediatric unit	Long term care
8.99	2.04	1.58	2.12	0.58

➤ Infection site

respiratory	urinary	« purulent collection »	blood	catheter
0.76	0.37	0.34	0.03	0.02

Susceptibility (%) to antibiotics of *P. aeruginosa* (N = 1129)- ARECLIN



TIC = ticarcillin, CAZ = ceftazidime, IPM = imipenem,
CIP = ciprofloxacin, AN = amikacin

6 serogroups represent 80% of the *P. aeruginosa* strains

Serogroup	GERPA France	ARECLIN
6	25%	14.7%
11	16%	13%
4	10%	8.3%
1	10%	8.3%
3	6%	6.6%
10	6%	
12	4%	4.1%

Susceptibility of *P. aeruginosa* according to the main serogroups: comparison France 2004- ARECLIN 2001

SERO GROUP	TIC		CAZ		IPM		AN		CIP	
	GERPA	ARECLIN	GERPA	ARECLIN	GERPA	ARECLIN	GERPA	ARECLIN	GERPA	ARECLIN
6	70	70	83	86	85	68	91	80	79	77
11	44	37	60	55	74	63	77	52	47	51
4	50	36	67	73	78	69	91	82	43	24
1	60	62	84	84	87	85	93	80	78	80
3	72	68	86	88	90	76	90	86	83	79
12	11	12	61	72	61	49	39	35	28	26

TIC= ticarcillin, PIP = piperacillin, ATM = aztreonam, CAZ=ceftazidime,
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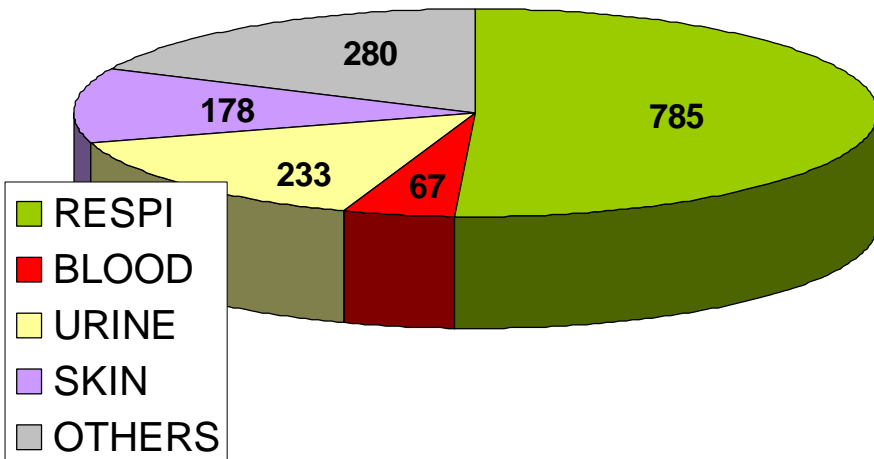
GERPA; RICAI 2004 400/81P

C. Cattoën - Lille 12 Avril 2002 -submitted

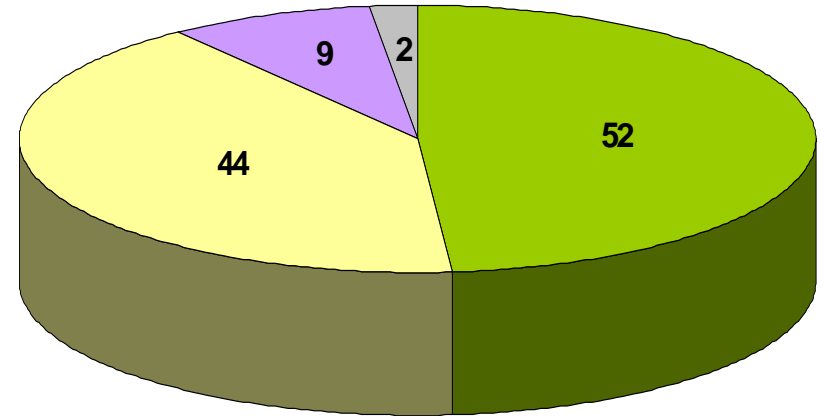
Susceptibility (%) of *P.aeruginosa* in France and in Lille hospital

