Decisioni Cliniche e Prove di Efficacia

Riccione, 5-6 aprile 2002

Workshop Clinici Interattivi

Vecchi e nuovi chinolonici
Vantaggi per chi?

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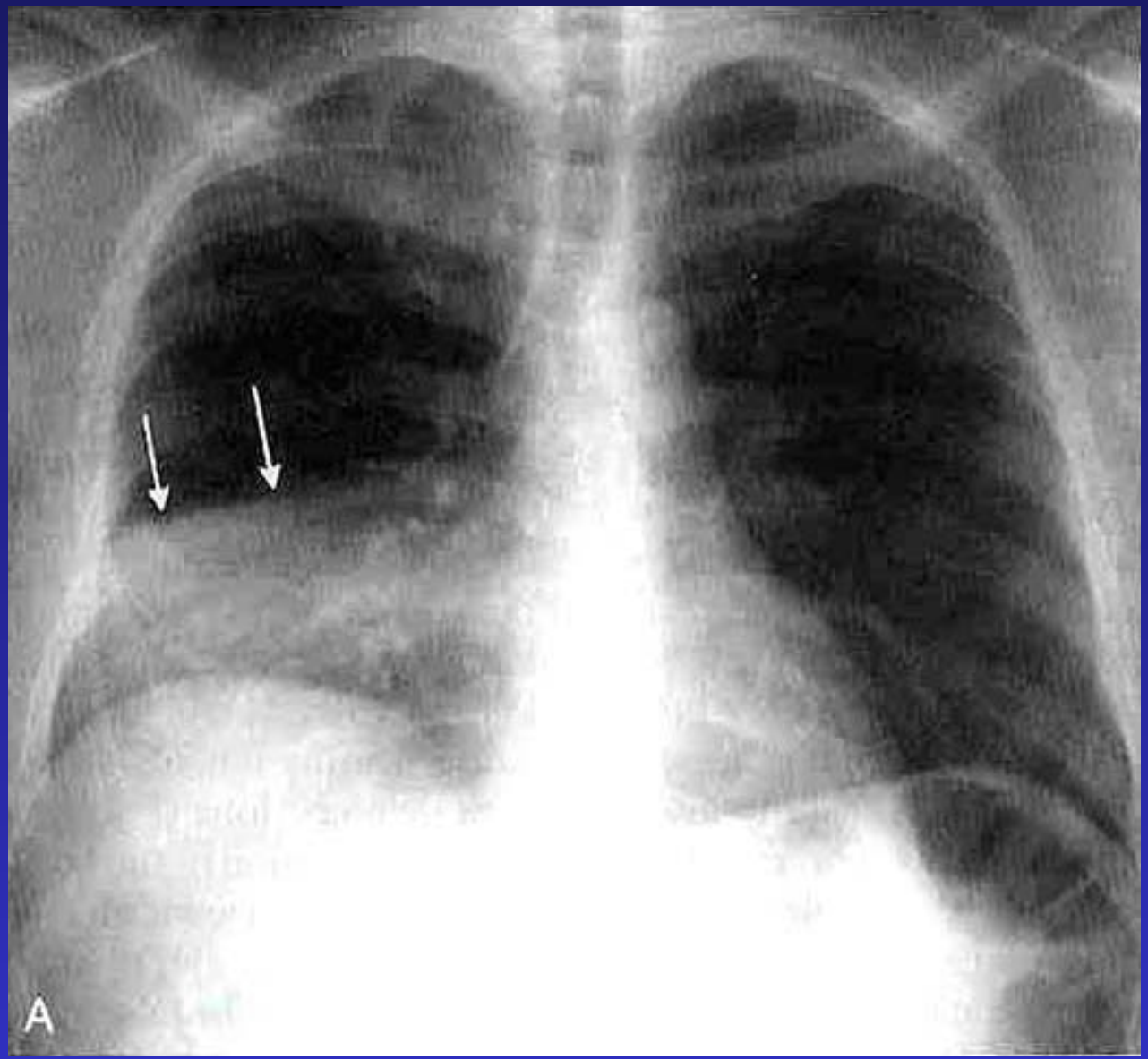
Scenario Clinico (1)

