*Original Report*

# The decision-making process in antibacterial treatment of pediatric upper respiratory infections: a national prospective office-based observational study

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**Background:** The identification of patient management practices and the sources of medical information is crucial for rationalizing the treatment of respiratory tract infections, whose high incidence, especially in children, makes them one of the maior areas of unnecessary health expenditure.

**Materials and Methods:** This national prospective study was designed to investigate the diagnostic and prescribing habits of 100 office-based pediatricians managing upper respiratory tract infections in 1111 pediatric patients (604 males, mean age 6.79±2.77 years; 507 females, mean age 6.73±2.8 years) sequentially enrolled when an antibiotic treatment was deemed necessary.

**Results:** The most frequently diagnosed diseases were acute tonsillopharyngitis (56.2%) and acute otitis media (18.1%). Penicillins were prescribed in 34.3% of the cases, cephalosporins in 38.1%, and macrolides in 26.1%: oral drugs accounted for 92.2% of the prescriptions. The treatments were administered once or twice daily in 75.8% of the patients, and prescribed for ≥8 days in more than 80%; 76.7% also received supportive or symptomatic treatment (antipyretics, corticosteroids, cough suppressants and non-steroidal anti-inflammatory drugs). Laboratory or radiologic investigations were rarely requested. The main sources of medical information indicated by the participating pediatricians were pharmaceutical companies (35.6%) and meeting or congress reports (27.3%).

**Conclusions:** The results indicate that more active education is still needed to improve the decision-making processes of office-based pediatricians.

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## INTRODUCTION

The management of acute upper respiratory infections (URIs) in children is one of the major tasks of office-based pediatricians. Young children may experience several episodes a year, and, although frequently of viral origin, these may lead to secondary bacterial infections such as otitis media and sinusitis.[1] The increasing incidence of the infections can be attributed to the growing use of daycare centers (especially in large cities and if both parents work) and the effects of smoking and air pollutants.

The treatment of respiratory tract infections frequently involves the use of antibiotics, which represent the second most commonly prescribed group of drugs and are mainly prescribed for infections diagnosed in ambulatory settings.[2] However, the predominance of viral etiologies raises doubts about the real efficacy of such treatments,[3,4] and the widespread use of, particularly, the new extended-spectrum oral compounds has contributed to the emergence of increasingly resistant bacterial strains.[5]

Acute URIs not only represent a health problem in terms of the costs of diagnosis and treatment, but also have considerable non-medical implications. They have a considerable socio-economic impact because, as they are usually only mildly or moderately severe, the affected children are normally cared for at home, which means that a member of the family has to stay with them (with a consequent loss of working days) or a baby-sitter needs to be hired.

Only limited prospective data are currently available concerning the medical and social impact of pediatric URIs, which makes it difficult to document their medical and social costs. The relatively few studies of antibiotic drug use are usually based on overall statistics or small populations,[6–8] and cannot provide an adequate description of the complete medical and social process.

This national survey was carried out in Italy in January–March 1998 and designed to investigate how office-based pediatricians manage the primary care of URIs.

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## METHODS

This was a prospective observational study aimed at documenting the procedures used by 100 National Health Service office-based pediatricians throughout Italy in managing children with community-acquired URIs requiring antibiotic treatment. The physicians were selected on the basis of criteria such as age, time since qualification, and patient allotments, and asked to enrol consecutively at least the first 10 patients aged ≥3–16 years requiring, according to the pediatrician's judgment, an antibiotic treatment course. No financial incentives were offered.

A clinical chart was prepared on which to record the patients' demographic information, clinical data, infection-related symptoms, concomitant pathologies, prescribed antibiotics and other drugs, and requested laboratory (hematology, throat and nasal swabs) or radiologic investigations. The physicians were also asked to record the reason(s) for the choice of antibiotic, and the sources of their information and education concerning antibiotic therapy.

A second examination was planned for the patients whose clinical condition had not normalized or if it was otherwise deemed necessary. In such cases, the physicians also recorded the disappearance or otherwise of the symptoms, any adverse event observed, and their judgment of the clinical results of the treatment.

The social impact of URIs was investigated by asking the parents how many schooldays had been lost, whether the illness had required them to take time off work, and whether they had to hire a baby-sitter to care for the child.

The data were analyzed using SAS version 6.97 software. All of the collected data were descriptively analyzed. Frequency distributions were used for discrete data; the continuous variables were described in terms of mean frequencies, standard deviations, and mean, minimum and maximum values.

