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Practical Considerations When Treating Children with Antimicrobials in the Outpatient Setting

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Summary

Over the past decade new antimicrobial agents have been introduced used to treat common paediatric infectious diseases such as acute otitis media and sinusitis. These agents vary with respect to their mechanism of action, dosage and duration of therapy, cost, taste and type of adverse effects. More recently, there has been concern about the overuse of antibiotics and increasing bacterial resistance, particularly *Streptococcus pneumoniae*, to these agents.

Dosage and duration of therapy, cost, taste, and adverse effects play important roles in determining success or failure of antimicrobial medications in paediatric patients. Use of potential alternatives and adjuncts to antimicrobial treatment, such as vaccination, control of environmental risk factors, surgical techniques and alternative medical therapies may also be employed, and the practitioner must ascertain if their paediatric patients are being treated by any of these methods. Rather than listing the therapeutic challenges for all common outpatient paediatric infectious diseases, acute otitis media (accounting for over 50% of the antimicrobial prescriptions dispensed in childhood) is used to illustrate each issue.

Clinicians are faced with a growing number of possible antimicrobial choices; concomitantly, there is increasing concern that these agents are overused. When

prescribing antimicrobial agents, we need to be familiar with what we can do to optimise the care we provide. By avoiding inappropriate or trivial use of antimicrobials, we can preserve and even strengthen our armamentarium against disease. Simple strategies can improve compliance with therapeutic regimens and improve parental satisfaction.

Paediatricians and family practice physicians are faced not only with a plethora of antimicrobials available to treat common outpatient paediatric infectious diseases, but also with conflicting recommendations and practices concerning antimicrobial selection. In addition there is a growing concern in the scientific community about bacterial resistance and parental pressures to dispense antibiotics. Recent investigations have added to our understanding of these issues.

We pooled our collective clinical and research experience in private and academic settings to identify the practical considerations faced by physicians when treating paediatric patients with antimicrobials. Pertinent studies and review articles were found after a systematic search of these topics in the recent literature using MEDLINE. In this article, we discuss common topics related to the selection of antimicrobials such as their indications, treatment options and factors affecting compliance. We focus on antibacterial agents and use acute otitis media (AOM) as a clinical example for many of these issues – since this disease accounts for the majority of antimicrobial use in children.[1,2] We also address emerging trends in patient care with respect to factors related to treatment failure and relapses, the rise in bacterial resistance to antimicrobials, and the promise of alternative therapies.

1. Background

Children are most commonly exposed to antimicrobials at an early age. In the US, two-thirds of all infants are exposed to antimicrobials within the first 200 days of life. [1,3] In national surveys, antimicrobial agents account for more than one-third of all prescriptions written for children under 10 years of age.[4,5] Common diagnoses that prompt physicians to prescribe antimicrobials include AOM, bronchitis and pneumonia, pharyngitis, sinusitis and acne. It is noteworthy that the second most common diagnosis prompting antimicrobial prescription, upper respiratory tract infection, has a viral aetiology.[6]

AOM accounts for approximately one-fifth of all antimicrobials prescribed in the US. According to the US Centers for Disease Control and Prevention, 23.6 million prescriptions of antimicrobial drugs for AOM in 1992 were presented – double the number of prescriptions from the preceding decade.[6] When following a cohort of children in Pittsburgh, researchers found approximately one-half of infants under 6 months, three-quarters of children under 1 year, and more than 90% of children under 2 years had developed at least one episode of AOM. Each year, these children spent the equivalent of 1 month on antibiotics.[7]

2. Indications

Antimicrobials prescribed in the outpatient setting may be divided into the following groups; cephalosporins (first, second and third generations), macrolides, penicillins, sulphonamides, tetracyclines, various combinations and other miscellaneous agents (see table I). In general, antimicrobial therapy is initiated on a clinical judgement of a bacteriological diagnosis, the most likely infecting micro-organism, and the known susceptibilities of the organism. Therapy suppresses the growth of micro-organisms, helps to reduce clinical signs and symptoms of disease and helps to prevent complications associated with ongoing infection.[8]

The treatment of AOM provides a good example of several principles associated with prescribing antimicrobials. After determining if a child has signs and symptoms consistent with an AOM, the clinician considers whether or not to prescribe an

antimicrobial agent. He or she considers the present standard of care, weighs the benefits and risks associated with the therapy, and determines under what circumstances alternative decisions would be reached.

