

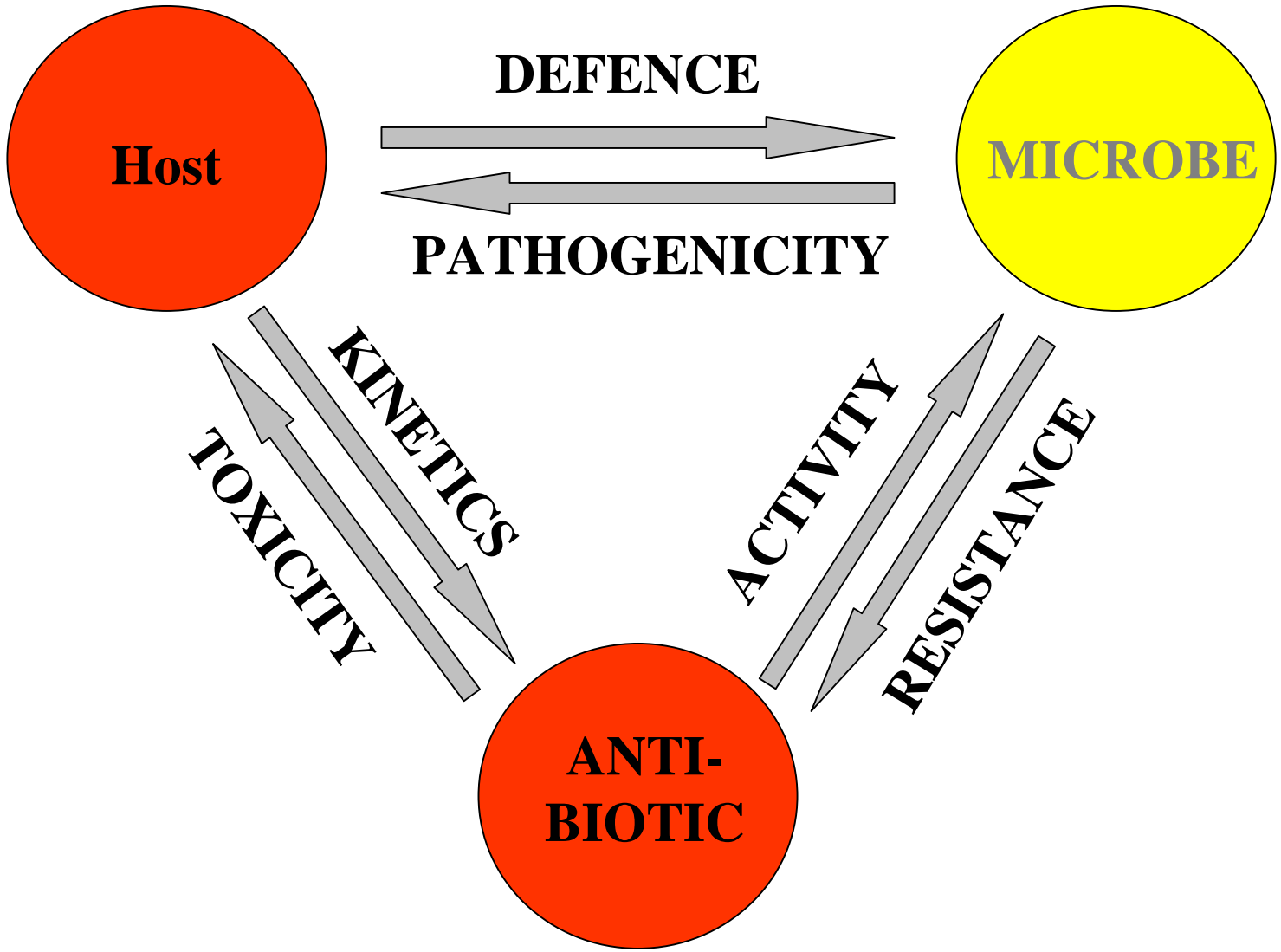
Resistance and Strategies for *Streptococcus pneumoniae*

Vanhoof, R.

**Unit of Antibiotic Research
Institute Pasteur Brussels**



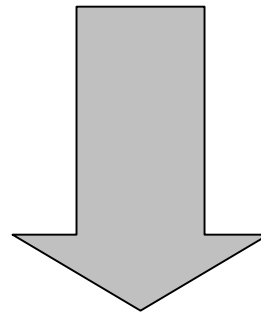
UCL, Brussels,
07/04/2005



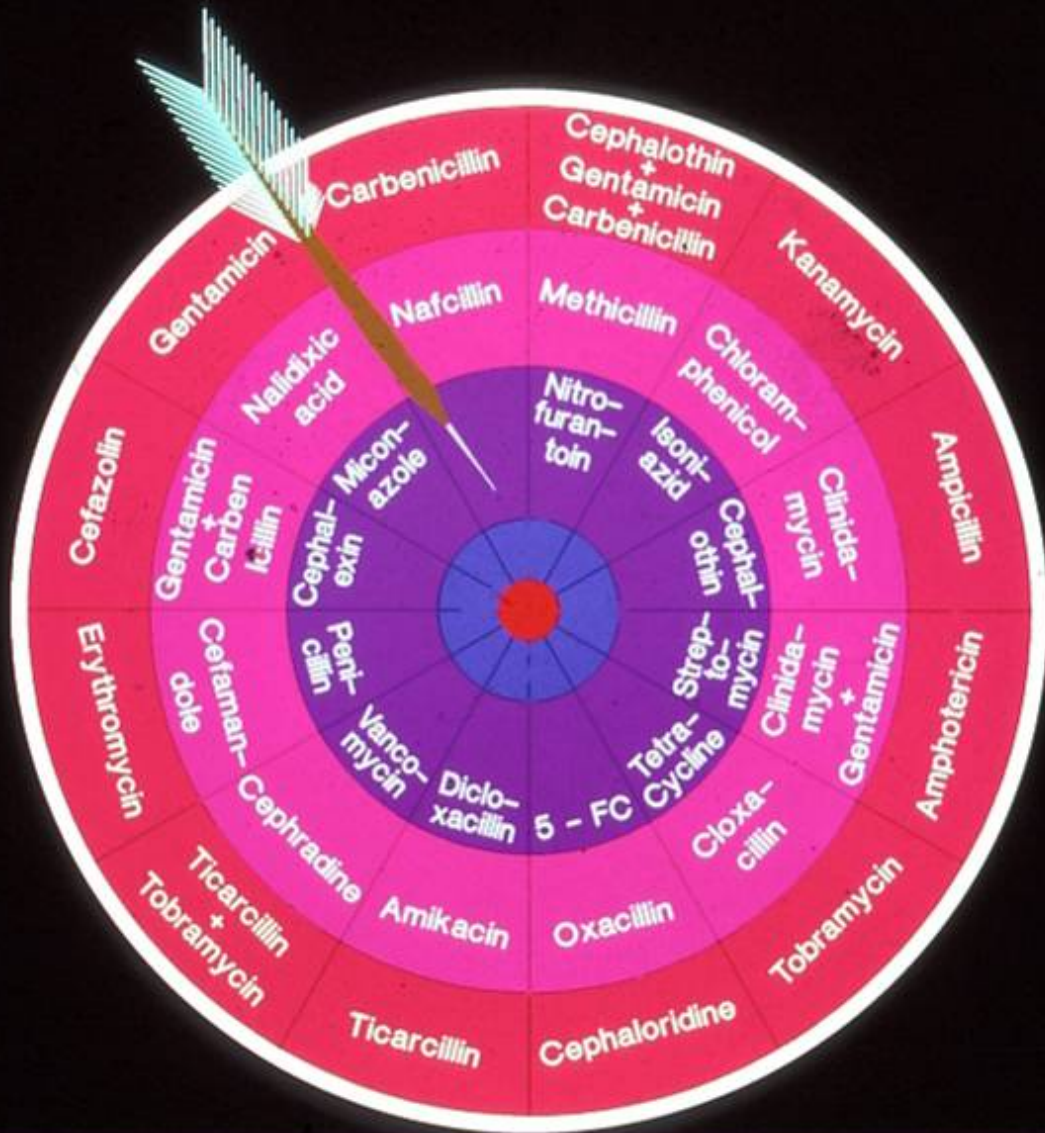
ANTIBIOTIC

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★ MICROBE ★



**ANTIBIOTIC RESISTANCE
PROBLEM**



Streptococcus pneumoniae is one of the most important pathogens exhibiting both a high degree of morbidity and a considerable rate of mortality.

Penicillin G has been considered as the drug of choice in the treatment of pneumococcal infections, though its clinical utility has been hampered by the appearance of **penicillin-insusceptible** isolates.

In 1967, the first **penicillin-insusceptible** *S. pneumoniae* was reported from Australia.

In **Belgium**, the first isolates with reduced susceptibility to penicillin were reported in **1980** by Vanhoof et al.

In **Belgium**, steadily **increase** of reduced susceptibility to penicillin since **1994-1995**.