## RESULTS

### Patients and diagnoses

Between January and March 1998, 1111 pediatric patients (604 males, mean age 6.79±2.77 years; 507 females, mean age 6.73±2.8 years) were recruited. Ninety-one (8.2%) had a history of allergy, which was mainly respiratory (5.2%).

The examinations took place in the pediatricians' offices (61.1%) or the patients' homes (38.9%). The majority of the children (82.6%) were examined 1–3 days after the onset of symptoms.

The predominant diagnosis was pharyngotonsillitis (PT: 56.2%), followed by acute otitis media (AOM: 18.1%) and recurrent pharyngitis (9.4%); the other diagnoses were much less frequent (Table 1). The diseases were classified as mild, moderate or severe in, respectively, 22.4%, 70.8% and 6.8% of the cases.

**Table 1.** Upper respiratory tract infections by diagnosis

| | *No. of patients* | *Percentage* |
|---|---|---|
| Acute pharyngotonsillitis | 625 | 56.2 |
| Acute otitis media | 201 | 18.1 |
| Recurrent pharyngitis | 105 | 9.4 |
| Sinusitis | 52 | 4.6 |
| Tracheitis | 27 | 2.5 |
| External otitis | 20 | 1.8 |
| Chronic otitis | 16 | 1.4 |
| Rhinitis | 11 | 1.0 |
| Influenza | 10 | 0.9 |
| Acute pharyngitis | 8 | 0.8 |
| Bronchitis | 4 | 0.4 |
| Laryngitis | 3 | 0.3 |
| Other | 29 | 2.6 |

### Treatments

#### *Antibiotics*

The prescribed antibacterial treatments included a wide range of compounds. As shown in Table 2, penicillins were prescribed in 34.3% of the patients, the most frequently used being amoxicillin and amoxicillin–clavulanate (45.9% and 44.6% of penicillin prescriptions, and 15.8% and 15.3% of all prescriptions). Oral ampicillin (together with its pro-drug bacampicillin or in combination with sulbactam) accounted for 5.3% of the penicillin prescriptions (1.76% of all prescriptions).

Of the 12 cephalosporins, 42.4% were third-generation and 39.2% second-generation oral compounds; the most frequently prescribed drugs in these two groups were cefixime and cefaclor (23.9% and 26.2% of the cephalosporin prescriptions; 9.1% and 10% of all prescriptions). Third-generation parenteral extended-spectrum cephalosporins were used in 17% of the cases (6.7% of all prescriptions).

Macrolides accounted for 26.1% of all prescriptions, the most frequently administered being clarithromycin (45.4%; 11.9% of all prescriptions) and azithromycin (31.1%; 8.1% of all prescriptions).

The three main drug classes were equally prescribed for acute PT (34.1% penicillins; 34.8% cephalosporins; 30.1% macrolides), with second- and third-generation oral cephalosporins being prescribed in, respectively, 11.7% and 15.7% of the cases, and parenteral compounds in 7.4%. Penicillins, cephalosporins and macrolides were prescribed in, respectively, 34.8%, 47.6% and 14.4% of the patients with AOM.

Oral antibiotics were used in 92.2% of the patients and parenteral drugs in 7.5%. Once- or twice-daily regimens were used in 78.5% of the cases, and more than 80% of the patients were treated for ≥8 days.

#### *Supportive and symptomatic treatment*

Supportive or symptomatic treatment was prescribed in 76.7% of the patients: 49.6% received one drug, 18.8% two, and 8.4% three or more. Antipyretics were the most frequently used (49.8%), followed by mucolytics

