

CAP GUIDELINES :

Why differences between Belgian and American/Canadian

UCL

23/11/2001

Yvan Valcke

Belgian situation

= different, in terms of :

1. Epidemiology :

- incidence of CAP pathogens**
- resistance patterns**

2. Availability of anti-microbial drugs :

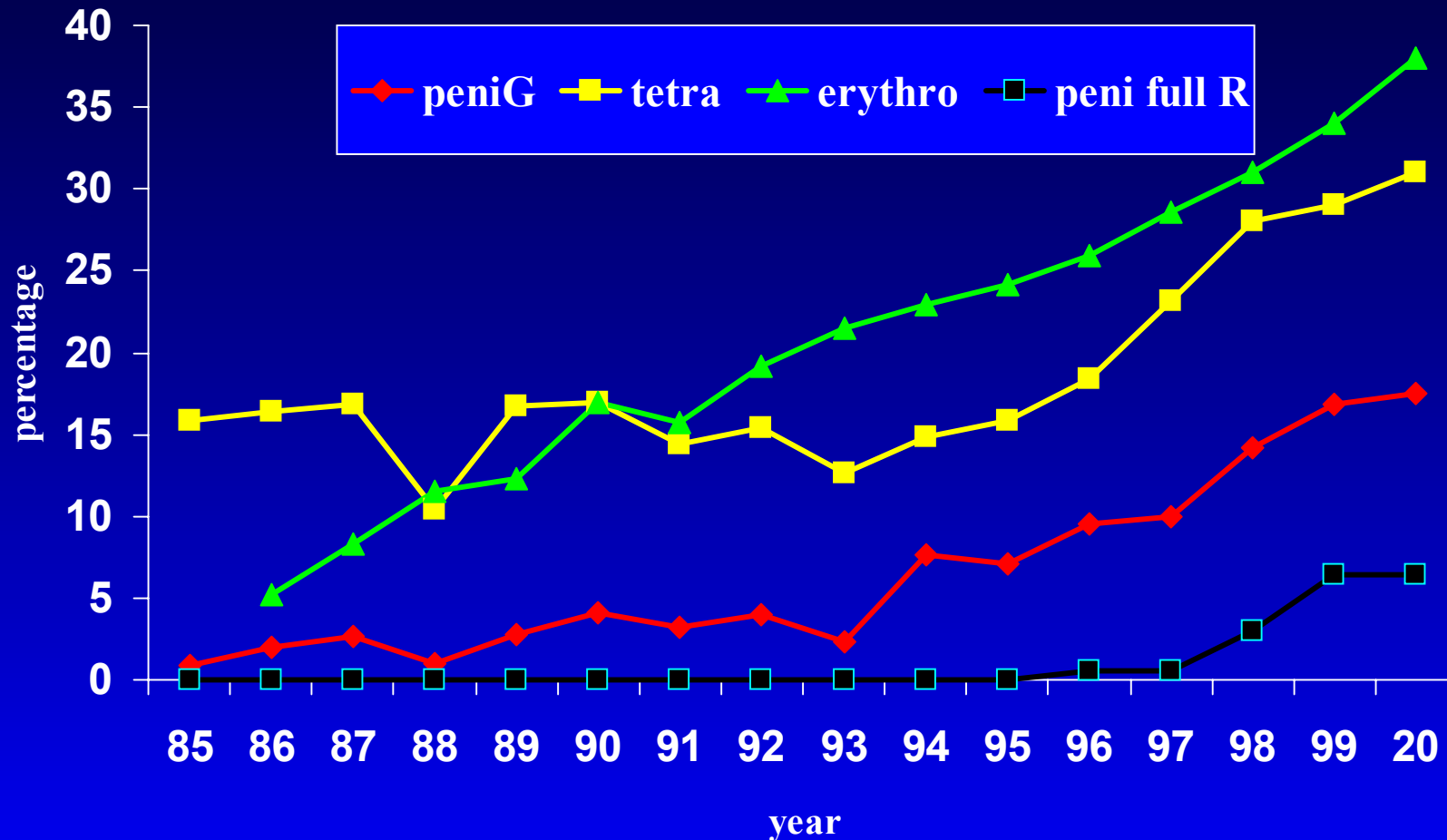
- In new FQ group: only levofloxacin available**