At present, AOM is most commonly treated with oral antibiotics at the time of initial diagnosis. Antimicrobials hasten the resolution of the clinical signs of AOM[9,10] and improve microbiological clearance.[11] Complications, although infrequent, include mastoiditis, chronic otorrhoea, hearing loss, labyrinthitis and facial nerve paralysis.[12] However, particularly in the treatment of AOM, there is a renewed interest in withholding antimicrobial therapy due to concern for emerging bacterial resistance (section 6).

Table I. Antimicrobials used in the treatment of common outpatient paediatric diseases: dosage and comparative cost

Generic drug	Route	Dosage (mg/kg/day)	Interval	Adult dose[a] (mg)	Daily cost[b] ($US)
Amoxicillin	PO	40	q8h	750-1500	+
Amoxicillin/clavulanic acid[c]	PO	40	q8h *or* q12h	750-1500	++++
Ampicillin	PO	50-100	q6h	1000-2000	+
Azithromycin[d]	PO	5	q24h	250-500	++++
Cefaclor	PO	40	q8h *or* q12h	750-1500	++++
Cefadroxil	PO	30	q12h	1000-2000	+++
Cefalexin	PO	25-100	q6-12h	1000-4000	++/+++
Cefixime	PO	8	q12h *or* q24h	400	+++
Cefpodoxime proxetil	PO	10	q12h	200-800	+++
Cefprozil	PO	30	q12h	500-1000	++++
Ceftibuten	PO	9	q24h	400	++++
Ceftriaxone	IM	50 mg/kg	Once	1000-4000	++++
Cefuroxime axetil	PO	20-30	q12h	500-1000	++++
Clarithromycin	PO	15	q12h	500-1000	++++
Dicloxacillin	PO	12-25	q6h	500-2000	+
Erythromycin	PO	30-50	q6h	1000-4000	+
Erythromycin (ETM)/sulfafurazole (sulfisoxazole) (SFZ)	PO	50 (ETM) 150 (SFZ)	q6h-q8h	1600 4800	+
Loracarbef	PO	15-30	q12h	400-800	+++
Minocycline[e]	PO	4	q12h	200	+++
Mupirocin[f]	Topical		q6-12h		+++/++++
Benzathine benzylpenicillin (penicillin G-benzathine)	IM	25-50 000 U/kg	Once	1.2 million U	+
Phenoxymethylpenicillin (penicillin VK)	PO	25-50	q6h-q8h	750-1500	+
Rifampicin (rifampin)	PO	10-20	q12h-q24h	600	+++
Sulfadiazine	PO	120-150	q4h-q6h	4000-8000	++/+++
Sulfafurazole (sulfisoxazole)	PO	120-150	q4h-q6h	4000-8000	++/+++
Tetracycline[e]	PO	25-50	q6h	1000-2000	+
Cotrimoxazole [trimethoprim (TMP)/ sulfamethoxazole (SMX)]	PO	6-12 TMP 30-60 SMX	q12h	320 1600	+
Vancomycin	PO	10-50	q6h	500	++++

a Maximal dose in a 24h period.

b Acquisition cost based upon the 24h, 10kg child dosage given over a 10-day period (unless otherwise specified).

c Dosage of amoxicillin component.

d Initial dose is doubled. Usual treatment course is 5 days.

e Not indicated for young children.

f Based on use of a single 15g tube.