**Table 2.** Antibiotic prescriptions

| | *No. of Prescriptions* | *% of Antibiotic Class* | *% of Total Prescriptions* |
|---|---|---|---|
| Penicillins | 381 | – | 34.3 |
| Amoxicillin | 175 | 45.9 | 15.8 |
| Amoxicillin–clavulanate | 170 | 44.6 | 15.3 |
| Ampicillin | 1 | 0.3 | 0.08 |
| Ampicillin–sulbactam | 1 | 0.3 | 0.08 |
| Benzathine G penicillin | 6 | 1.6 | 0. |
| Bacampicillin | 18 | 4.7 | 1.6 |
| Flucloxacillin | 10 | 2.6 | 0.9 |
| Total intramuscularly | 6 | 1.6 | 0.5 |
| Cephalosporins | 423 | – | 38.1 |
| Cefetamet pivoxyl | 13 | 3.1 | 1.2 |
| Cefixime | 101 | 23.9 | 9.1 |
| Cefodizime | 2 | 0.5 | 0.2 |
| Cefonicid | 6 | 1.4 | 0.5 |
| Cefotaxime | 4 | 0.9 | 0.4 |
| Cefpodoxime proxetil | 7 | 1.7 | 0.6 |
| Ceftazidime | 11 | 2.6 | 1 |
| Ceftibuten | 58 | 13.7 | 5.2 |
| Ceftriaxone | 51 | 12.1 | 4.5 |
| Cefuroxime axetil | 55 | 13 | 5 |
| Cefazolin | 4 | 0.9 | 0.3 |
| Cefaclor | 111 | 26.2 | 10 |
| Third-generation oral cephalosporins | 179 | 42.4 | 16.1 |
| Second-generation oral cephalosporins | 166 | 39.2 | 15 |
| Third-generation parenteral cephalosporins | 74 | 17.1 | 6.7 |
| First-generation parenteral cephalosporins | 4 | 0.9 | 0.36 |
| Macrolides | 290 | – | 26.1 |
| Clarithromycin | 132 | 45.4 | 11.9 |
| Josamycin | 2 | 0.7 | 0.2 |
| Miocamycin | 3 | 1.1 | 0.3 |
| Roxithromicin | 63 | 21.7 | 5.7 |
| Azithromicin | 90 | 31.1 | 8.1 |
| Others | 17 | – | 1.5 |
| Rufloxacin | 1 | 5.8 | 0.08 |
| Tiamfenicol | 1 | 5.8 | 0.08 |
| Trimethoprim–Sulfamethoxazole | 14 | 82.6 | 1.3 |
| Rifamicin | 1 | 5.8 | 0.08 |

(15.5%), corticosteroids (9.8%), cough suppressants and non-steroidal anti-inflammatory drugs (4.4%). Oral administration was preferred (49.2%), followed by the use of rectal suppositories (30.7%).

## Laboratory and radiologic investigations and specialist consultations

The pediatricians rarely felt it necessary to request microbiological or serologic investigations. A throat culture was made before starting PT treatment in 111/625 cases (17.8%), and a complete blood count with differential and the determination of acute-phase reactants in only 77/1111 (6.9%).

Radiologic studies (mainly chest or paranasal sinus X-rays) were requested for 35 subjects.

Fifty-four ENT and 12 allergologic specialist consultations were requested.

## Follow-up visits

Four hundred and fifty-two patients (40.7%) were followed up (74.8% office visits; 12.6% home visits; 12.6% phone consultations): the reason was persisting signs and symptoms indicating possible treatment failure in 13.7% of cases (36.9% were judged to be responding). New symptoms were recorded in 41 patients (9.1%).

Twenty per cent of the treatment failures were switched to another drug, which was a parenteral compound in 30.6% of the cases. The main reasons for the changes were persisting signs and symptoms and possible microbiological failure.

Eighty-nine of the patients underwent a third and final check-up, at which 98.1% were cured or had markedly improved.

## Tolerability

The treatments were generally well tolerated. Ninety-four adverse events were recorded in 74 (16%) of the 452 patients. Diarrhea was documented in 43 patients (mild in 41, possibly iatrogenic in 27), nausea in 14, vomiting in 11, gastric discomfort in 13, rash in 9, and itching in 2. Two cases were undetermined.

## Reasons for antibiotic choice

The reasons for the choice of drug were a high degree of antimicrobial activity in (only) 30.4% of the cases, treatment compliance in 17.2%, general tolerability in 14%, and cost-effectiveness in 10.3%. Twenty-six per cent of the prescriptions were based on the patient's personal experience with a specific antibiotic treatment (indicating a substantial demand for an 'authorized' form of self-medication), whereas the personal experience of the physicians themselves accounted for no more than 2.1%.

## Sources of information on antibiotics

Table 3 shows that books or scientific journals were reported as the main source of continuing education on antibiotic treatment by only 9.9% of the physicians, whereas 22% obtained their information from non-peer-reviewed bulletins. Medical meetings were cited in 27.3% of the reports. The substantial impact of non-

**Table 3.** Sources of continuing education

| | *Percentage of Answers* |
|---|---|
| Meetings | 27.3 |
| NHS courses | 3.6 |
| Pharmaceutical company courses | 5.8 |
| Information directly provided by pharmaceutical companies | 29.8 |
| Newsletters | 22.2 |
| Scientific books or journals | 9.9 |
| Personal experience | 1.4 |

independent education is indicated by the fact that 35.6% of the reports cited pharmaceutical company promotional meetings and direct information.