- Gustavo è un ex dirigente d'impresa di 66 anni, con storia d'ipertensione arteriosa trattata con nifedipina. Fuma sigari
- Da due giorni presenta febbre elevata (sino a 40 °C), che non è sensibile al paracetamolo.
- All'esame obiettivo: murmure vescicolare normotrasmesso, crepitazioni in campo medio dx. Toni cardiaci validi, ritmici, pause libere. Non edemi declivi. Non segni di TVP
- Rx torace: esteso focolaio broncopolmonare del lobo medio di dx. Non segni di versamento pleurico



Scenario Clinico (2)

- In considerazione delle buone condizioni generali, l'assenza di fattori di rischio - score di Fine 81 (Classe III) - e di insufficienza respiratoria, il paziente viene inviato in Day Hospital, dove inizia terapia antibiotica (ceftriaxone 1gr IM + claritromicina 500 mg 1 cpr x 2) .

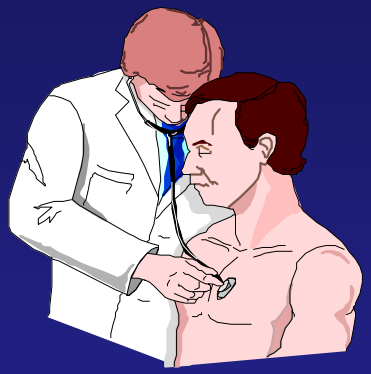
- Il sig. Gustavo viene quindi inviato al proprio domicilio dove sfebbra al terzo giorno di trattamento.

- Le sierologie per Legionella, Mycoplasma e Chlamydia risultano negative

Scenario Clinico (3)

- In ottava giornata esegue controllo Rx: “detersione del parenchima polmonare in regione lobare media di dx per parziale risoluzione del grossolano addensamento segnalato”.

- Sospende terapia antibiotica in 14° giornata, ed una Rx di controllo in 20° giornata mostra “ulteriore riduzione in estensione e densità dell’addensamento parenchimale in sede lobare media dx”



CLINICAL QUESTIONS

?

2. Vecchi e nuovi chinolonici. Vantaggi per chi?

2A. Ritieni corretta la decisione di non ospedalizzare il paziente?

1. Sì
2. No

2. Vecchi e nuovi chinolonici. Vantaggi per chi?

2B. Nella gestione domiciliare del paziente con CAP è sufficiente il trattamento con antibiotici per via orale?