Antibiotic	GERPA** 2004	
	France N = 450	Lille N = 30
TIC	62	43
TCC	61	43
PIP	79	63
TZP	80	60
CAZ	78	57
FEP	64	53
IPM	83	63
CIP	68	53
AN	86	76

Lille hospital: *P. aeruginosa*: Origin of samples

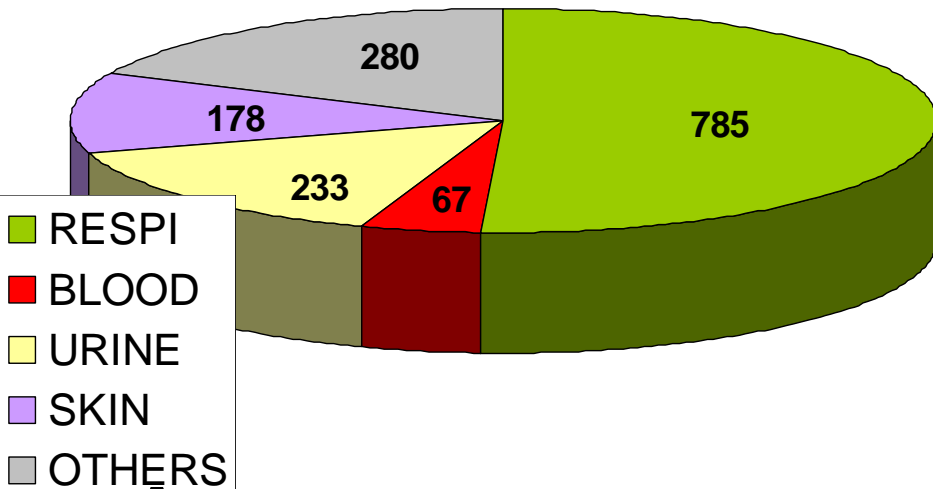


**Acute
hospitalisation
n =1543**



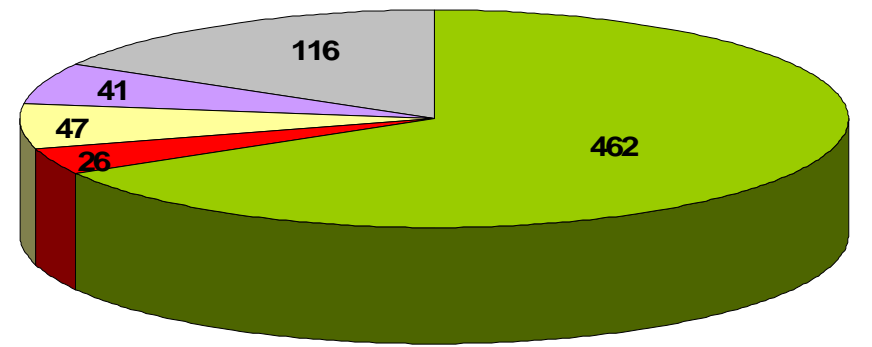
**Long term care
n =107**

P. aeruginosa: Sample origins

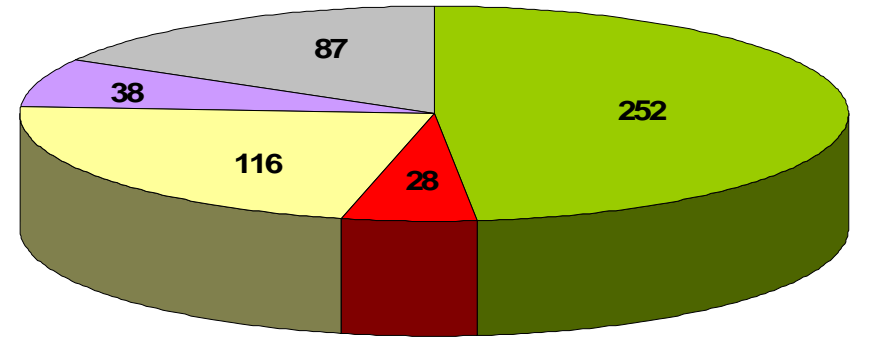


**Acute
hospitalisation
n = 1543**

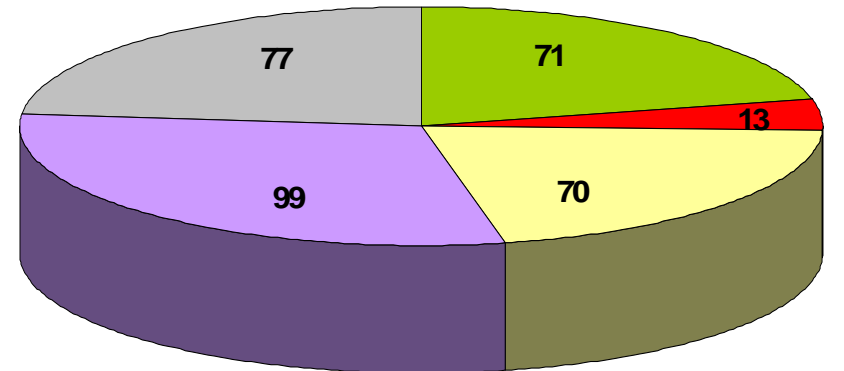
**(N= 6621
Gram negative bacilli)**



Intensive care(n=692)