Follow-up of Antibiotic Resistance in *S. pneumoniae*

- **National Reference Centre,
University Hospital Gasthuisberg.**

- **The Belgian SPN Study Group.**
 - **Institute Pasteur Brussels.**
 - **15 participating Centres**
 - **National Reference Centre**

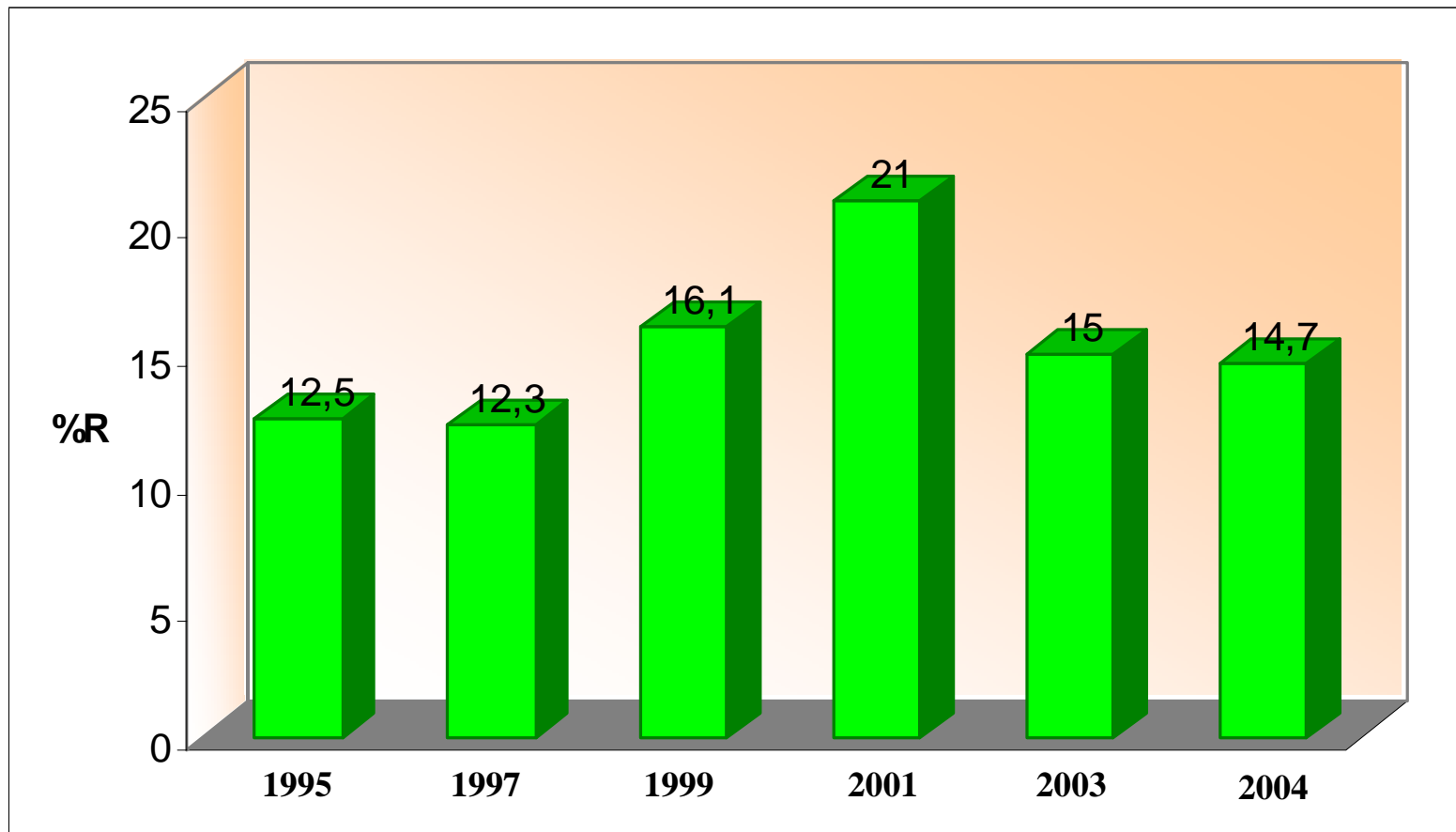
Factors impacting Resistance in *S. Pneumoniae*

- Usage and clones
- Geography
- Population density (urban/rural)
- Specimen source
- Vaccine use
- Travel
- Social/cultural behaviour
- Climate
- Hospitalisation, day care, LCF
- Age, gender
-

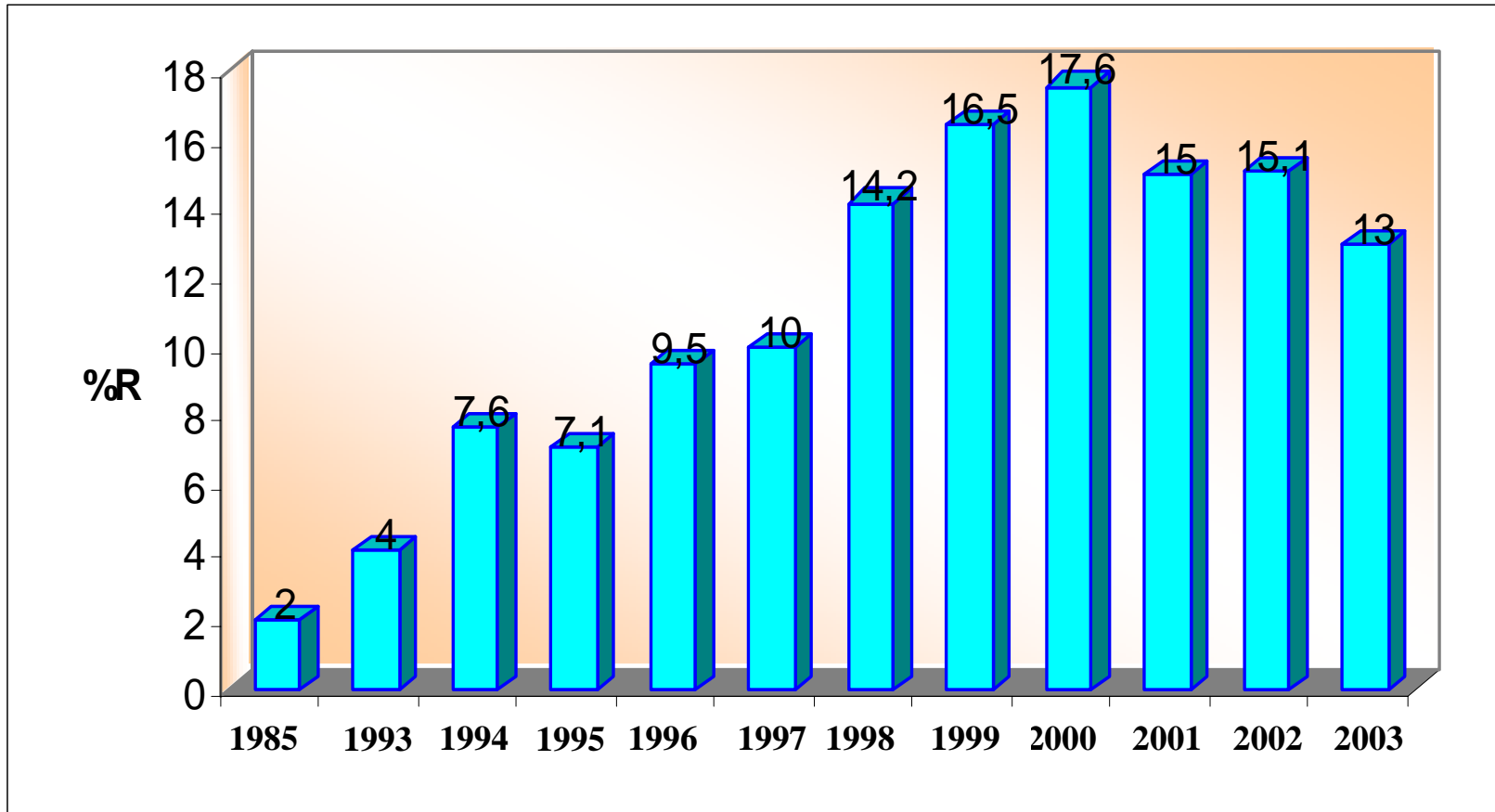
***S. Pneumoniae*: epidemiology of resistance**

➤ **Resistance Rates**

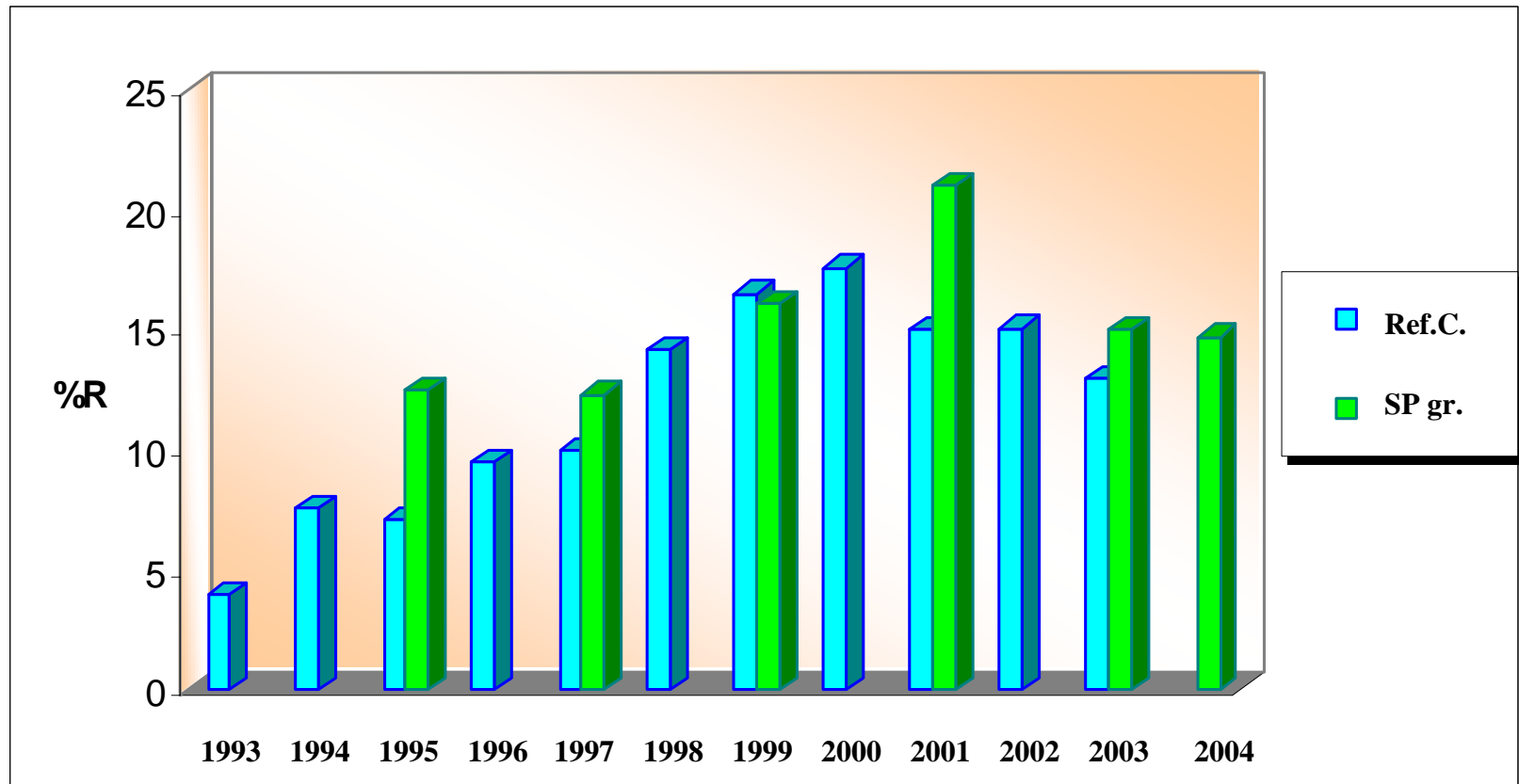
Evolution of Penicillin Resistance in Belgium following the Belgian SP-Study Group (Vanhoof et al)