Abbreviations and symbols: IM = intramuscular; PO = oral; + ≤ $US0.50, ++ $US0.50-0.99, +++ $US1.00-1.99, ++++ ≥ $US2.00.

Table II. Risk features for acute otitis media (AOM) [after Klein & Bluestone[11]]

Host features
Age of first episode appears to be the most powerful predictor of recurrent AOM
Early onset of disease
Very low birthweight (<1500g) and gestational age <33wk
Male sex
Race and ethnicity: Native Americans, Alaskan and Canadian Inuit, Australian Aborigines
Familial aggregation: disease in siblings and parents
Altered host defences (structural defects and immunological deficiencies)
Environmental features
Group daycare
Exposure to environmental antigens and pollutants
Exposure to smoke
Not breast-fed (as little as 3mo provides significant protection)
Season: autumn, winter, early spring
Poverty: crowded living conditions, poor sanitation and lack of access to medical care
Prone sleeping position
Use of a pacifier or dummy

The benefits of universal antimicrobial therapy are modest (reduced risk of pain and fewer AOM in a small subgroup of patients); to prevent 1 child suffering ear pain 2 to 7 days after presentation, 17 children are treated early. A further complication of universal treatment with antimicrobials is a doubling of the incidence of emesis, diarrhoea and rashes among patients.[9] Finally, the risk of a dire complication among untreated children in developed countries has become exceedingly rare.[13] Therefore, a policy of selective use of antimicrobials for AOM unresponsive to initial palliative therapy (e.g. analgesia) has been implemented by some.[14,15] Under selective treatment, approximately 14% of patients will have ear pain persist beyond 24 hours of presentation and then be placed on antimicrobials.[9] Discussing treatment options (universal antimicrobial treatment versus selective use with analgesia) with parents will aid the clinician in finding the appropriate therapy for a child.

There are additional factors (table II) that need to be considered when thinking about initiating therapy for AOM. Host factors (such as male sex, a sibling's history of recurrent AOM and, most significantly, age at the time of the first AOM before reaching 6 months[3]) and environmental factors [such as low socioeconomic status, lack of breast feeding and exposure to other children (within the household or with group day care attendance)][7] are associated with greater disease prevalence. When considering withholding treatment for children with AOM, clinicians should recognise that children with these risk factors are at increased risk for recurrent AOM and may require prompt therapy.

3. Treatment Options

There are a large number of recommended antimicrobial agents available to treat paediatric infectious diseases, including AOM.[16] They vary with respect to spectrum of action, dosage and duration of therapy, cost, taste and predominant adverse effects.

3.1 Spectrum of Action

Increasingly, more expensive, broad spectrum antimicrobial drugs like second- and third-generation cephalosporins are being prescribed for common paediatric, respiratory tract–related disease and the use of less expensive drugs such as the penicillins has been decreasing.[6] Perhaps this trend is fuelled by concerns for bacterial resistance, by the effective promotion by pharmaceutical companies of their newest 'best' antimicrobial, or by attempts to ensure treatment compliance. However, with the new β-lactam drugs demonstrating efficacy similar to that of amoxicillin against many diseases, it is often difficult to justify the use of newer, more broad spectrum and expensive antimicrobial agents.[16-18]

There is an apparent contradiction between the prevalence of bacterial pathogens commonly resistant to antimicrobials isolated from middle ear aspirates of children with AOM (table III) and the efficacy of amoxicillin. This phenomenon may be related to the concentration of the antimicrobial agent achieved in the ears of patients – which will exceed the minimal inhibitory concentration

Table III. Prevalence of prominent pathogens and mechanisms of antimicrobial resistance

Organism	Approximate prevalence of pathogen in children with AOM (%)	Mechanism of resistance	Approximate prevalence of antimicrobial resistance in these pathogens
Streptococcus pneumoniae	40	Altered penicillin binding proteins	20% of bacterial strains are resistant (one-third of resistant strains are considered highly resistant)
Haemophilus influenzae	25	Produces β-lactamase	30-40% of bacterial isolates produce the enzyme
Moraxella catarrhalis	10	Produces β-lactamase	80% of bacterial isolates produce the enzyme; however, amoxicillin appears to be effective in eradicating 80% of these resistant strains – possibly due to the low β-lactamase concentration achieved in the middle ear by the microbe or due to the spontaneous clearance of the microbe

Abbreviation: AOM = acute otitis media.