**Medical unit
(n=521)**

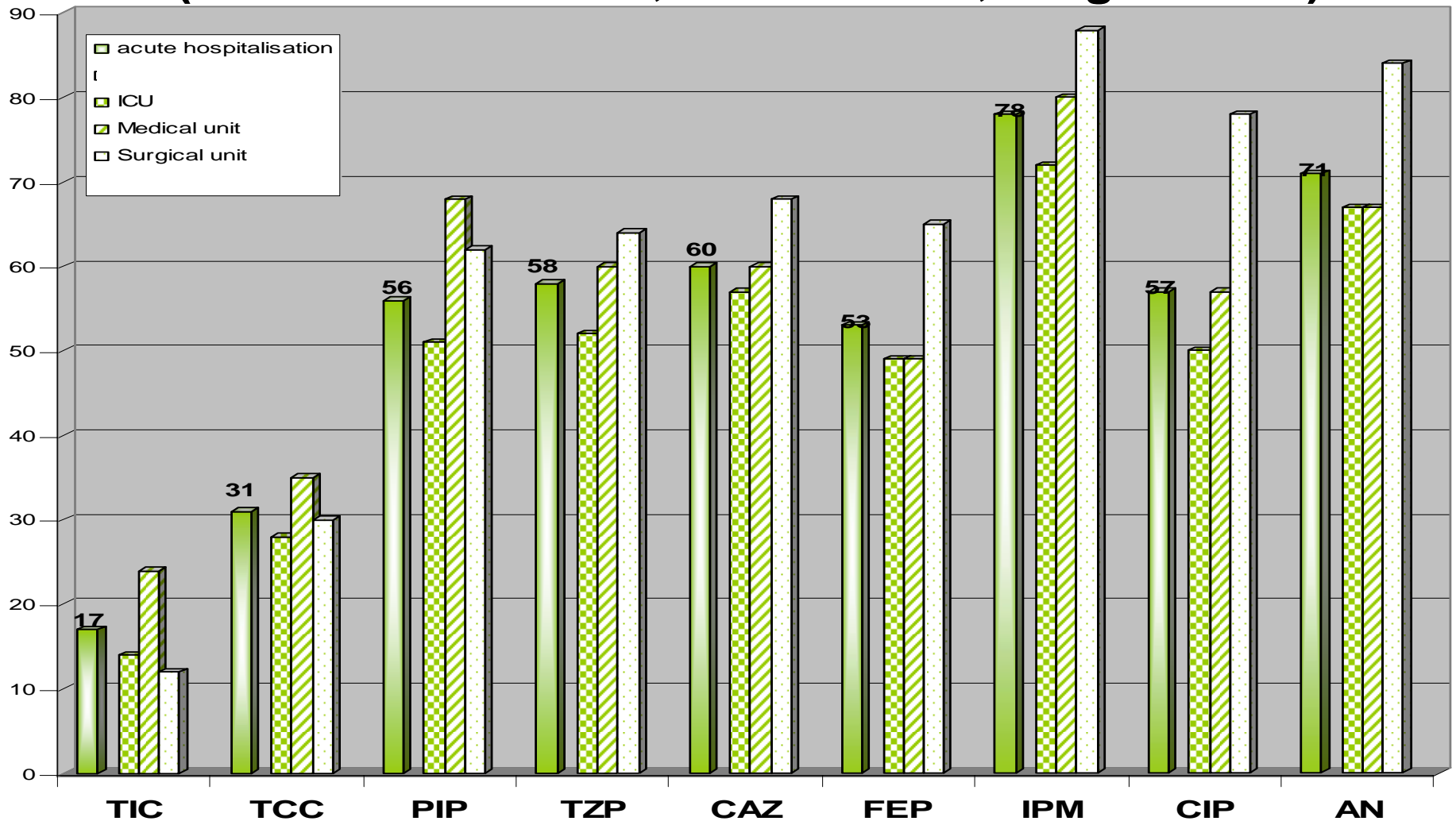


**Surgical unit
(n=330)**

Susceptibility (%) of *P. aeruginosa* to antibiotics

Lille hospital 2004

(Intensive Care Unit, medical unit, surgical unit)

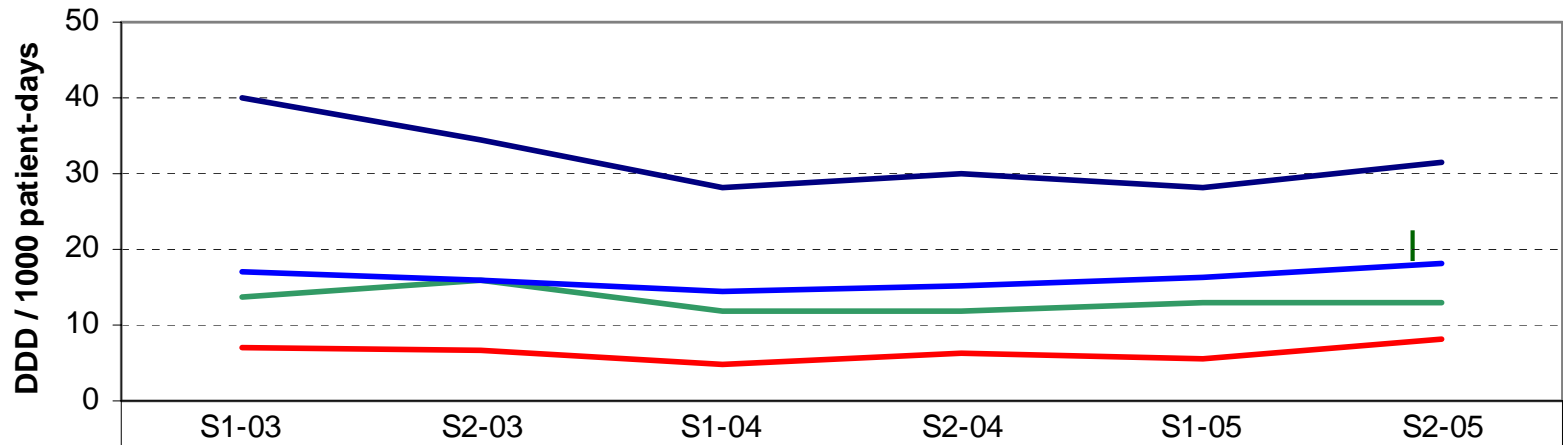


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 TZP = piperacillin + tazobactam, CAZ = ceftazidime, FEP = cefepime, IPM = imipenem
 CIP = ciprofloxacin, AN = amikacin

Volume of antibiotics consumed during a 1 000 patient-days since 2003: Lille hospital

Total antibiotics = 892.8 DDJ/1000JH Variations 2003-2005 = + 5.1%

Lille hospital



— Ciprofloxacin	40,2	34,4	28,2	30,1	28,0	31,5
— Ceftazidime	6,9	6,6	4,8	6,5	5,6	8,3
— Imipenem	13,9	15,7	11,8	11,7	12,8	12,9
— Tazocillin	17,17	16,04	14,5	15,31	16,12	18,03

