

INCREASED RESISTANCE TO MACROLIDE ANTIBIOTICS

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The DANMAP (Danish Antimicrobial Resistance Monitoring and Research Programme) annual reports deal with antibiotic consumption in agriculture and medicine and antibiotic resistance in bacteria from farm animals, foods and humans, EPI-NEWS 3/99 and 4/99. Based on the report for 1999, this issue of EPI-NEWS describes the problem of increasing macrolide (erythromycin) resistance in pneumococci and its possible relation to the relatively high macro-lide consumption over recent years in Denmark.

Susceptibility tests on pneumococcal isolates from blood and cerebrospinal fluid sent to the Streptococcus Laboratory at Statens Serum Institut show that the frequency of erythromycin resistance in pneumococci has slowly risen from close to 0% in 1990 to 3.4% in 1999, Fig. 1. There is cross-resistance between erythromycin and the other macrolides used in Denmark, azithromycin, clarithromycin and roxithromycin. During the period 1994-1999 total macrolide consumption in Denmark has been around 2 DDD (Defined Daily Doses) per 1,000 inhabitants per day, or an average of 7.3 prescriptions per 1,000 inhabitants per month, Fig. 1. No comparable data are available for erythromycin consumption prior to 1994.

Increased macrolide consumption during mycoplasma epidemic

In November and December 1998 a marked rise in Danish macrolide consumption was noted, which exceeded the seasonal variation, Fig. 2. This rise could be related to an epidemic of mycoplasma infections, EPI-NEWS 46/98. Macrolide consumption only fell to a "normal" level, i.e. to that of the same period of previous years, in April 1999. Perhaps the use of macrolides contributed to stopping the mycoplasma epidemic, but a few months later a rise in the frequency of erythromycin resistance was noted in Copenhagen and Frederiksberg Municipalities, reaching 3-7% in several Gram-positive bacteria, e.g. pneumococci, haemolytic streptococci of groups A, C and G, and Staphylococcus aureus, as reported by H. Westh, Dept. of Clinical Microbiology, Hvidovre Hospital.

Fig. 1. Macrolide consumption and macrolide resistance

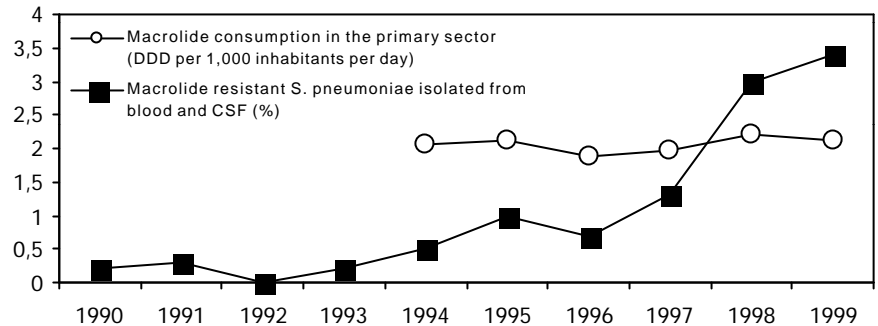
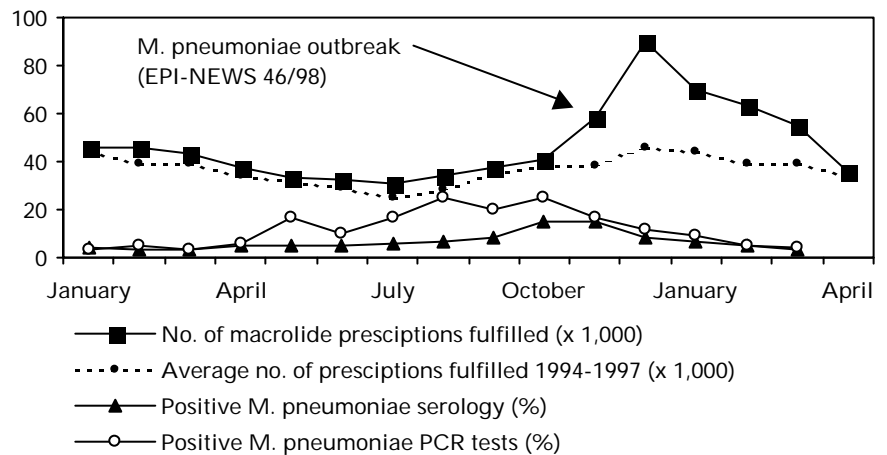


Fig. 2. Macrolide prescriptions fulfilled and diagnoses of M. pneumoniae infection, January 1998 - April 1999