Belgian situation

Incidence of Respiratory Pathogens in CAP

- **Few epidemiological studies !!!!**
- **No pathogen identified in 50-60 % of CAP**
- **S. pneumoniae most frequent**
- **“Atypical”**
 - **incidence = ??????**
 - **value of serological testing = ????**
 - **only few studies using surface-gen detection (PCR): incidence very low !!!!**

Evolution of *S. pneumoniae* resistance in Belgium



Belgian situation

Antibiotic resistance

Streptococcus pneumoniae

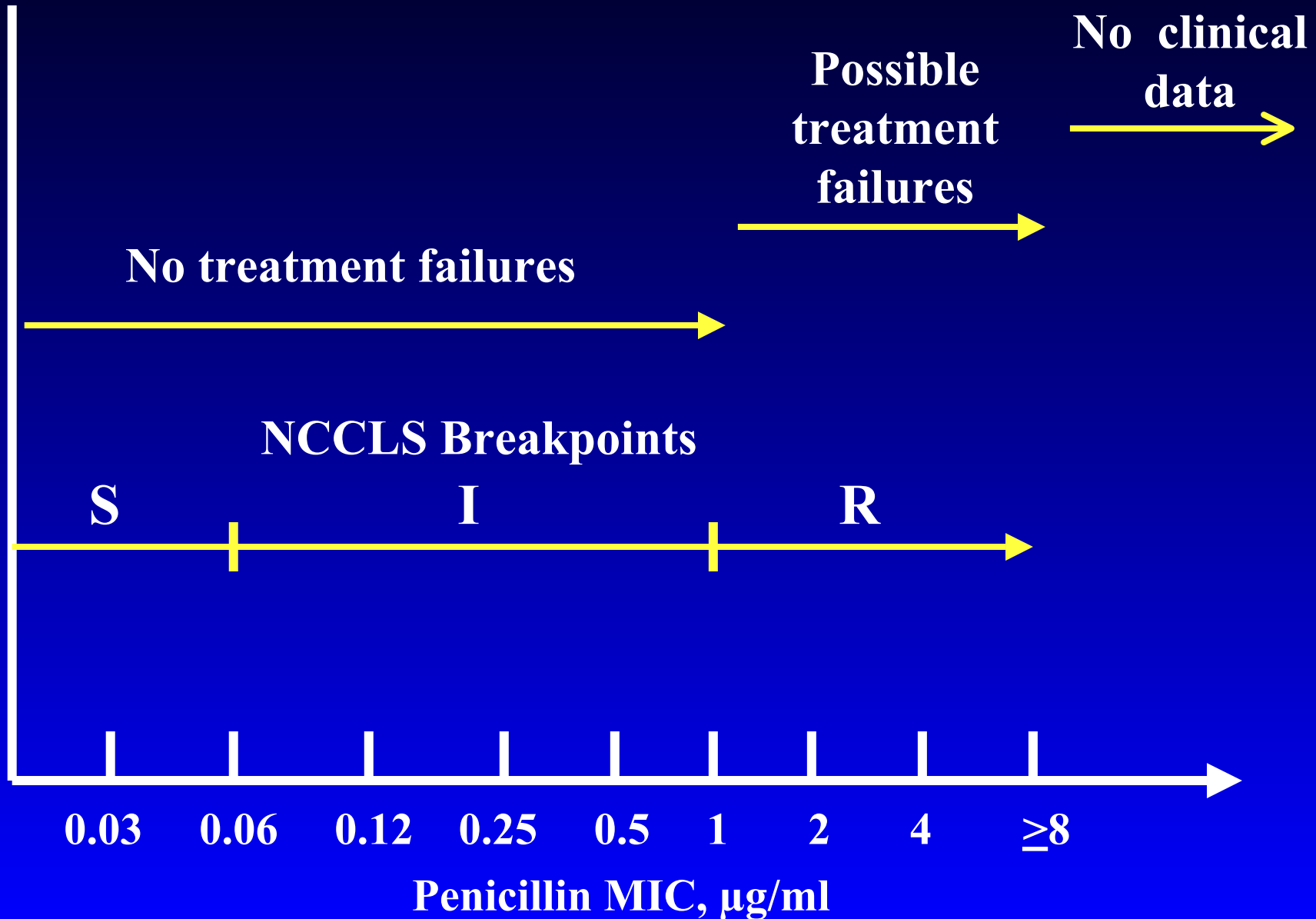
	2000 invasive n=1216 (1)	1998 - 1999 respiratory n=205 (2)	1999 - 2000 respiratory n:637 (3)
penicillin G (I + R)	17,6 % 11,6 + 6,0	16,1 % 6,8 + 9,3	18,2 % ND
cefotaxime	5,7 %	12,7 %	ND
erythromycin	36,5 %	36,1 %	38,5 %
tetracycline	31,7 %	22,9 %	33 %
ofloxacin / ciprofloxacin	0,3 %	1,5 %	1,1 %