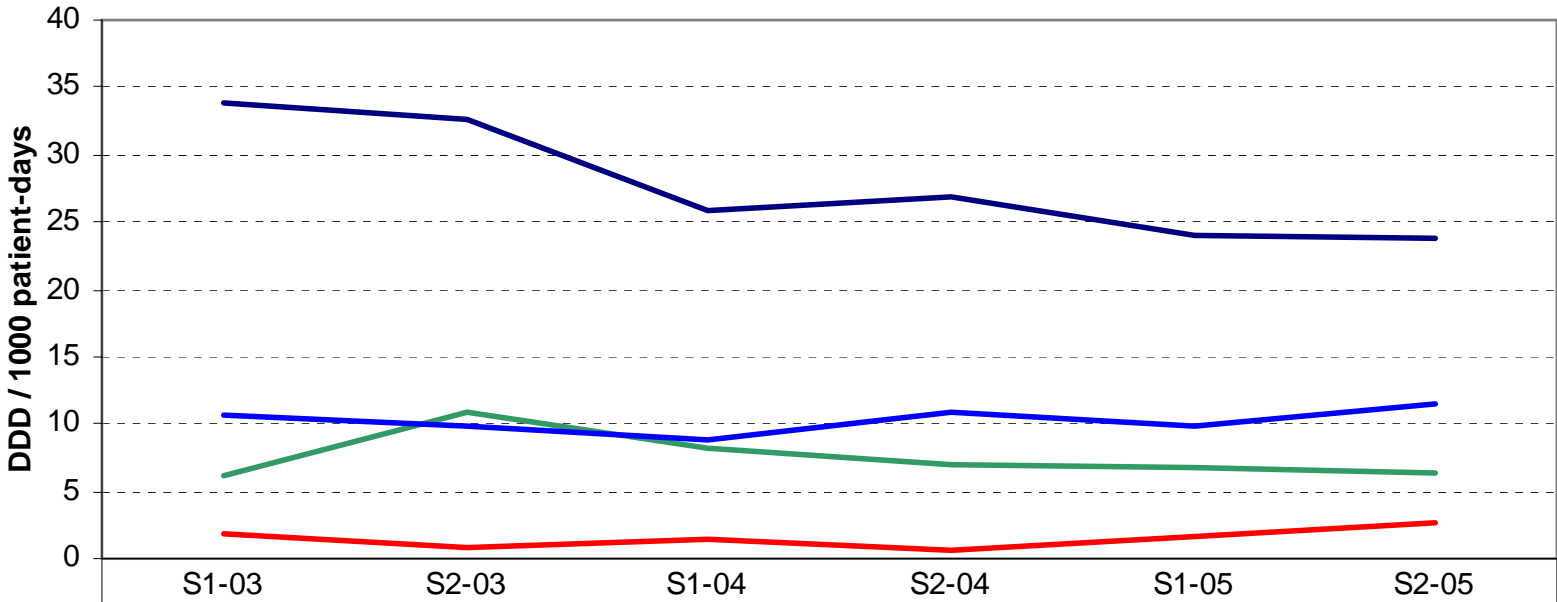
— Ciprofloxacin — Ceftazidime — Imipenem — Tazocillin

NB: Ciprofloxacin = -22% , but Levofloxacin = +28.2% and Ofloxacin = +13.8%

Volume of antibiotics consumed during a 1 000 patient-days since 2003: Lille hospital

Total antibiotics = 949.5 DDJ/1000JH Variations 2003-2005 = + 2.2%

Surgical unit



— Ciprofloxacin	33,9	32,6	25,9	26,8	24,0	23,8
— Ceftazidime	1,8	0,8	1,4	0,6	1,7	2,7
— Imipenem	6,1	10,9	8,1	7,0	6,7	6,4
— Tazocillin	10,61	9,85	8,72	10,83	9,8	11,5