1. Sì
2. No

2. Vecchi e nuovi chinolonici. Vantaggi per chi?

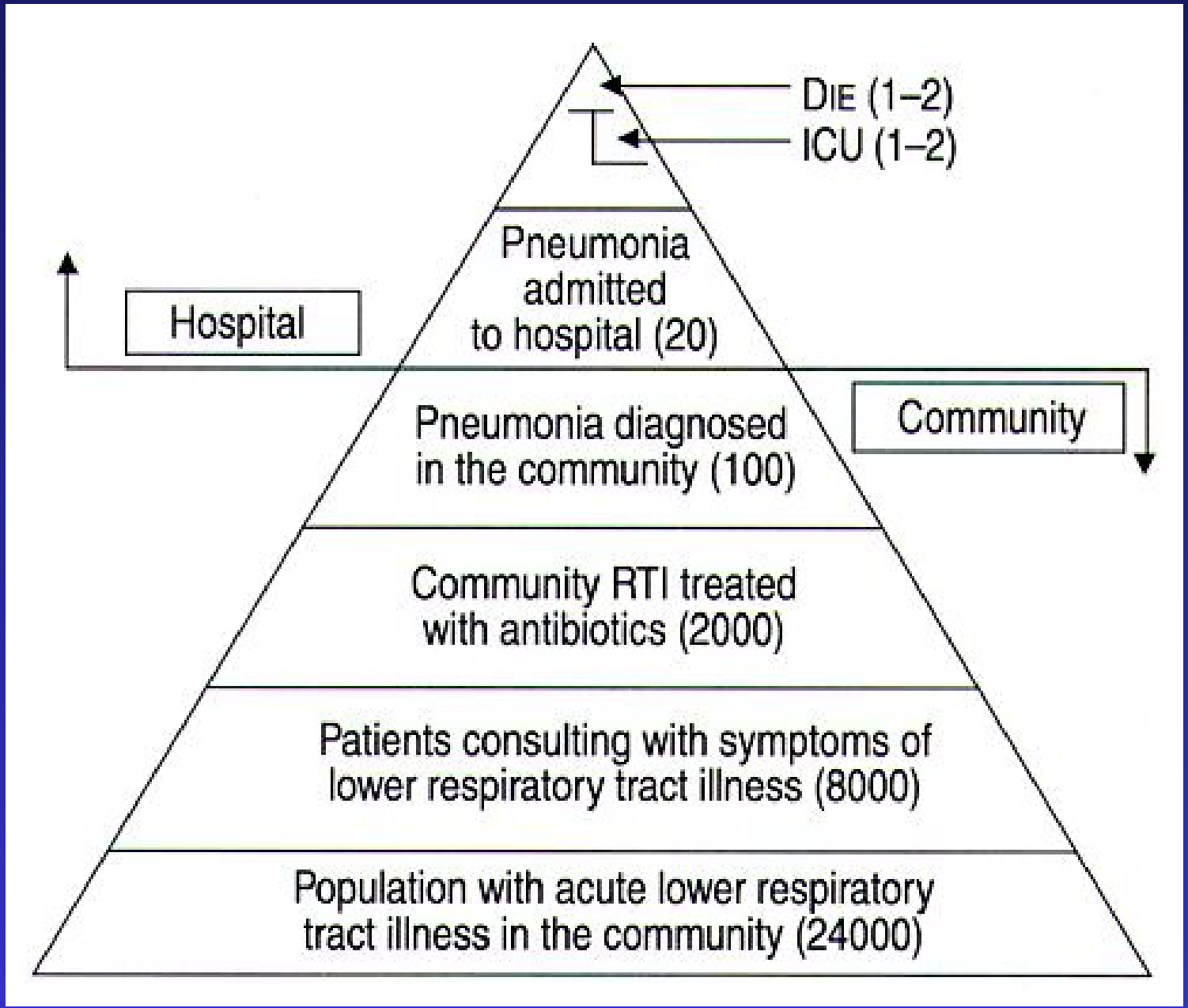
2C. Quale classe di antibiotici ritieni più appropriata per il trattamento ambulatoriale delle CAP?

1. Beta-lattamici
2. Cefalosporine
3. Macrolidi
4. Fluorochinolonici
5. Una variabile associazione dei precedenti

2. Vecchi e nuovi chinolonici. Vantaggi per chi?

2D. Ritieni che i chinolonici di nuova generazione, rispetto ai “vecchi”, offrano vantaggi considerevoli per il paziente?