(MIC) even for moderately resistant organisms. In the case of resistant *Streptococcus pneumoniae*, amoxicillin easily surpasses the threshold (MIC ≥ 2.0 mg/L) for middle ear fluid concentration.[19,20] However, clinicians may want to consider the use of a broad spectrum antimicrobial agent in the initial therapy for AOM and acute sinusitis if the child recently has (less than 4 to 6 weeks previously) been on antibiotics or is immunocompromised.

3.2 Dosage and Duration of Therapy

Depending on the specific agent, antimicrobials are prescribed in dosage intervals of 6, 8, 12 and 24 hours (table I). For most common, acute, outpatient paediatric infectious diseases, such as AOM, bronchitis/pneumonia, pharyngitis, sinusitis and cellulitis, the majority of antimicrobials are prescribed for a 10-day period. Certain specific agents have shorter recommended courses; for example, in treating AOM ceftriaxone is pending approval in the US as a single intramuscular injection[21] and azithromycin has been approved as a single dose daily for 5 days.[22]

Is the usual prescribed duration of therapy appropriate? It may be possible that a subset of children can be adequately treated with less than the standard length of antimicrobial therapy. For example, in a group of 868 children treated with amoxicillin/clavulanic acid for AOM, a 5-day antimicrobial regimen was found as effective as a 10-day course for children over 2 years of age.[23] In the treatment of AOM, providing antimicrobial therapy for longer than the standard duration has no long term, and limited short term, benefit.[24]

3.3 Cost

Consideration of the cost of antimicrobials for both families and society should play a greater role in the selection of a specific agent. Physicians need to understand how a family will pay for a prescribed antimicrobial and what barriers may delay or prevent them from obtaining the drug. In the US, medical costs for the majority of children (86%) are covered to a varying degree by private and public health insurance.[25] The benefit packages of insurance plans differ and may require copayment fees, fixed deductibles, use of restricted formularies and other elements contributing to the cost of prescriptions. For those families who are responsible for out-of-pocket payment for prescription drugs, or have no health insurance, the cost of antimicrobials may impose a significant financial burden and a barrier to compliance.

The average retail cost of a prescription in the US ranges from under $US5 to over $US60 for a 10kg child. Newer agents are far more expensive than older, commonly used antimicrobials such as amoxicillin, cotrimoxazole (trimethoprim plus sulfamethoxazole), and erythromycin plus sulfafurazole (sulfisoxazole) [table I]. In a study of the fee-for-service Medicaid programme in Colorado, although the lower cost antimicrobials accounted for two-thirds of the total antibiotic prescriptions filled, they contributed only 21% of the expendi-

Table IV. Palatability of antimicrobials used in the treatment of common outpatient paediatric diseases (after Steele et al.[28] Demers et al.[29] and Samulak et al.[30])