Evolution of Penicillin Resistance in Belgium following the National Reference Centre



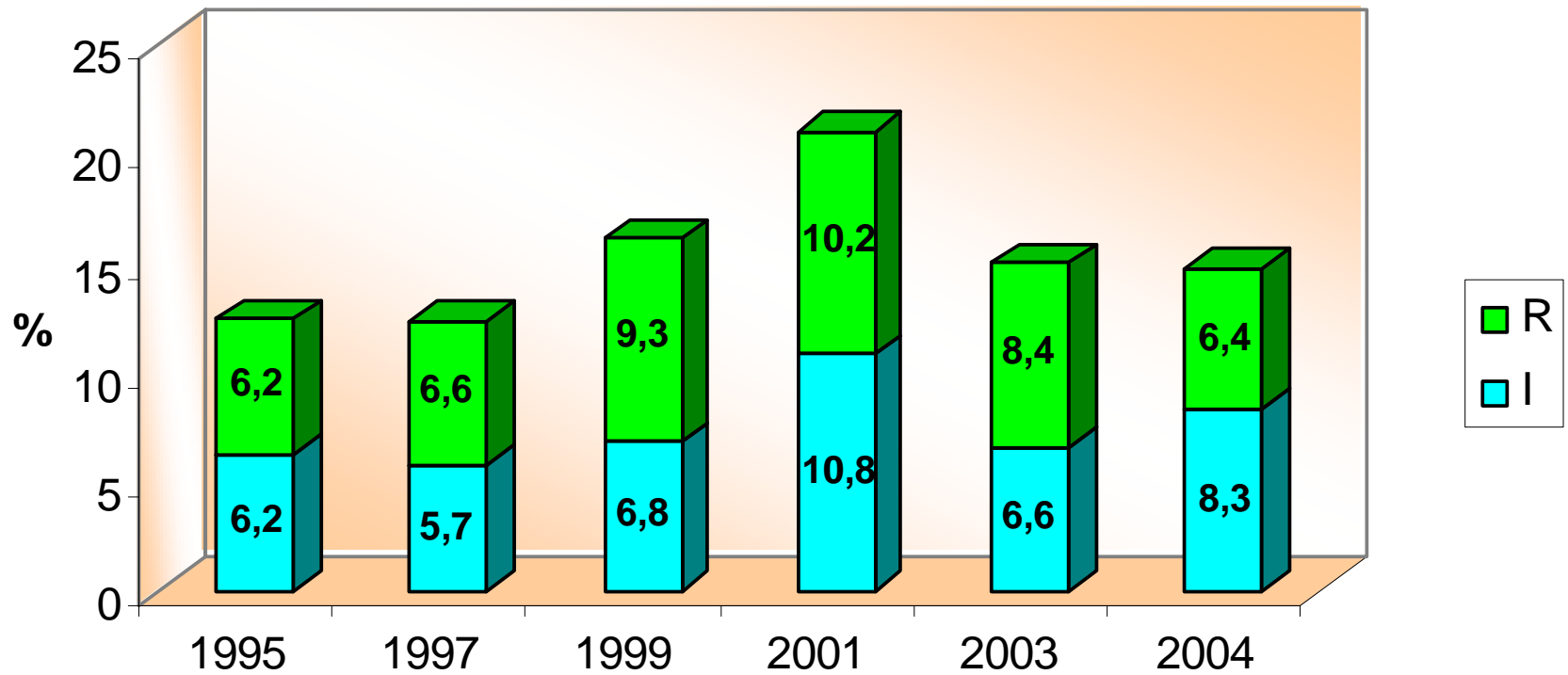
Comparison of the Evolution of Penicillin Resistance in Belgium



RESULTS

Resistance rates

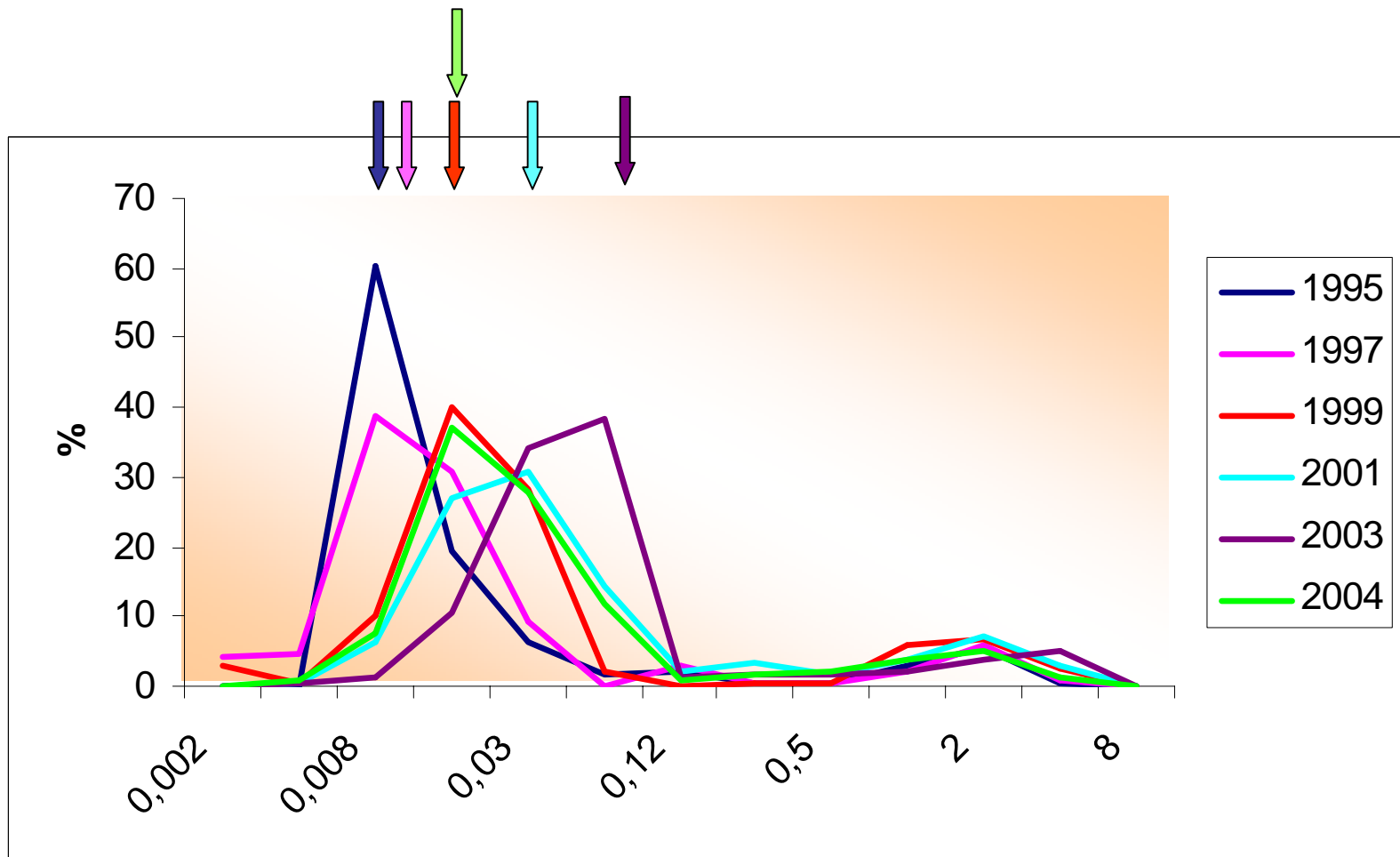
Evolution of Pen-insusceptibility



Resistance rates (%): β -lactams

Antibiotic	1995	1997	1999	2001	2003	2004
PEN	12.5	12.3	16.1	21.0	15.0	14.7
AMX/C	0	0	1.0	1.6	2.6	1.2
CRX	9.1	9.9	15.1	16.9	13.6	12.7
CTX	6.2	7.6	12.7	7.3	4.9	6.2