1: J. Verhaegen. Nat Reference Laboratory.

2: R. Vanhoof et al. Acta Clin Belg 2000; 55: 312-322.

3: J. Verhaegen, et al. Telithromycin study ICAAC 2000.

CAP : Peni-Resistance vs. Clinical Outcomes



Belgian antimicrobial resistance patterns of respiratory pathogens

- *S. pneumoniae* :
 - tetracycline resistance : 31.7 %
 - erythromycin resistance : 36.5 %
 - complete cross-resistance between all (neo-) macrolides/azalides (including miocamycin) in 90% of erythromycin-resistant strains
 - No cross resistance with telithromycin (ketolide)

Macrolide-resistant *S. pneumoniae*

RESISTANCE MECHANISMS

- BELGIUM

methylation of ribosomal RNA (erm B gene): 92 %

efflux (mef E gene): 3 %

both (erm B gene + mef E gene): 5 %

J Antimicrob Chemother 2000; 45: 119-121.

- USA

mostly efflux mechanism

MIC efflux << MIC ribosomal :
In Belgium: macrolide resistance = treatment failure

Belgian antibiotic resistance :

Haemophilus influenzae

- **M. Delmée et al. Acta clin Belg 1996; 51: 237-243.**
 - beta-lactamase-positive: 16,7 %
 - bla-neg ampi R: 1,1 %
- **P. De Mol unpublished results 2000 (n=474)**
 - beta-lactamase-positive: 16,0 %
 - bla-neg amp R: 3,0 %

Belgian antibiotic resistance:

Moraxella catarrhalis

- **P. De Mol. unpublished data 2000 (n=164 clinically significant isolates)**
 - beta-lactamase positive: 75 %**
- **remain susceptible to amoxi-clav, cephalo 2, macrolides and fluoroquinolones**

Antimicrobial resistance patterns of respiratory pathogens : conclusions

- Very high resistance rates for all (neo-) macrolides, azalides and tetracyclines make them contra-indicated in monotherapy if *S. pneumoniae* is a possible cause of CAP
- *S. pneumoniae* increasingly penicillin-resistant but (increased dosages of) b-lactams still first choice for *S. pneumoniae* CAP
- Production of b-lactamase in *H. influenzae* stable around 17%

Belgian situation

Availability of antimicrobials

- **Levofloxacin is the only NFQ available**
- **Levofloxacin: weaker antipneumococcal in vitro activity :
gemifloxacin > moxifloxacin > levofloxacin**
- **Weaker in vitro activity may lead to higher rates of
resistance selection, therefore when FQ are indicated:
USE THE MOST POTENT**
- **Reports of treatment failure and resistance development
with levofloxacin**



Levofloxacin : Reserved for selected patients with CAP :