Generic drug	Trade name	Colour	Flavour	Appearance	Smell	Texture	Taste	Aftertaste	Overall
Amoxicillin	Amoxil®	Pink	Strawberry	++++	+++	++++	+++	++++	+++
Amoxicillin/clavulanic acid	Augmentin®	Cream	Banana, orange	+++	+++	+++	++	++	+++
Ampicillin	Omnipen®	Pink	Strawberry	+++	+++	+++	+++	++	+++
	Principen®	Pink	Mixed fruit/ blackcurrent/ peppermint	+++	++	+++	+++	+++	+++
Azithromycin	Zithromax®	Pink	Cherry	+++	++++	+++	+++	++	+++
Cefaclor	Ceclor®	Pink	Strawberry	++++	++++	+++	+++/++++	+++/++++	+++/++++
Cefadroxil	Duricef®	Cream	Orange/ pineapple	+++	++++	+++	++++	++++	++++
Cefalexin	Keflex®	Pink	Bubble gum	+++	++++	++++	++++	++++	++++
Cefixime	Suprax®	White	Strawberry	+++	+++	++++	++++	++++	++++
Cefpodoxime proxetil	Vantin®	White	Lemon/crème	+++	++++	+++	++	+	++
Cefprozil	Cefzil®	Pink	Bubble gum	++++	++++	++++	++++	+++/++++	+++/++++
Ceftibuten	Cedax®	Pink	Cherry	+++	+++	+++	++++	++++	+++
Cefuroxime axetil	Ceftin®	White	Tutti-frutti	+++	++++	++	++	++	++
Clarithromycin	Biaxin®	White	Vanilla	+++	+++	++	+++	++	+++
Dicloxacillin	Dynapen®	Pink	Orange/ pineapple	+++	++++	+/++	+	+	+
Erythromycin	EES400®	Yellow	Banana	+++	++++	+++	++	++	+++
Erythromycin/sulfafurazole (sulfisoxazole)	Pediazole®	White	Strawberry/ banana	++	+++	++	++	++	++/+++
Loracarbef	Lorabid®	Pink	Strawberry/ bubble gum	++++	++++	++++	++++	++++	++++
Oxacillin	Prostaphlin®	Pink	Apricot passion cola	++++	++	++	+	+	+
Phenoxymethylpenicillin (penicillin VK)	Veetids®	Red	Strawberry	++++	+++	++++	++	+/++	+++
Sulfafurazole (sulfisoxazole)	Gantrisin®	White	Raspberry	+++	+++	+++	+++	+++	+++
Cotrimoxazole (trimethoprim/ sulfamethoxazole)	Bactrim®	Pink	Cherry	++++	+++/++++	+++	+++	++	+++

Symbols: + poor; ++ fair; +++ better; ++++ best.

tures.[26] Cephalosporins and amoxicillin plus clavulanic acid accounted for an inordinately high proportion of expenditures. Contrary to expectations, in the Colorado study, the use of more expensive antibiotics was not associated with improved clinical outcome.

Antibiotic suspensions are dispensed in a variety of fixed concentrations and bottle sizes (quantities). Since the dose prescribed is dependent on the child's weight, it is common to have excess antibiotic remaining after a treatment course. Prescribing antibiotics to minimise wastage helps to reduce cost.[27] For example, 40% of clarithromycin remains in the bottle after completing a 10-day course of therapy when prescribed for both 10 and 20kg children. A similarly efficacious agent with less wastage will cost less. For younger children, the amount of antibiotic 'left over' can vary between 10 and 60%.

Prescribing the precise amount of antibiotic needed for the treatment course will not only reduce costs but will also avoid future self-medication without consultation – a potentially serious concern. If antibiotic is left over, parents may ini-

tiate inappropriate treatment on their own and treat a viral infection with an antibiotic or treat a bacterial infection with the wrong agent. Reconstituted antimicrobial suspensions become inactive over time and parents may delay medical attention believing that they have adequately treated a serious infection. Finally, once the excess antibiotic has been used, the clinician will be faced with a dilemma about continuing therapy while guided by fewer available physical findings on examination and without the ability to obtain reliable cultures. We strongly recommend that clinicians minimise antibiotic wastage, explicitly advise their patients' parents to complete antibiotic courses and encourage them to discard any unused suspension or tablets at the conclusion of therapy.