Evolution of MIC Distributions: Penicillin



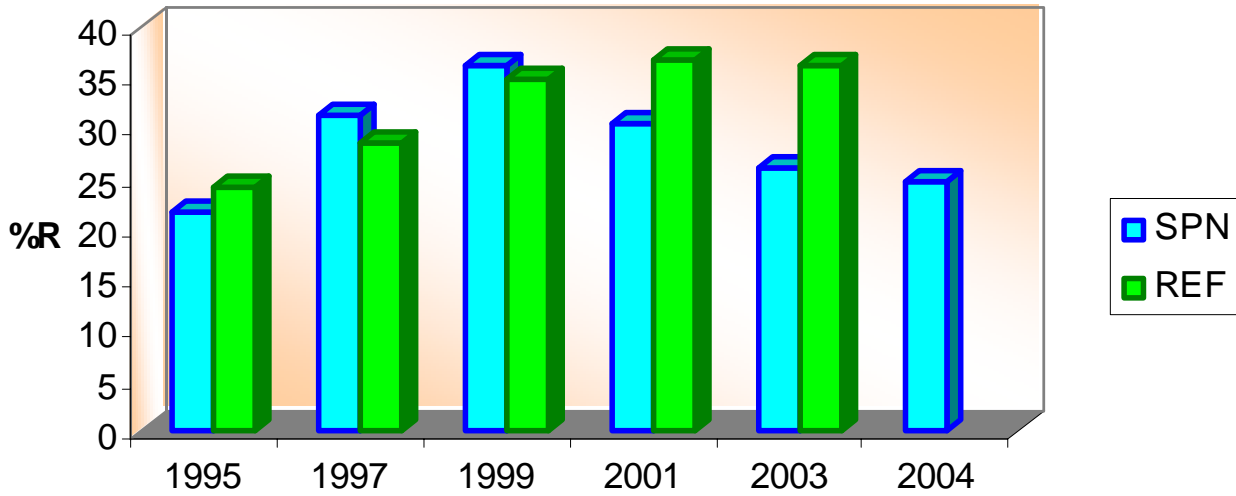
Resistance rates (%): Fluoroquinolones

Antibiotic	1995	1997	1999	2001	2003	2004
CIP	NT	NT	15.6	11.2	13.8	9.0
LEV	NT	NT	2.0	2.5	3.3	2.8
MOX	NT	NT	NT	NT	0.6	0.2
OFL	NT	NT	NT	NT	13.5	9.0

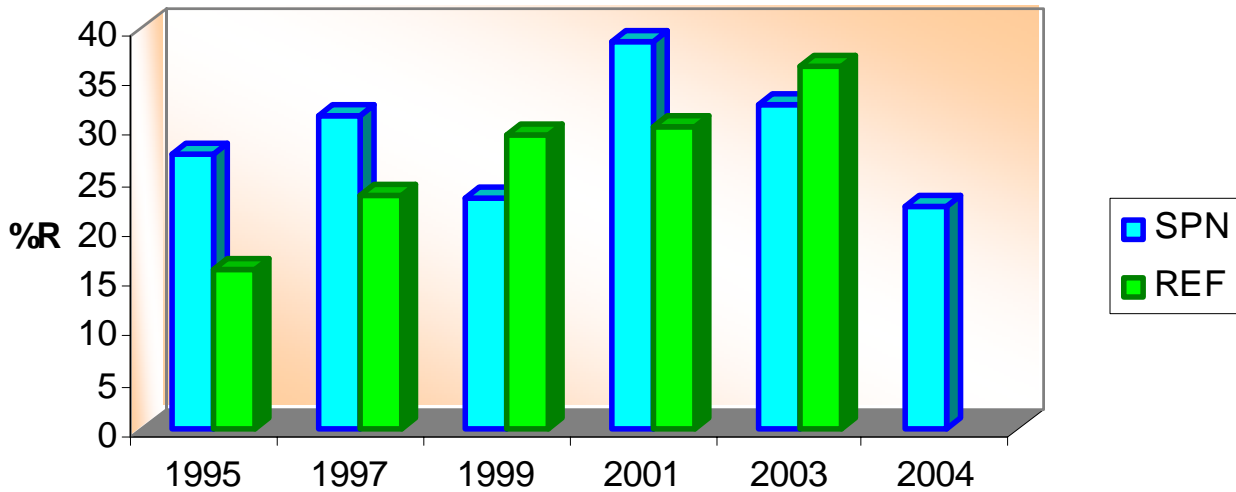
Resistance rates (%): MLS + TET

Antibiotic	1995	1997	1999	2001	2003	2004
ERY	21.6	31.4	36.1	30.3	26.1	24.7
TEL	NT	NT	NT	NT	0.8	0.2
TET	27.3	31.1	22.9	38.5	32.3	22.1

Evolution of ERY Resistance

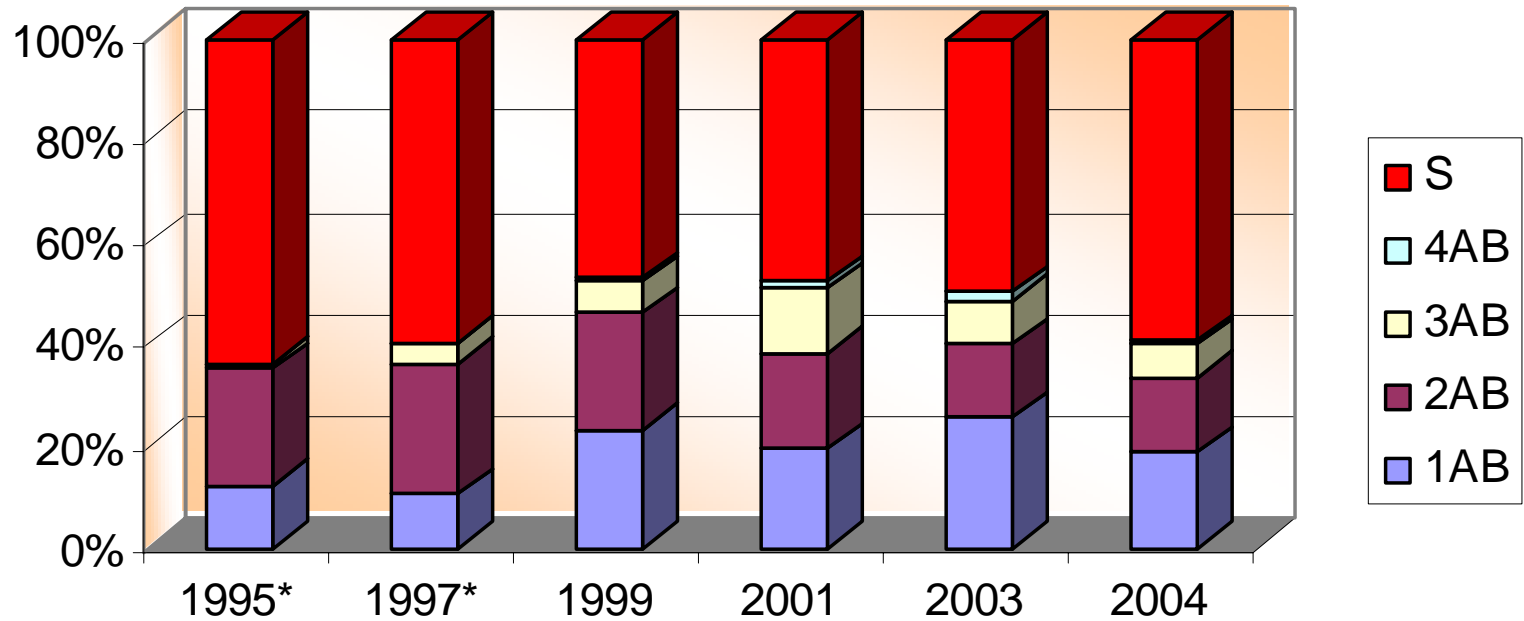


Evolution of TET Resistance



Distribution of the susceptibility Phenotypes

Evolution of Phenotypes



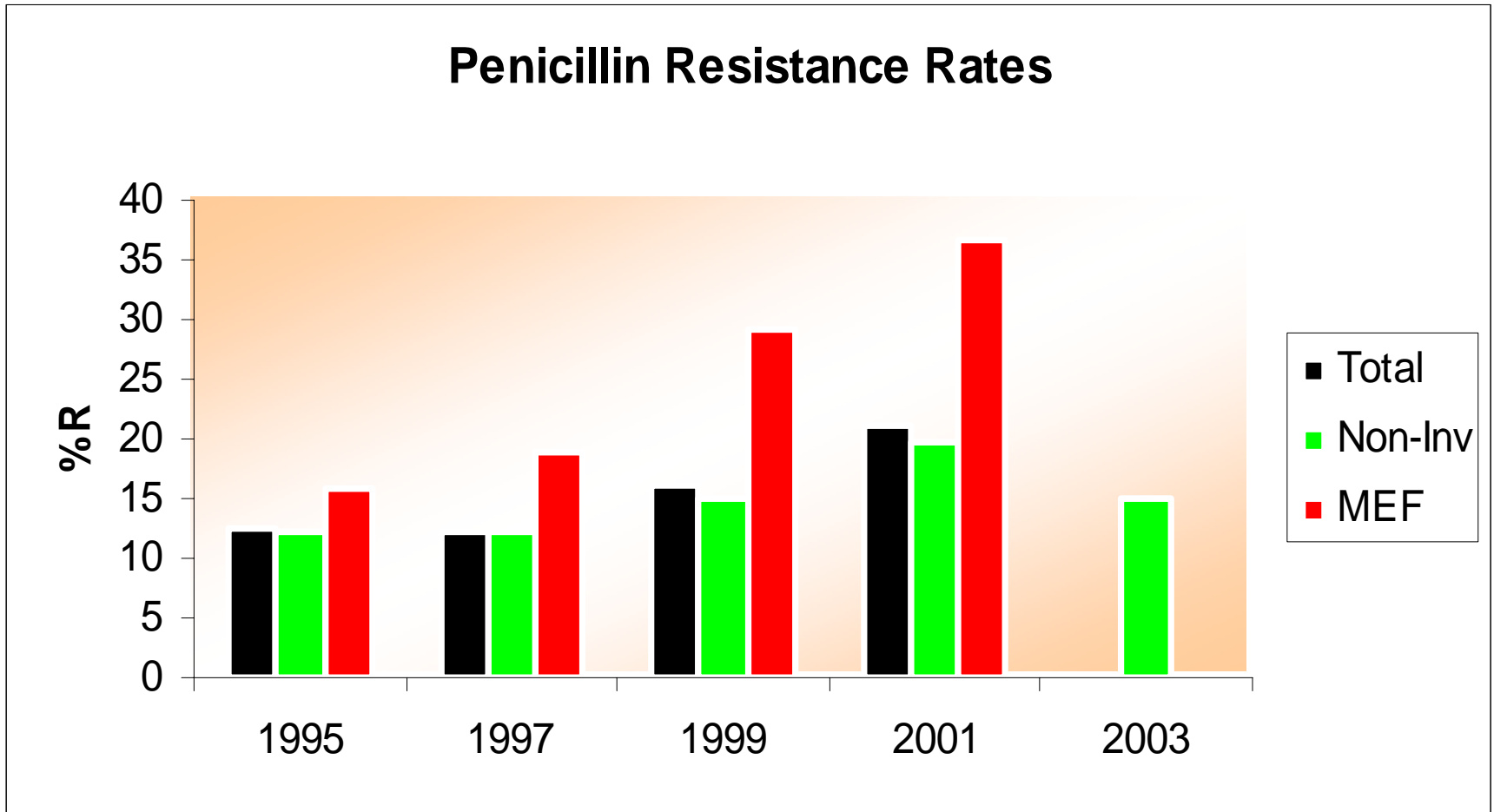
***S. Pneumoniae*: epidemiology of resistance**