### Family impact of URIs

Normal family life was frequently affected. Only 2.4% of the children did not lose any day of school, whereas 15.4% lost 1–3 days, 73.4% lost 4–8 days, and 8.9% lost 10 or more days.

Furthermore, 18.1% of the parents reported that they had had to take days off work, and 4.2% of those who could not lose working days had to hire a baby-sitter to care for their child.

## DISCUSSION

Acute URIs comprise the most frequent medical reason for visiting a physician's office. In a large European observational cohort study,[9] they accounted for 44.8% of 1466 visits. Furthermore, 22.7% involved children aged <10 years, who were prescribed 31.2% of all of the antibiotics prescribed for URIs.

The accurate diagnosis and treatment of acute URIs in children is difficult for various reasons. First, the diagnostic criteria are vague: for example, AOM is diagnosed by some practitioners when they find myringitis, and by others only when there is redness, dullness and purulent material behind the tympanic membrane. Second, even if the clinical diagnosis is sound, therapy is still empirical because of the lack of pathogen tests: for example. microbiological confirmation is rarely available in the case of otitis and sinusitis, and acute pharyngitis is the only clinical condition in which the main causative bacteria (group A β-hemolytic streptococci—GABHS) can be easily demonstrated by means of a standard throat culture or rapid antigen testing.[10] Finally, the difficulty in distinguishing antibiotic-responding diseases from those of viral origin leads to overtreatment.

Further pressure to use antimicrobial agents in outpatient settings may come from non-medical considerations, including patients' (or parents') expectations and previous experiences, and the physician's desire not to alienate the patient.[11]

As general pediatricians often consider acute URIs to be benign and spontaneously resolving clinical entities, the propensity to prescribe antibiotics may partially arise from the belief that they are effective in reducing complications, particularly pneumonia. However, the protective advantage of antibiotics over placebo against such complications has been estimated in a review of 12 randomized clinical trials,[12] in which a relative risk of 0.71 (95% CI: 0.45–1.12) was calculated, thus indicating that 35 children need to be treated in order to prevent one case of complications.

The main concern of general pediatricians is to provide symptom relief and reassure mothers that their children's illness is being adequately considered and appropriately treated; antibiotics are the only available approach, because of the lack of major signs and symptoms indicating a viral etiology. Complete blood counts or acute-phase reactants (such as C-reactive protein or the erythrocyte sedimentation rate) might help in differential diagnosis, but are only available in offices with at least basic laboratory facilities (which are rare in Italy and many other countries).

Although PT can be etiologically diagnosed, this is rarely done, and treatment is generally prescribed without any microbiological investigation: one study[13] found that 76% of the patients with acute tonsillopharyngitis received full courses of antibiotics before the test results were available.

Pediatricians are aware of the importance of tailoring treatment on the basis of the expectations of individual patients. Global patient acceptance is essential to ensure that the treatment is completed as indicated and not modified (or interrupted) when the symptoms disappear. This is particularly important in the case of tonsillopharyngitis, as the duration of treatment is directly related to the GABHS eradication rate.

The range of prescribed non-antibacterial treatments is mainly limited to antipyretics and mucolytics, and aimed at ensuring rapid relief and the effective control of signs and symptoms.

The frequency of URIs make them a problem for working families: 76.1% of the children in this study could not go to school or a daycare center for 3–7 days, and required home care by one of the parents or a paid baby-sitter.

It is not our aim to judge the magnitude or quality of the antibiotic treatment documented in this study. Like most of their counterparts in the Western world, Italian physicians are faced with the fact that children experience repeated URI episodes during the autumn and winter, with the children of working parents sent to daycare centers being exposed to a 1.7–2.2 relative risk.[14,15]

Parental pressure to prescribe may be difficult to resist, and it is time-consuming to explain the reasons for not prescribing. In a recent survey of 915 office-based pediatricians,[16] 48% reported that parents pressure them to prescribe antibiotics even when they are not considered to be indicated. Furthermore, some physicians may consider prescribing because of the placebo effect.[17]

Thousands of guidelines aimed at providing a rationale for every clinical condition have been published throughout the world, but the misuse of antibiotics has not significantly changed. A new approach is now needed, and should be based on rapid 'bedside' diagnostic facilities and simplified treatment schedules that maximize patient compliance.

'It is a long way from the Petri dish to community pediatrics', and only continuing collaboration between pediatricians and general practitioners, and between science and society, will help us to understand the complex medical and social dynamics of acute community-acquired infections such as URIs.

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