- 1. Adults for whom one of the first-line regimens failed**
- 2. Allergy to first-line agents**
- 3. Documented infection with highly resistant *S. pneumo* (MIC \geq 4.0 μ g/ml).**

Working group CAP of IDAB 2000

- **Herman Goossens**
- **Paul Jordens**
- **Willy Peetermans**
- **Yves Sibille**
- **Yvan Valcke (chairman)**
- **Johan Van Eldere**
- **Yves Van Laethem**
- **Walter Vincken**

**Belgian guidelines on the initial
diagnostic and therapeutic approach of
CAP
in the immunocompetent patient**

**Update of the CAP consensus text of
the IDAB
2000**

BELGIAN CAP - GUIDELINES

Premises (1)

- 1. No demonstrated need for systematic coverage of atypicals in subgroups 1, 2 and 3**



atypicals in subgroups 1, 2 and 3 should be covered only when suspected on clinical or epidemiological grounds

- 2. In Belgium, presently available macrolides, azalides and older quinolones offer inadequate coverage of *S. pneumoniae***

BELGIAN CAP - GUIDELINES

Premises (2)

3. High β lactam dosages are preferred :
 - ↓ resistance selection
 - adequate time > MIC for Peni I
Peni R | S. pneumoniae
4. First generation cephalosporins (also cefaclor) are less active than amoxicillin or cefuroxime against Peni I / R S. pneumoniae

BELGIAN CAP - GUIDELINES

Premises (3)

- 5. Parenteral 3rd generation cephalosporins are only first choice in subgroup 4, especially when :**
 - previous b-lactam treatment (within last 15 days ?)**
 - previously hospitalized patients**
 - proven/potential simultaneous CNS spread**

- 6. DD atypical *versus* bacterial CAP :**
 - only reliable in subgroup 1**

CAP - Classification

SUBGROUPS

- 1. Outpatient, < 60 yr, no comorbidity**
- 2. Outpatient, \geq 60 yr and/or comorbidity**
- 3. CAP requiring hospitalization**
- 4. CAP requiring ICU-hospitalization**

1. Outpatient, < 60 yr, no comorbidity

ATYPICAL

versus

BACTERIAL

λ **M. pneumoniae**

λ **S. pneumoniae**

λ **C. pneumoniae**

λ **H. influenzae (rare)**

λ **Virus**

λ **(Legionella)**



λ **Neo-macrolide/azalide PO**

λ **Doxycycline PO**



λ **Amoxicilline 0.5-1g q8h PO**

λ **Cefuroxime-axetil 0.5g q8 PO**

λ **NFQ (beta-lactam allergy)**

2. Outpatient, ≥ 60 yr and/or comorbidity

- **First choice:**

amoxi/clav 875/125 mg q8h PO

+/- neo-macrolide or azalide PO

- **Alternative:**

- cefuroxime - axetil 500 mg q8h PO

+/- neo-macrolide or azalide PO

- NFQ (beta-lactam allergy)

3. Hospitalized CAP

- **First choice:**

- amoxi/clav **1g q6h IV**

or

- cefuroxime **0.75 - 1.5 g q8h IV**

+/- neo-macrolide or azalide PO or IV

- **Alternative:**

- NFQ (beta-lactam allergy)

→ sequential to oral: when afebrile for 24 - 48 h,
declining inflammatory parameters, and O2 Sat > 95 %

4. ICU - hospitalized CAP

- **First choice :**

- cefotaxime 2g q8h IV
with
(clarithromycin 0.5g q12h IV or NFQ IV)

OR

- ceftriaxone 2g q24h IV
with
(clarithromycin 0.5g q12h IV or NFQ IV)

+/- aminoglycoside OD IV

4. ICU - hospitalized CAP

- **Alternative :**

- **amoxi/clav 1g q6h IV
with
(clarithromycin 0.5g q12h IV or NFQ IV)**

OR

- **cefuroxime 1.5 g q8h IV
with
(clarithromycin 0.5g q12h IV or NFQ IV)**

+/- aminoglycoside OD IV