➤ **Resistance and sampling site**

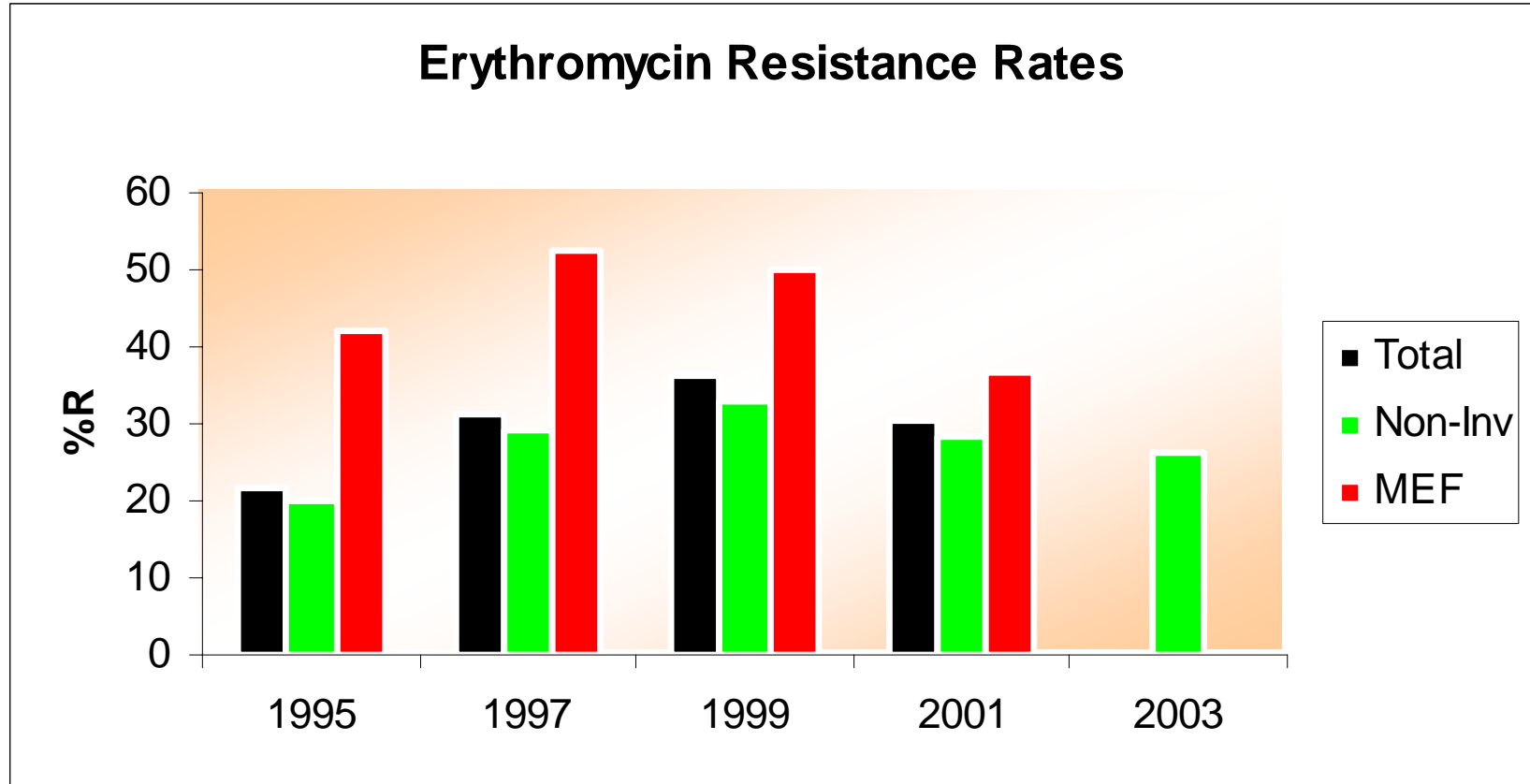
- **MEF: 1.63 more likely than blood to be Pen-NS**
- **MEF: 1.43 more likely than CSF to be Pen-NS**

Multivariate logistic regression analysis of Belgian Data (Reference Centre) by R. Mera (USA).

Impact of MEF isolates on Resistance rates (1)



Impact of MEF isolates on Resistance rates (2)

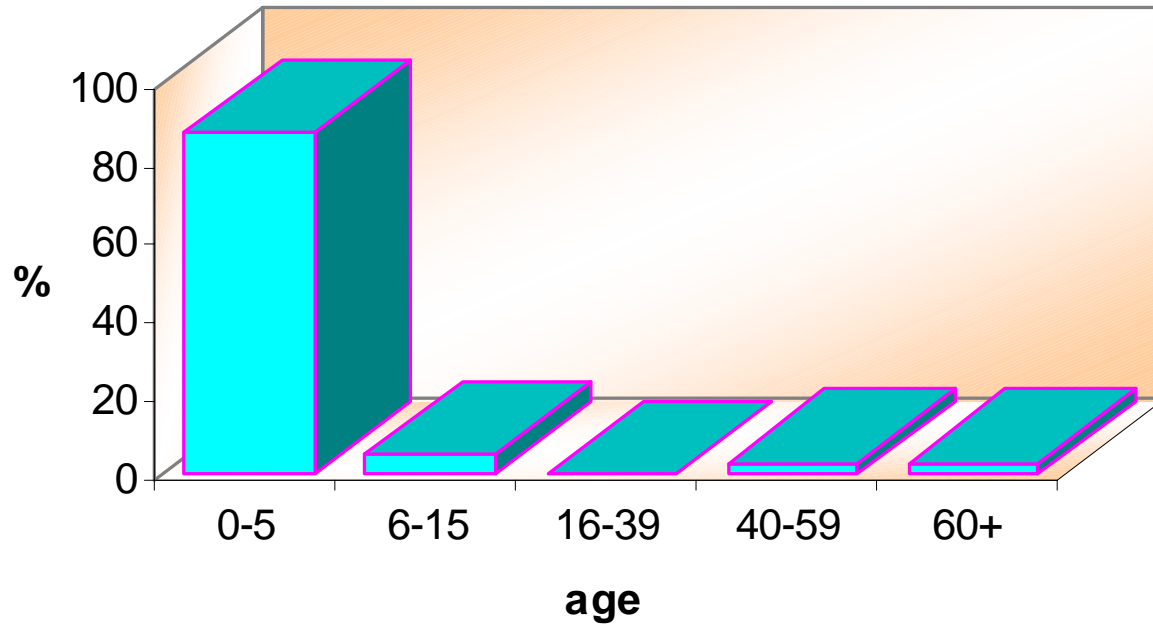


RESULTS

Resistance rates (%) in MEF and Non Invasive isolates

Antibiotic	MEF isolates	Non Inv.	
Penicillin	26.6	15.4	0.01>P>0.001
Amoxicillin	1.1	1.0	NS
Cefotaxime	1.1	3.2	NS
Imipenem	3.2	3.0	NS
Ciprofloxacin	9.3	14.1	NS
Erythromycin	44.7	27.7	P<0.001
Tetracycline	36.2	29.8	NS