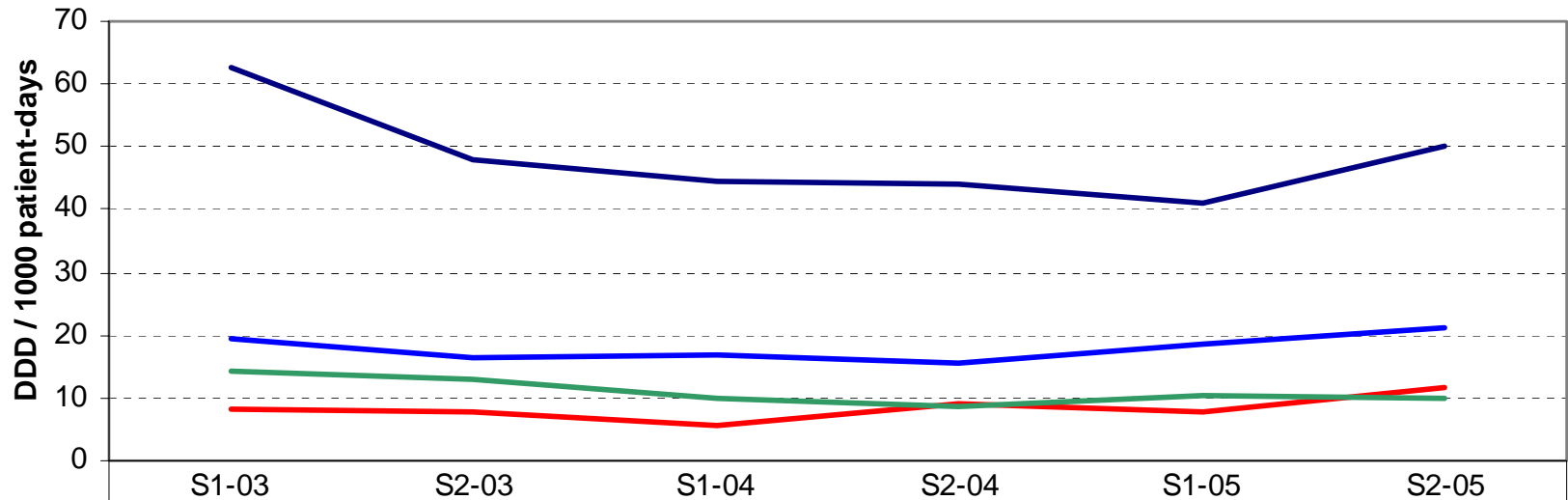
— Ciprofloxacin — Ceftazidime — Imipenem — Tazocillin

NB: Ciprofloxacin = -22% , Ofloxacin +1.6% and Levofloxacin + 4.4%

Volume of antibiotics consumed during a 1 000 patient-days since 2003: Lille hospital

Total antibiotics = 1051.4 DDJ/1000JH Variations 2003-2005 = +2.3%

Medical unit



— Ciprofloxacin	62,7	47,9	44,4	44,0	41,2	50,0
— Ceftazidime	8,3	7,6	5,4	9,1	7,9	11,5
— Imipenem	14,2	13,1	10,1	8,8	10,5	9,8
— Tazocillin	19,39	16,36	16,73	15,42	18,53	21,03