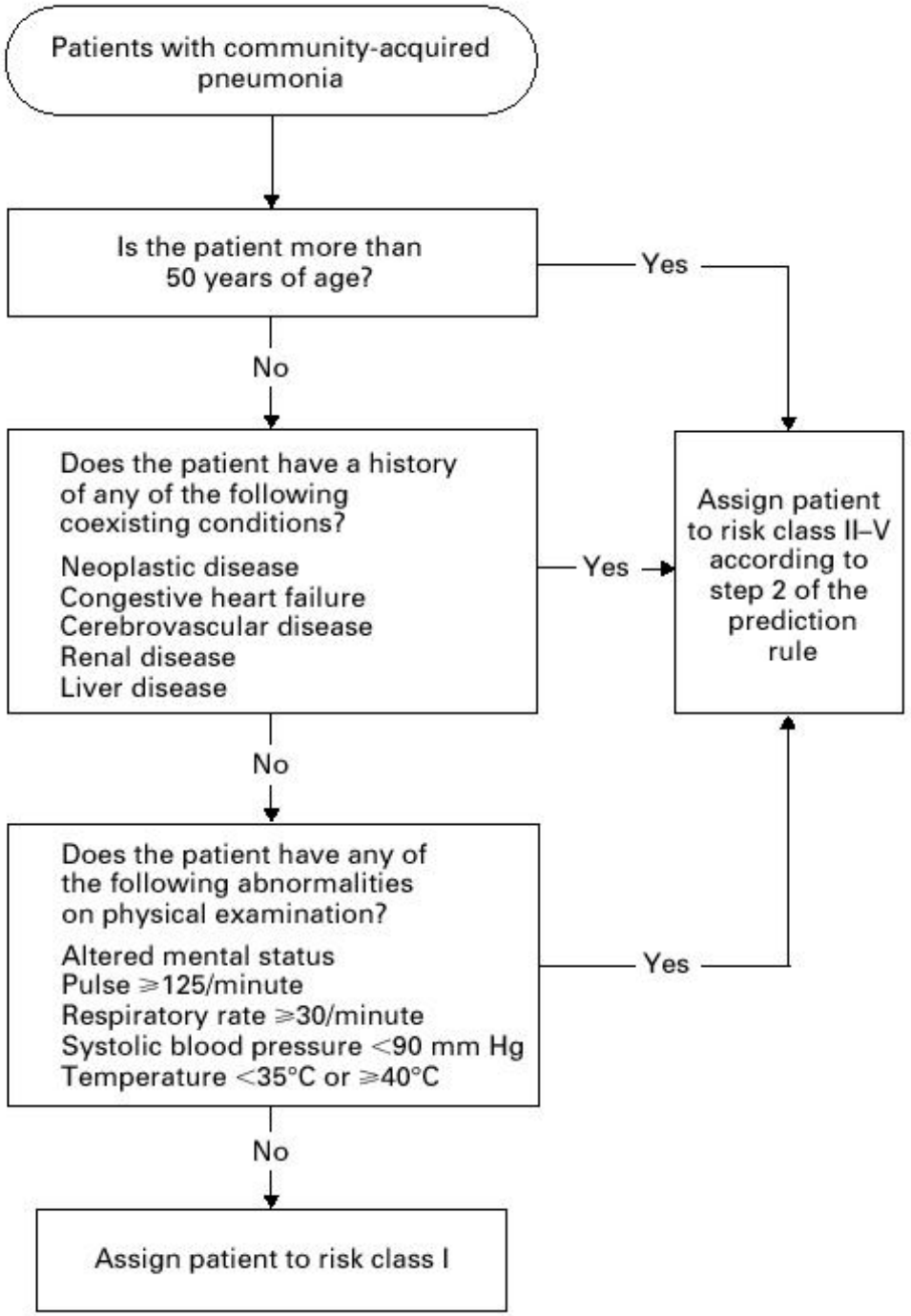
1. Sì
2. No
3. Non so, non rispondo



Fine MJ, Auble TE, et al.

A prediction rule to identify low-risk patients with community-acquired pneumonia

N Engl J Med 1997;336:243-50



Da Fine MJ, et al.

N Engl J Med 1997

TABLE 2. POINT SCORING SYSTEM FOR STEP 2 OF THE PREDICTION RULE FOR ASSIGNMENT TO RISK CLASSES II, III, IV, AND V.