3.4 Taste

In table IV we have gathered the results of several studies[28-30] evaluating the palatability of common antimicrobial suspensions available in the USA based on appearance, smell, texture, taste, aftertaste and overall assessment. Although adult volunteers have provided much of these data, taste preference in children appears to be similar.[31,32] The cephalosporins cefadroxil, cefixime, cephalexin and the carbacephem loracarbef appear to be the most palatable. However, numerous antibiotics, including amoxicillin, are fairly well tolerated. The effect of taste on patient compliance is be discussed additionally in section 4.

3.5 Adverse Effects

The most commonly reported adverse drug reactions include gastrointestinal symptoms (nausea, vomiting and diarrhoea) and skin rashes. Severe anaphylactic reactions are rare and severe adverse effects to other organ systems are rarer still.[2] Adverse effects occur with similar frequency (approximately 6% of antimicrobial prescriptions) with both amoxicillin and newer, more expensive antibiotics.[26] Amoxicillin plus clavulanic acid, certain cephalosporins like cefixime and the macrolides are known to produce gastrointestinal symptoms more commonly than other adverse effects. Amoxicillin and the sulphonamide drugs more commonly produce skin rashes. Factors that are associated with a greater likelihood of a parental report that an adverse drug reaction has occurred include high socioeconomic status, young age of the child and administration of a total daily dose greater that the therapeutic range recommended by the manufacturer.[33,34]

4. Compliance with Antimicrobial Therapy

Presentation of a prescription for an antibiotic does not guarantee that the child will in fact receive the agent. Several practices can contribute to improved compliance with treatment plans (table V). First, the parents must appreciate that their child has a treatable illness and that the therapy is necessary for both recovery and avoidance of complications.[35] Further, the parents need to be satisfied with the care provided.[36,37] This requires adequate communication with the parents and their child, clear explanations, display of an obvious concern for their child and clinical competence, as well as a helpful and courteous office staff.[38-40]

Secondly, parents need reassurance that the risk of adverse effects is minimal. They need to know what drug reactions to expect and in what circumstances they need to alert their physician. Despite the occurrence of an adverse reaction, antimicrobials are changed in less than 10% of treatment courses.[41]

Table V. Compliance-enhancing practices

Spend sufficient time during the patient visit to meet parental expectations
Alert parent that an adverse effect may occur, what can be done, and under what circumstances they should seek further medical care
Determine if financial concerns or other impediments will prevent prompt purchase of the antimicrobial
Clarify the dosage regimen in understandable terms
When prescribing liquid antibiotics, select a suspension that tastes good. Provide a premarked syringe and demonstrate its use
Use individualised written instructions, and consider the use of reminders

Thirdly, as discussed above, the costs of antimicrobials vary greatly. Depending on the family's financial resources, expensive drug prescriptions may not be filled or there may be delay in filling the prescription. The clinician should weigh cost with other factors, like taste, in these circumstances. In addition, providing sample antibiotics in order to initiate therapy sooner will also reduce the total amount of drug to be purchased. We suggest clinicians select among equally effective treatments the one that is least expensive and will result in the least amount of wastage.

Fourthly, as dosage frequency and length of therapy increase, compliance decreases.[33,41] Newer antimicrobials have the advantage of less frequent administration. The clinician needs to weigh the benefit of this convenience with the use of a broader spectrum, more expensive agent.[18] Whatever the dosage regimen, the physician should be clear about when the antibiotic should be taken. It is helpful for a family to incorporate administration of the medication into their daily routine by associating the schedule with meals, sleep and other regular activities.