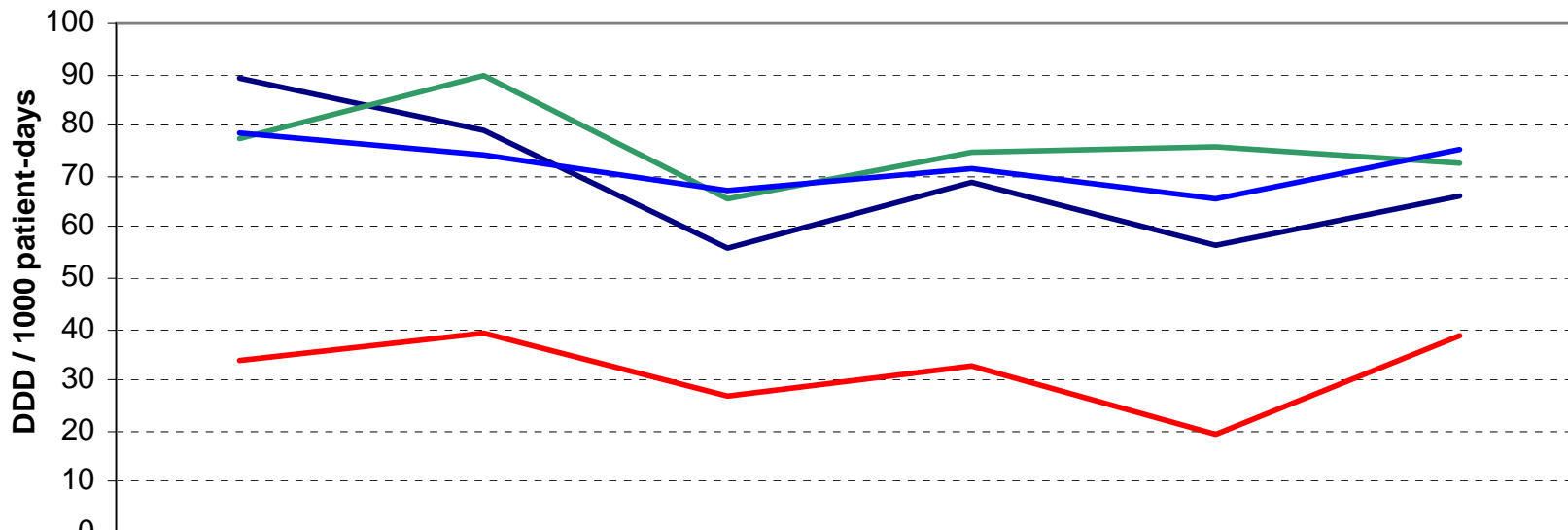
— Ciprofloxacin — Ceftazidime — Imipenem — Tazocillin

NB: Ciprofloxacin = -21.5% , Ofloxacin = -2.6% but Levofloxacin = +39%

Volume of antibiotics consumed during a 1 000 patient-days since 2003: Lille hospital

Total antibiotics = 1849.5 DDJ/1000JH Variations 2003-2005 = 9.7%

Intensive care unit



	S1-03	S2-03	S1-04	S2-04	S1-05	S2-05
Ciprofloxacin	89,4	79,0	55,8	68,7	56,4	66,1
Ceftazidime	33,7	39,4	26,9	32,8	19,2	38,6
Imipenem	77,4	89,9	65,9	74,8	75,6	72,7
Tazocillin	78,41	73,94	66,94	71,64	65,68	75,26



NB: Ciprofloxacin = -23.3% , % and Ofloxacin = -25.7% but Levofloxacin = +89.6% !