CHARACTERISTIC	POINTS ASSIGNED*
Demographic factor	
Age	
Men	Age (yr)
Women	Age (yr) − 10
Nursing home resident	+10
Coexisting illnesses†	
Neoplastic disease	+30
Liver disease	+20
Congestive heart failure	+10
Cerebrovascular disease	+10
Renal disease	+10
Physical-examination findings	
Altered mental status‡	+20
Respiratory rate ≥30/min	+20
Systolic blood pressure <90 mm Hg	+20
Temperature <35°C or ≥40°C	+15
Pulse ≥125/min	+10
Laboratory and radiographic findings	
Arterial pH <7.35	+30
Blood urea nitrogen ≥30 mg/dl (11 mmol/liter)	+20
Sodium <130 mmol/liter	+20
Glucose ≥250 mg/dl (14 mmol/liter)	+10
Hematocrit <30%	+10
Partial pressure of arterial oxygen <60 mm Hg§	+10
Pleural effusion	+10

Da Fine MJ, et al.
N Engl J Med 1997

Tabella 2 - Classi di rischio nei pazienti con CAP (da 17, adattata)

Classe	Score	N.pazienti	Mortalità (%)	Setting assistenziale raccomandato
I	*	3.034	0,1	Ambulatoriale
II	≤ 70	5.778	0,6	Ambulatoriale
III	71-90	6.790	2,8	Ambulatoriale o day-hospital
IV	91-130	13.104	8,2	Ospedaliero
V	> 130	9.333	29,2	Ospedaliero

*assenza di fattori predittivi

Da Fine MJ, et al. (semplificata)
N Engl J Med 1997

Verheij T, Kochen M, Hoepelman IM, Lammers JW, Macfarlane J, Woodhead M.

Antibiotics for community acquired pneumonia in adult outpatients

(Protocol for a Cochrane Review)

The Cochrane Library. Issue 1, 2002. Oxford: Update Software.

- **Objectives**
  - To assess the effectiveness of the different antimicrobial therapies in adult outpatients with CAP

- **Types of outcome measures**
  - Clinical response
  - Frequency of hospitalization
  - Mortality

Verheij T, et al. Cochrane Library, 2002

Pomilla PV, Brown RB

Outpatient treatment of community-acquired pneumonia in adults

Arch Intern Med 1994;154:1793-802

• Etiologic diagnosis is helpful in determining appropriate outpatient treatment for community-acquired pneumonia, and usually requires only sputum Gram's stain analysis.

• Viral, mycoplasmal, and chlamydial agents are among the most common pathogens encountered in individuals treated as outpatients, although much variability exists.

• Many oral antibiotic trials for community- acquired pneumonia have been published, but shortcomings in study design limit their clinical applicability.

• A treatment algorithm is offered, using the best available data.

Pomilla PV, Arch Intern Med 1994

- Two RCTs found evidence that, in immunocompetent people admitted to hospital who were not suffering life threatening illness, intravenous antibiotics were no more effective than oral antibiotics and were associated with increased length of hospital stay.

- Intravenous antibiotics are needed in people who cannot take oral medication because of severe nausea or vomiting, or who are bacteraemic or in septicaemic shock.

Siegel RE, et al. Chest 1996;110:965–971.
Ramirez JA, et al. Infect Med 1997;14:319–323.

Polmonite Acquisita in Comunità nell'Adulto
Principali linee guida

- British Thoracic Society, 2001
- American Thoracic Society, 2001
- Canadian Infectious Disease Society, 2000

- European Respiratory Society, 1998
- Infectious Diseases Society of America, 1998

British Thoracic Society

Guidelines for the Management of Community-Acquired Pneumonia in Adults

Thorax 2001;56 (suppl IV)

Keeley D

Guidelines for managing community acquired pneumonia in adults

Many recommendations remain based on the lowest grades of evidence

BMJ 2002;324:436-7

- New guidelines from the British Thoracic Society for managing community acquired pneumonia in adults were published in December 2001 in Thorax.

- They have been formulated using modern methods with explicit search strategies and appraisal criteria.

- Recommendations are graded according to the strength of the supporting evidence.

- They cover the assessment and management of pneumonia in the community as well as in hospital.

- Many of the practical recommendations remain based on the lowest grades of evidence.

Keeley D. BMJ 2002

Antibiotic management (section 8)

EMPIRICAL ANTIBIOTIC CHOICE IN THE COMMUNITY (TABLE 8)

- Amoxicillin remains the preferred agent but at a higher dose than previously recommended [**D**].
- A macrolide (erythromycin or clarithromycin) is offered as an alternative choice and for those patients who are hypersensitive to penicillins [**D**].
- For those patients referred to hospital with suspected CAP, general practitioners may consider administering antibiotics immediately where the illness is considered to be life threatening or where there are likely to be delays (over 2 hours) in admission [**D**].