Comments

European studies on patterns of antibiotic use in general practice and the frequency of pneumococcal erythromycin resistance have shown that there is a close relationship between the frequency of resistance and both macrolide and total antibiotic consumption. On the other hand, there was a negative relationship between the consumption of narrow-spectrum antibiotics, e.g. penicillin V, and macrolide resistance. In Finland, a doubling of macrolide consumption to 2 DDD per 1,000 inhabitants per day during the mid-1980's led to an increase in erythromycin resistance from less than 5% to over 20% in group A haemolytic streptococci. Similar findings have been reported in Spain. The experience of other countries shows that reducing macrolide consumption can bring about a fall in the frequency of resistance. The Danish experience shows that even if antibiotic consumption is generally low and the frequency of resistance correspondingly small, a temporary rise in con-

sumption of even a single class of antibiotic can upset this balance in an unfavourable direction. It also demonstrates the importance of continuous surveillance of bacterial resistance and antibiotic consumption.

Indications for macrolide treatment

The primary indication for macrolide treatment is in respiratory or urogenital infections due to chlamydia or mycoplasma. Secondary indications are the treatment of patients allergic to penicillin, mostly with infections of the upper or lower respiratory tract caused by erythromycin-sensitive pneumococci, streptococci or Branhamella, and the treatment of skin infections caused by erythromycin-sensitive staphylococci or streptococci.

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## Streptococci isolated from blood and CSF from infected patients

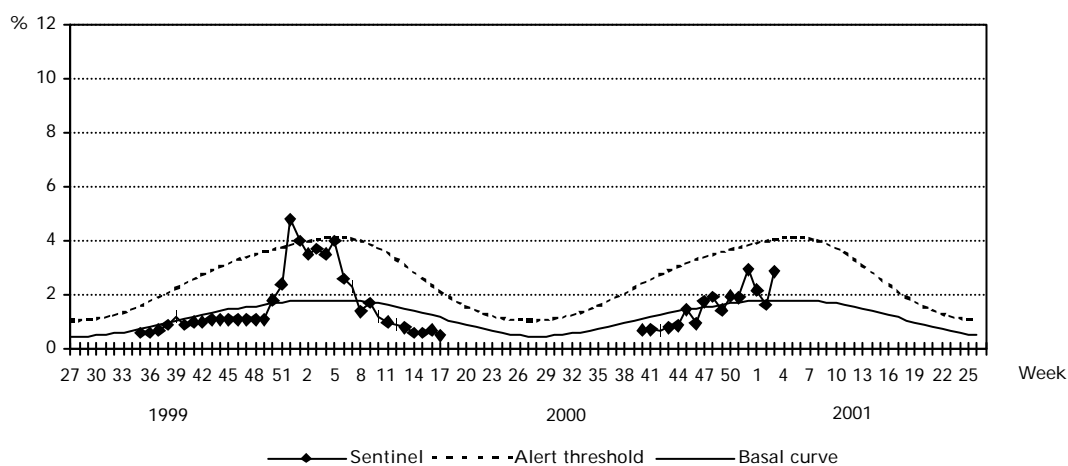
4th quarter 2000 compared with the same period of the two previous years

		4th quarter 2000				4th quarter	
		< 2 yrs	2-59 yrs	60 yrs +	Total	1998	1999
October	S. pneumoniae	5	14	25	44	58	54
	Group A strep.	-	2	-	2	8	5
	Group C strep.	-	-	2	2	1	-
	Group G strep.	-	2	6	8	5	5
November	S. pneumoniae	2	24	52	78	84	83
	Group A strep.	-	2	8	10	4	4
	Group C strep.	-	1	1	2	1	-
	Group G strep.	-	1	6	7	6	11
December	S. pneumoniae	3	32	39	74	125	80
	Group A strep.	-	7	2	9	12	9
	Group C strep.	-	2	-	2	3	3
	Group G strep.	-	2	10	12	6	4
4th quarter	S. pneumoniae	10	70	116	196	267	217
	Group A strep.	-	11	10	21	24	18
	Group C strep.	-	3	3	6	5	3
	Group G strep.	-	5	22	27	17	20

(Streptococcus Unit)

## Sentinel surveillance of influenza activity

Weekly percentage of consultations, 1999/2000/2001



- Sentinel:** Influenza consultations as % of total consultations  
**Basal curve:** Expected frequency of influenza consultations under non-epidemic conditions  
**Alert threshold:** Possible incipient epidemic

(Dept. of Epidemiology)