Age distribution in MEF isolates



***S. Pneumoniae*: epidemiology of resistance**

➤ **Geographic differences**

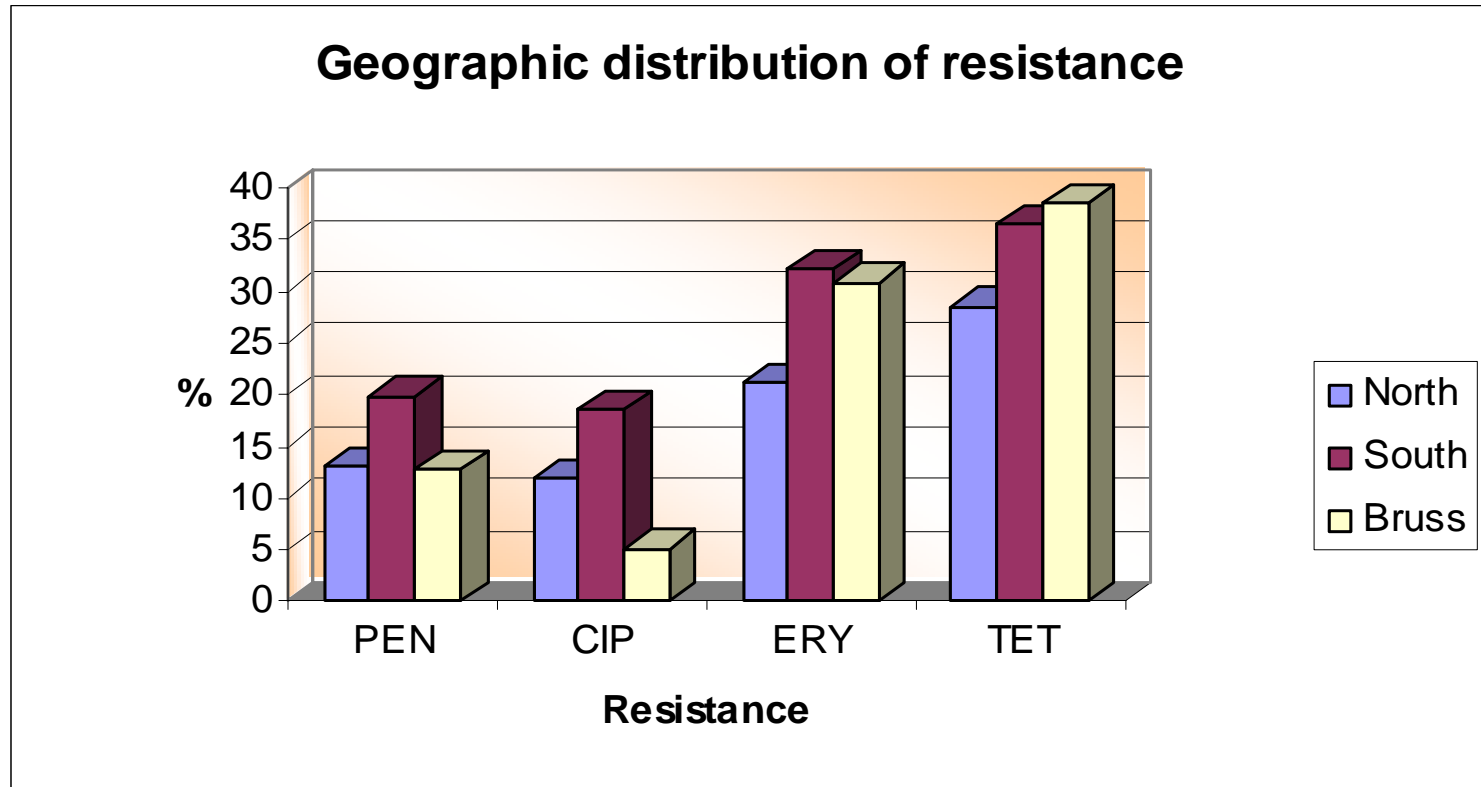
Penicillin insusceptibility (%) in France (2003)

Region	Total	Adult	Pediatric
France	50	43	62
Nord-Pas de Calais	48	35	68
Champagne-Ardennes	43	38	55
Lorraine	44	43	45
Alsace	45	42	52

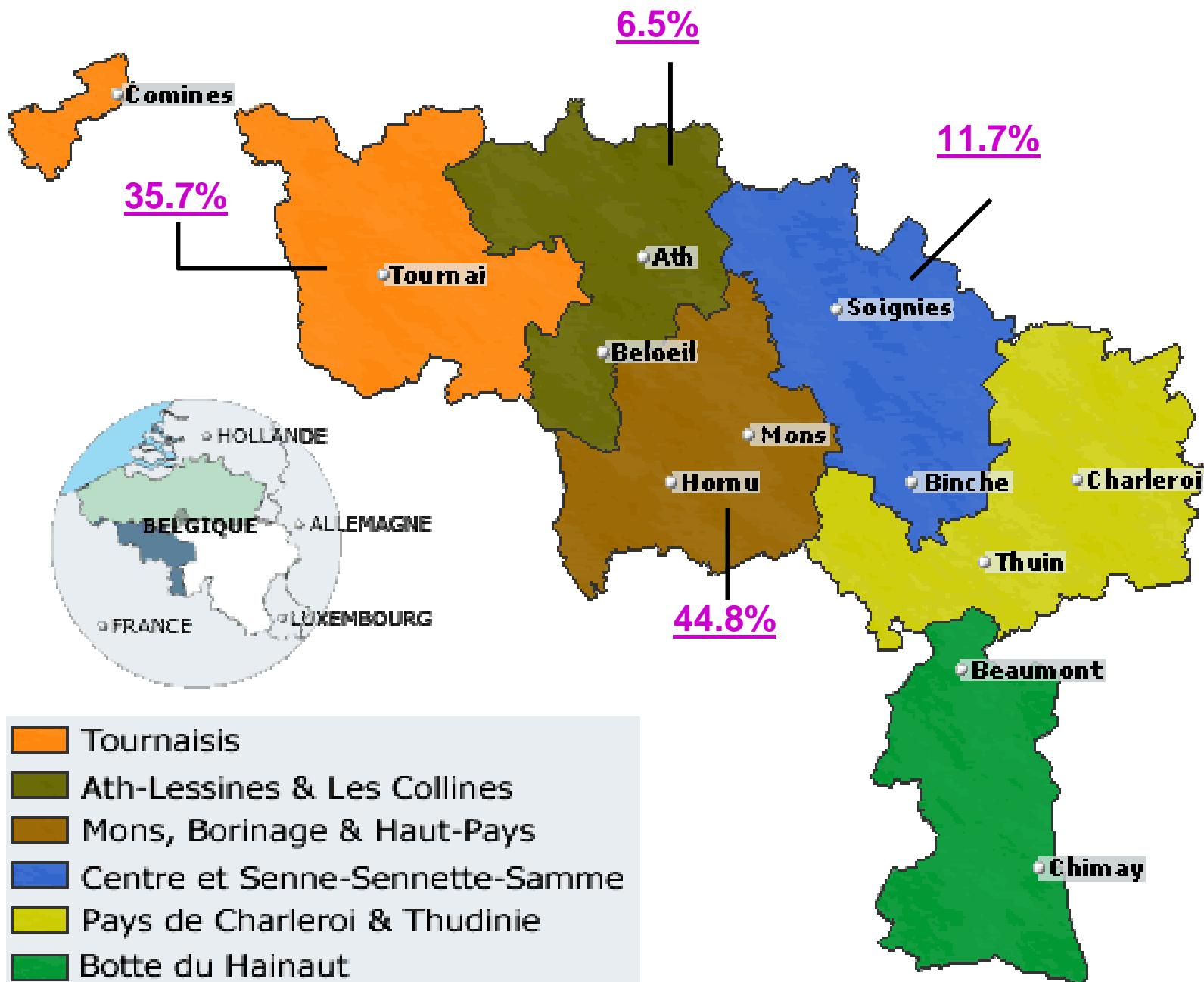
	1995	1997	1999	2001	2003	2004
France	38.0	40.5	44.0	55.0	50.0	NA

RESULTS

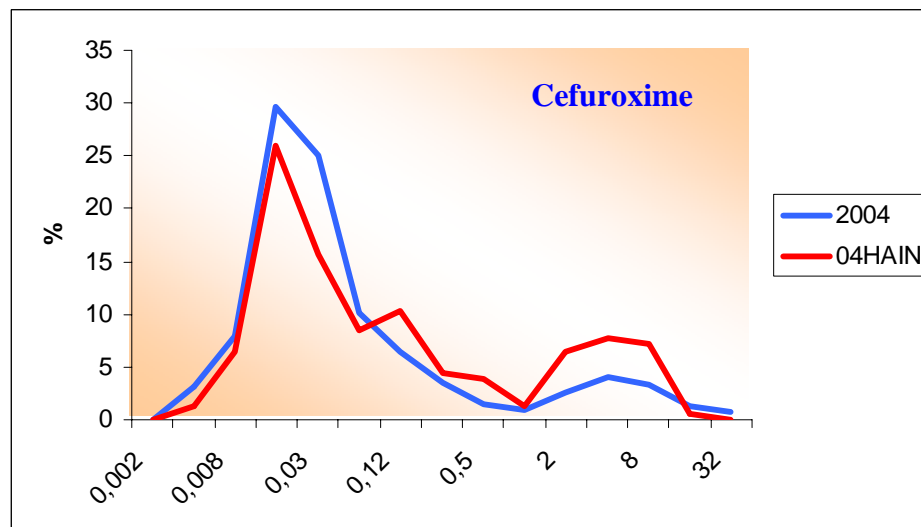
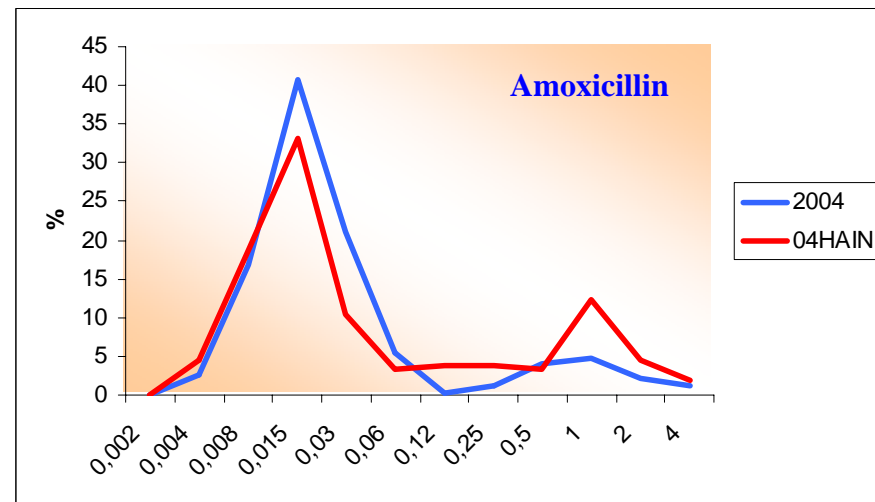
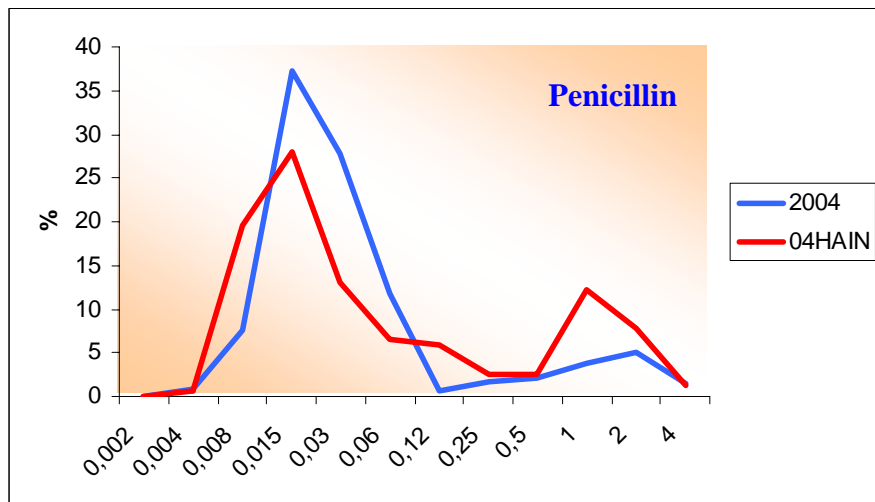
Resistance rates: geographic distribution