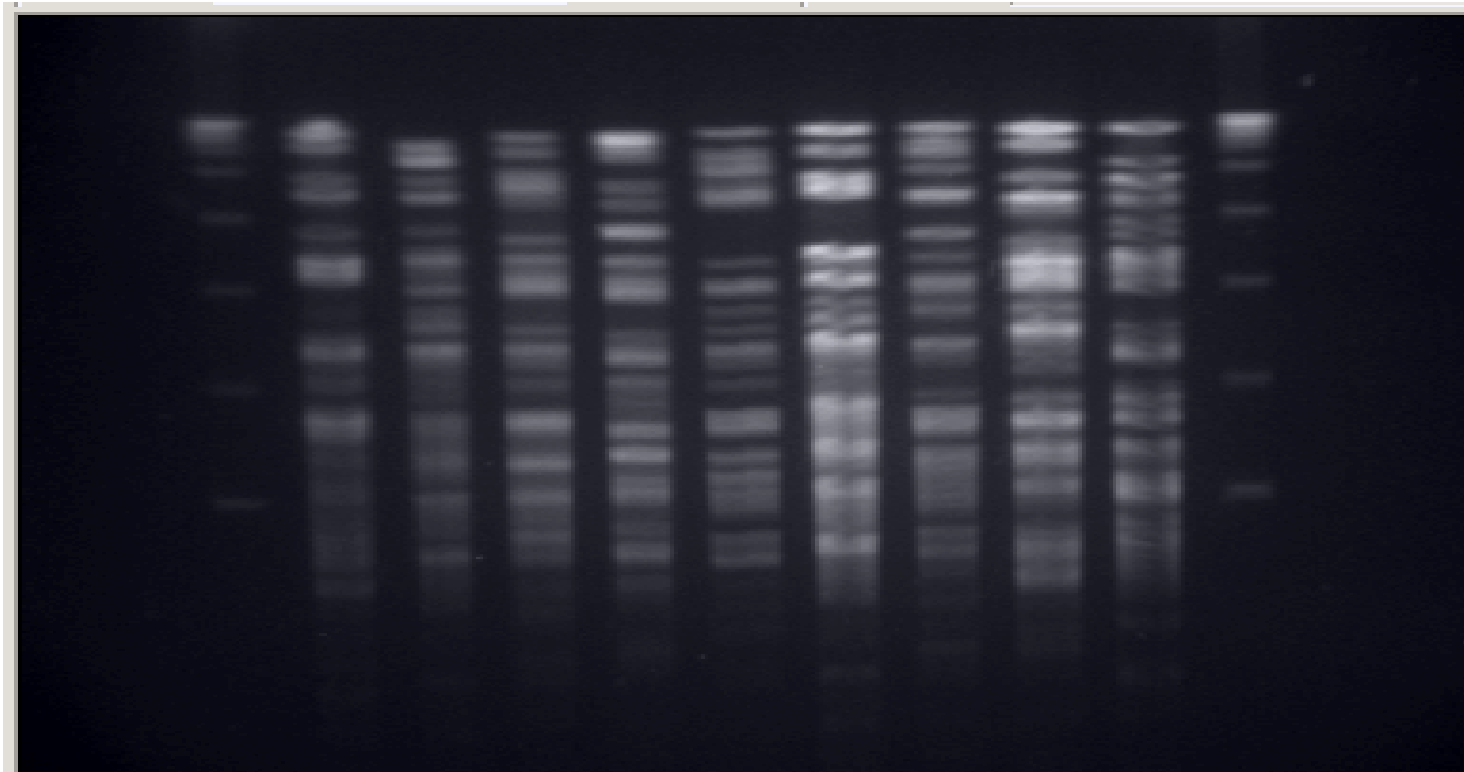
P. aeruginosa et multiresistance

- **18 *P. aeruginosa* O11** isolated in 2004 (increase/2003: 120%) among 17 hematology patients (12 acute leukemias).
- All strains were **multidrug resistant**:
100% TIC R, 72% CAZ I/R, CIP I/R, AN I/R et 50% IPM.
- Pulsed-field gel electrophoresis identified **multiple clones**.
- Among empirical treatment 50% included at least one antibiotic active on the strain.
- Median time between blood culture drawing and first administration of an active antibiotic was 2 days. Colimycin was employed in 10 cases. (7/10 susceptible strains)
- **12 cures, 5 deaths**, all due to infection.

TIC= ticarcillin, CAZ=ceftazidime, IPM=imipenem, CIP = ciprofloxacin, AN=amikacin

JB. Micol, et al ICAAC K-1542- 2005

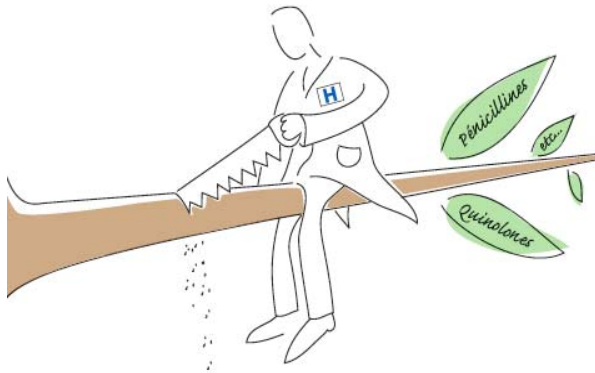
Pulsed-field gel electrophoresis of 14 clinical isolates and 2 environmental strains of *P. aeruginosa*



CONCLUSION

- ❑ **Worrying level of *P. aeruginosa***
 - In french hospital
 - In the north of France
- ❑ **Different level of resistance according to serogroups, samples, units.**
- ❑ **Worrying multidrug-resistance.**
- ❑ **Prevention:**
 - Hygiene
 - Antibiotic policy

**LES ANTIBIOTIQUES
C'EST PAS AUTOMATIQUE**



**Mieux utiliser les antibiotiques
pour préserver leur efficacité.**