BTS Guidelines, 2001

EMPIRICAL ANTIBIOTIC CHOICE FOR ADULTS HOSPITALISED WITH NON-SEVERE CAP (TABLE 9)

- New fluoroquinolones are not recommended as first line agents or for community use for pneumonia, but may provide a useful alternative in selected hospitalised patients with CAP [**C**].
- A fluoroquinolone active against *S pneumoniae* is an alternative regimen for those intolerant of penicillins or macrolides or where there are local concerns over *Clostridium difficile* associated diarrhoea. However, experience with such newer fluoroquinolones in the treatment of CAP and their interaction and side effect profile is at present limited and further reported experience is required [**B**–]. Levofloxacin is the only recommended agent currently licensed in the UK.

BTS Guidelines, 2001

Metge CJ, Vercaigne L, Carrie A, Zhanel GG.

The New Fluoroquinolones in Community-Acquired Pneumonia: Clinical and Economic Perspectives

Ottawa, November 2001
Canadian Coordinating Office for Health Technology Assessment
Technology Overview n°5

- The overall goal of this report was to assess the efficacy and cost-effectiveness of the new fluoroquinolones compared with other antibiotics available for the empirical treatment of CAP in Canada.

- A systematic review of randomized controlled trials was conducted as well as a cost-minimization analysis (CMA) and a cost-effectiveness analysis (CEA).

Metge CJ et al. CCOHTA, 2001

• Analysis of the trials on an intention-to-treat basis indicates that the orally-administered new fluoroquinolones offer no statistically significant additional clinical successes against other antibiotics for the empirical treatment of CAP.

• An evaluable subjects analysis found new fluoroquinolones to be slightly more effective in treating individuals diagnosed with CAP than comparator antibiotics.

• The CMA indicates that new fluoroquinolones approved for use in Canada have a small cost advantage for a 10-day course of outpatient (oral) treatment, when compared to some recommended alternative regimens (clarithromycin, cefuroxime axetil + erythromycin), but not others (amoxicilline)

Metge CJ et al. CCOHTA, 2001

• Decisions about the choice of empirical antibacterial treatment of CAP may involve other considerations:
- the regional pattern of bacterial resistance
- adverse drug reaction profiles
- patient convenience.

• Concerns about cross-resistance among fluoroquinolones resulting from overuse should also be considered.

Metge CJ et al. CCOHTA, 2001

Davidson R, Cavalcanti R, Brunton JL, et al.

Resistance to levofloxacin and failure of treatment of pneumococcal pneumonia

N Engl J Med 2002;346:747-50

- We describe four patients with pneumococcal pneumonia in whom empirical treatment with oral levofloxacin failed.

- In all four cases, an organism that either was resistant to levofloxacin before therapy or acquired resistance during therapy was isolated.

- None of the position papers published on community-acquired pneumonia since the introduction of fluoroquinolones for the treatment of pneumococcal pneumonia have suggested that a history of fluoroquinolone use should be a reason for caution in using one of these antimicrobials.

Davidson R, et al. N Engl J Med 2002

Nota informativa per i medici

Il testo di questa nota è stato concordato con il

Ministero della Salute

Dear Doctor Letter per la levofloxacina

Si sottolinea quindi che:

come tutti i fluorochinolonici la levofloxacina non deve essere usata in pazienti con affezioni tendinee insorte dopo un precedente uso di fluorochinolonici;

e si ricorda che:

- i pazienti anziani sono più predisposti alle tendiniti;
- il rischio di rottura di tendine sembra essere aumentato dal trattamento concomitante con corticosteroidi;
- se si sospetta una tendinite il trattamento con la levofloxacina (o un altro chinolonico) deve essere interrotto immediatamente e la tendinite trattata appropriatamente.