CIP: Bruss < South ($0.05 > P > 0.02$)*

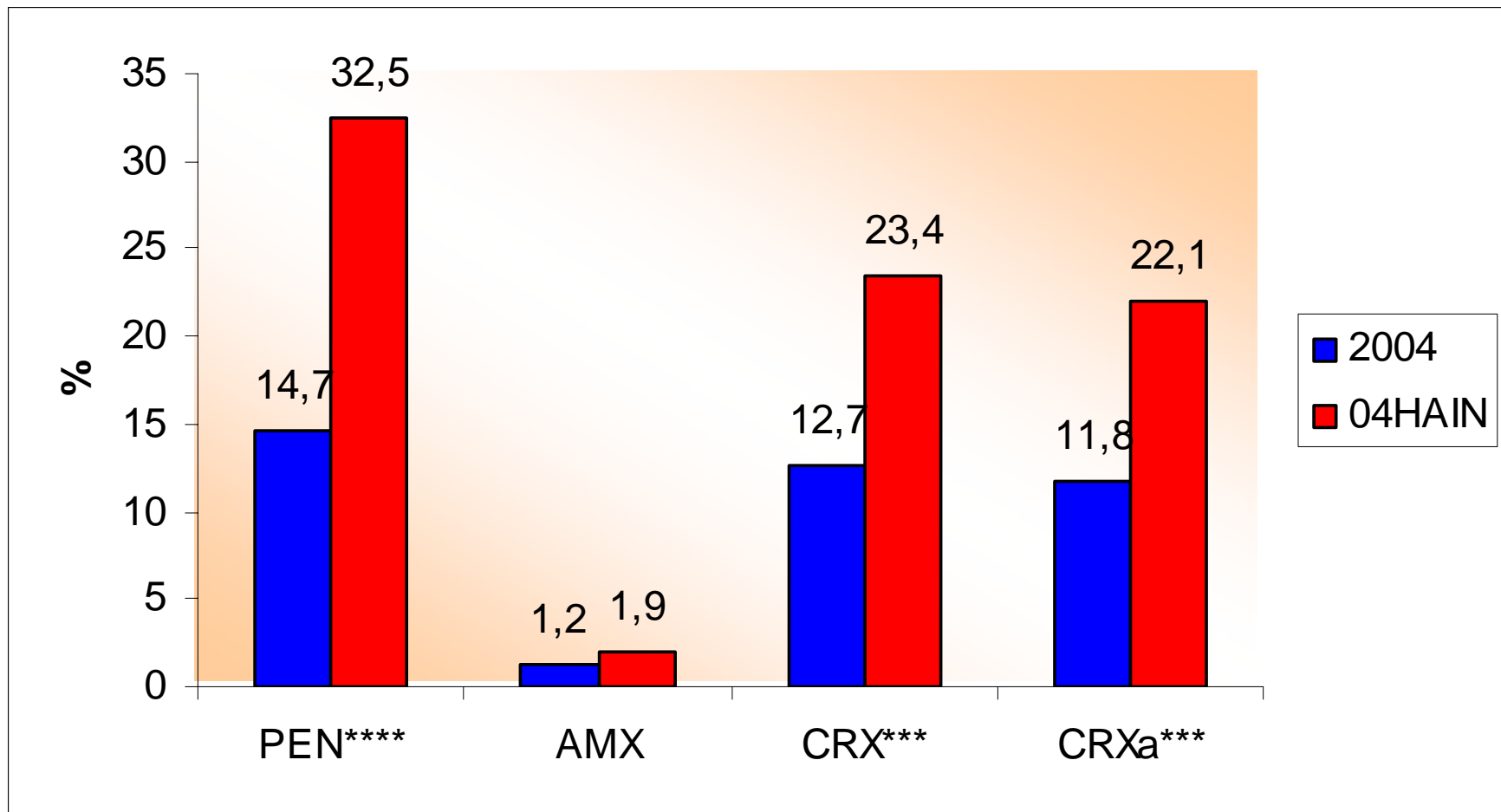


MIC Distributions: β -lactams



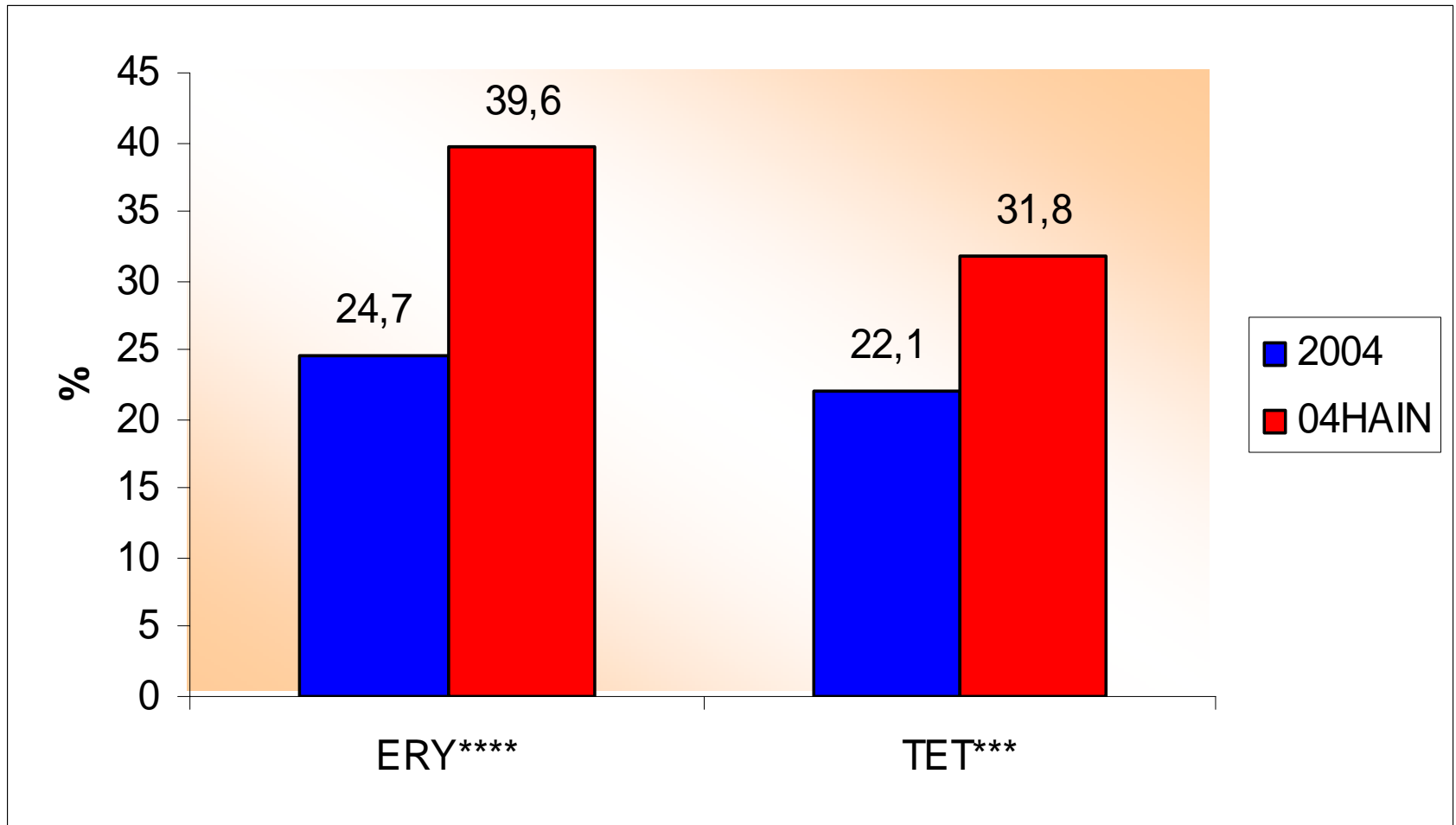
RESULTS

Resistance rates (%): β -lactams

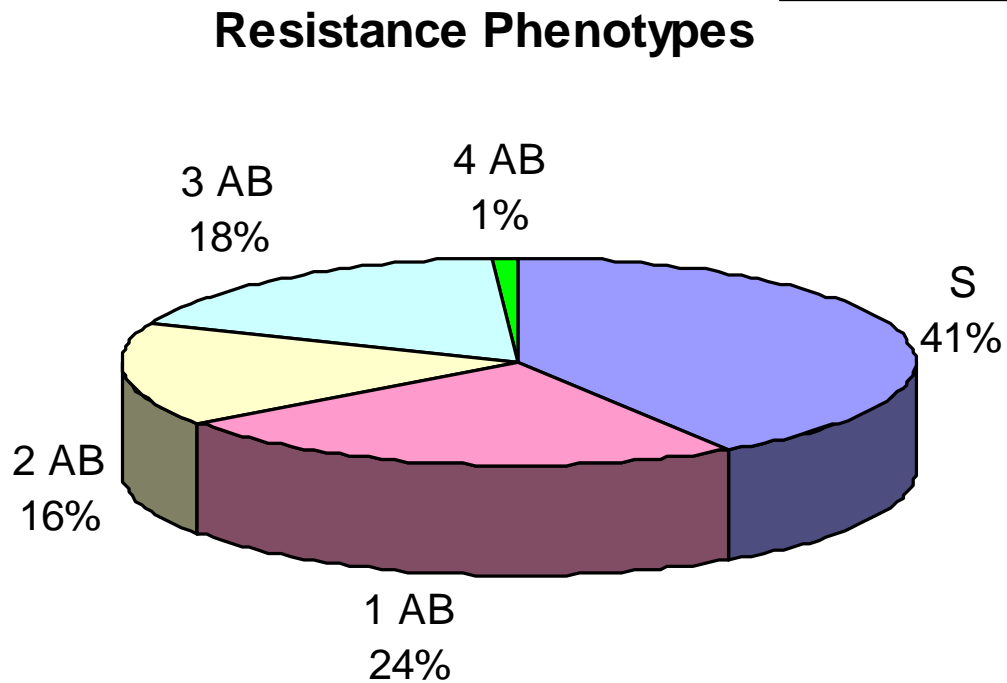
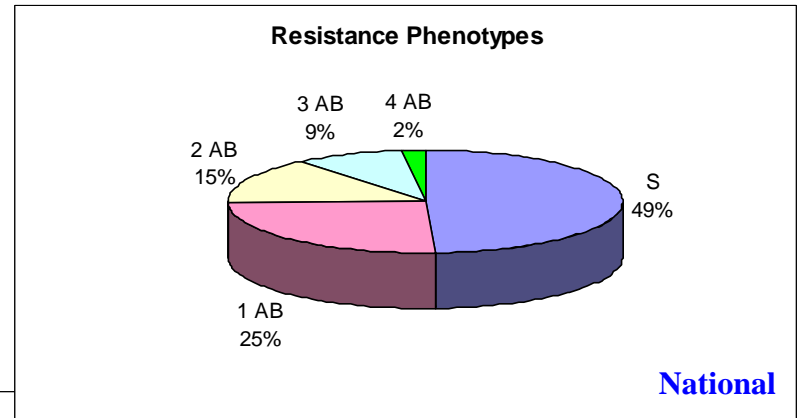


RESULTS

Resistance rates (%):MLS +Tetra



Distribution of the susceptibility Phenotypes



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***S. Pneumoniae*: epidemiology of resistance**

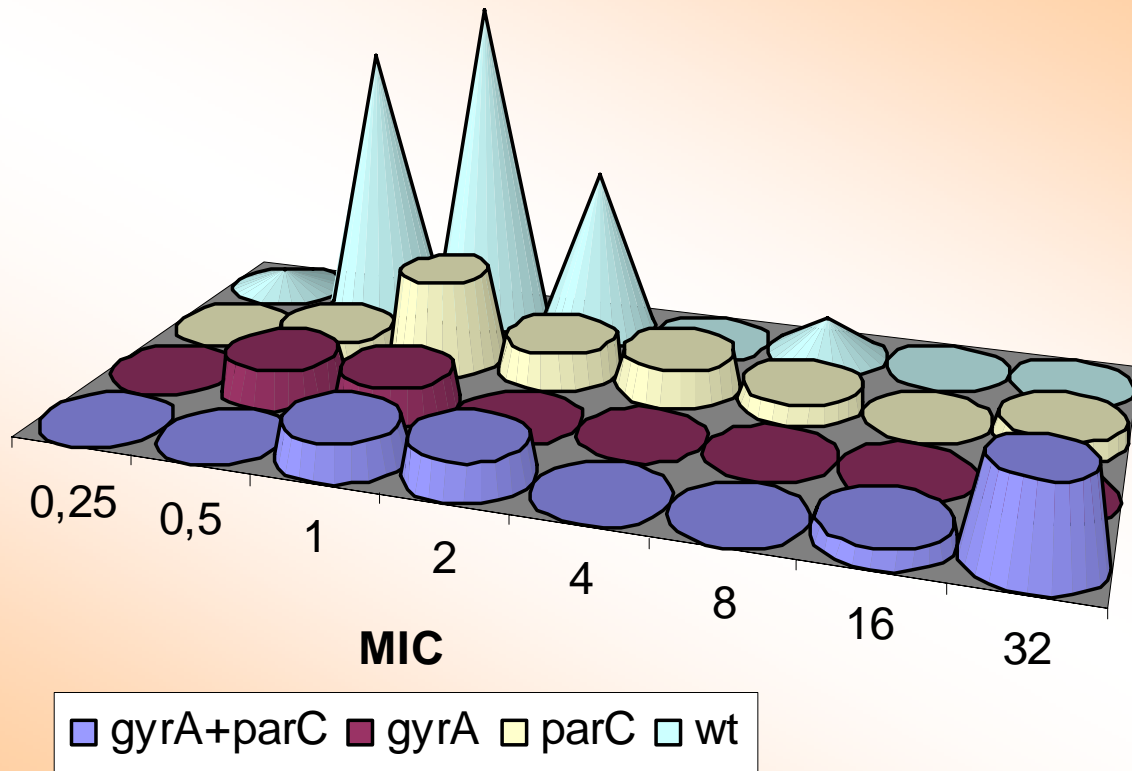
Resistance Mechanisms

➤ Fluoroquinolone Resistance

FQ Resistance Mechanisms in 71 *S.pneumoniae* isolates (1999-2003)

Type of Mechanisme	%
gyrA	5.6
parC	16.9
gyrA+parC	14.1
Wt and PmrA⁺	60.6
Wt and Pmr⁻	2.8

MIC distributions and type of mutation in *S.pneumoniae* isolates

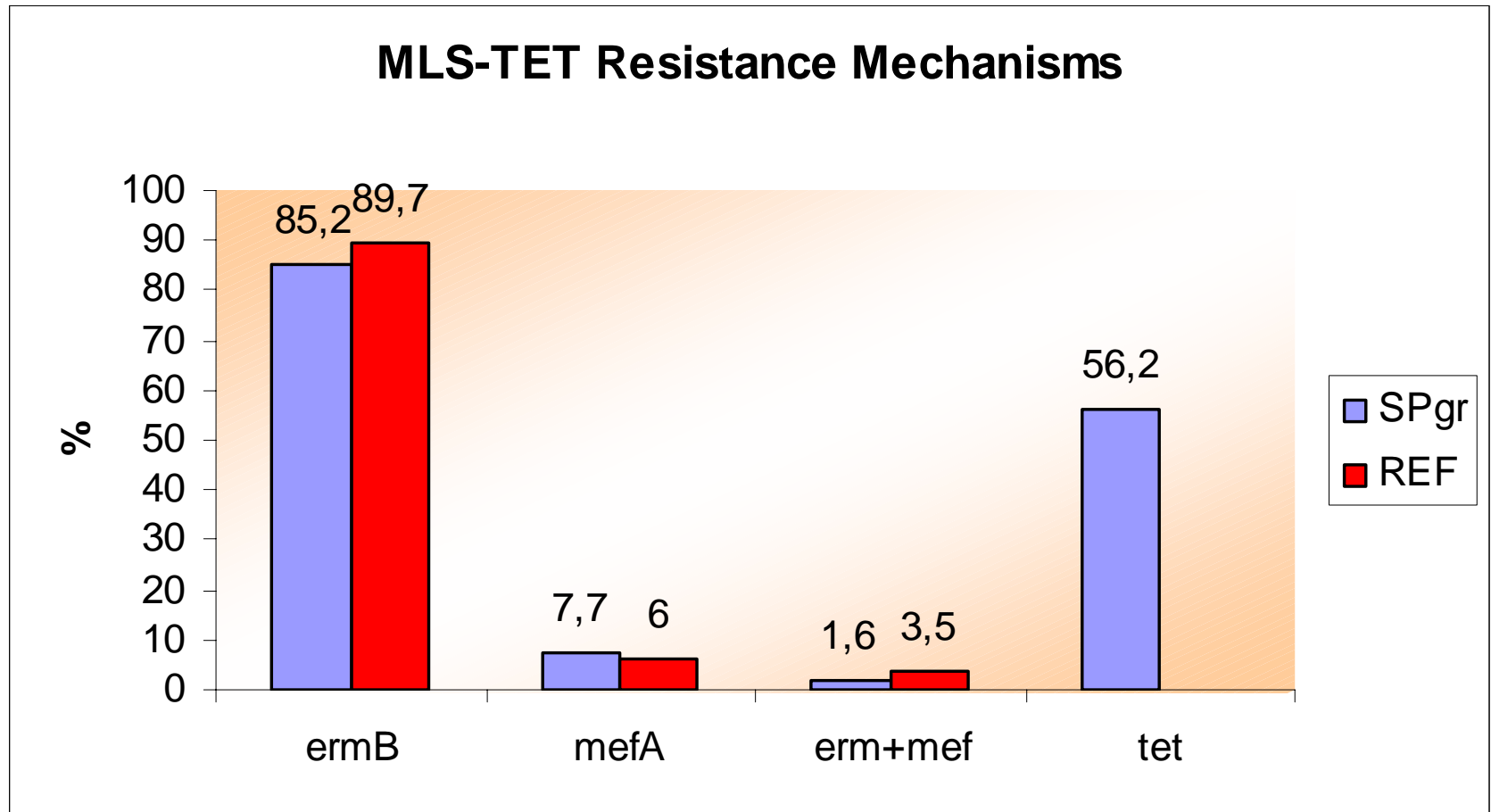


***S. Pneumoniae*: epidemiology of resistance**

Resistance Mechanisms

➤ MLS Resistance

MLS-TET Resistance Mechanisms in *S.pneumoniae* isolates



CONCLUSIONS

CONCLUSION (1)

SUVEILLANCE OF THE RESISTANCE EPIDEMIOLOGY

(resistance rates, population distributions,...)

STUDY OF FACTORS WITH IMPACT ON RESISTANCE DEVELOPMENT

(clinical, geographic, demographic,...)

STUDY OF RESISTANCE MECHANISMS

(importance of efflux,)