Fifthly, antimicrobials taken with difficulty generally result in more missed doses.[41] Generally, infants and young children prefer pleasant-tasting liquids or chewable tablets. Some suspensions become more palatable if chilled or are easier to take mixed in small aliquots of apple sauce or juice. As an alternative, many children by the age of 5 years can be trained to swallow a tablet or capsule. However, an ill child often regresses in behaviour and may lose this skill. The clinician needs to discuss with parents the most suitable form of the drug before to writing a prescription. Also, when prescribing liquid antimicrobials, the relatively simple intervention of providing a syringe with a line clearly marked at the prescribed dose and demonstrating its use dramatically improves the accuracy of dosage administration.[42]

Finally, in addition to providing verbal and written instructions to parents,[43] consider providing a reminder sticker or magnet for the patient's refrigerator[44] and a self-monitoring calendar.[45] In contrast, more elaborate procedures like telephone reminders and slide-tape presentations have not been shown to be greater motivators of improved compliance.[46]

5. Treatment Failure and Relapses

Within 48 to 72 hours of initiating antimicrobial treatment for most common outpatient paediatric infectious diseases, acute signs (e.g. fever) and symptoms (e.g. pain) usually resolve.[11,47,48] However, if signs and symptoms persist, the clinician needs to carefully re-examine the patient, inquire about compliance with the therapy and reassess the selected antimicrobial agent.[49] Benefits of changing the drug may include coverage of resistant organisms and improved compliance.

For respiratory tract–related illnesses, like AOM, the persistence of symptoms may be due to a concurrent viral syndrome and no benefit will be derived with further antimicrobial therapy. Risks of selecting a new antimicrobial include exposure to new adverse effects, increased cost and promotion of the perception that one antimicrobial is stronger than another. In the event that the parent has provided the therapy as prescribed and the physical examination demonstrates persistence of the illness, the clinician should first reconsider the initial diagnosis before prescribing a second-line antimicrobial agent. With persistent failure of treatment, further diagnostic tests (tympanocentesis and aspirate culture, etc.) may be necessary to obtain a sensitivity profile for the pathogen.

Recommendations concerning follow-up for outpatient paediatric infectious diseases are illness-specific. With respect to an AOM, when should a clinician re-evaluate the recovering child? Common practice varies greatly and we suggest making this treatment decision in part on the basis of the patient's age, environmental risk features and past history (table II). In particular, children should be considered to be at greater risk for persistent or recurrent disease if they are less than 6 months of age, in group or family day care, or have a history of multiple previous infections. Children under 15 months old are more likely to have per-

sistent AOM[50] and may lack the communicative skills to alert their parents – resulting in prolongation of discomfort and hearing deficit during a period of language acquisition. Follow-up visits for these children, especially if at risk for recurrent disease, should be performed by 3 to 6 weeks.[51,52]

If a child more than 15 months old is at low risk for recurrent AOM and will be seen within the next few months for routine healthcare maintenance, follow-up can wait until that visit. Middle ear effusion commonly persists for months and can be evaluated at that time.[2,53] In school-age children, routine re-evaluation after an AOM can be delayed for 4 to 6 months. Certainly, if parents feel their child has impaired hearing or if minor symptoms persist, the child should be seen sooner.

6. Emergence of Bacterial Resistance

Antimicrobial use exerts a potent selective pressure among bacteria, encouraging emergence of resistance by eliminating more susceptible strains, by promoting ascendancy of bacteria with rare mutations of resistance and by permitting the spread of resistant strains from infected individuals.[17,54] Often the emergence of resistant strains of bacteria may be linked to inappropriate antibacterial therapy: trivial use in viral syndromes, overuse in surgical prophylaxis or tendency of newly released antimicrobials to displace older, established drugs of similar efficacy.[6,17] As many as half of all patients with the principal diagnosis of 'cold' or upper respiratory tract infection are prescribed antimicrobials.[55,56] High antimicrobial use increases the prevalence of resistance to that agent; when treatment protocols reduce use, the emergence of resistance to antibiotics may be delayed and even reversed.[15,54,57]

Antimicrobial resistance to penicillins has progressively climbed among the primary bacterial pathogens causing AOM and acute sinusitis: *S. pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* (table III).[11] And yet, in the vast majority of cases, amoxicillin remains highly effective in the treatment of AOM and acute sinusitis.[16,21,24,47,58-60] The contributions of spontaneous clearance (as high as 48% in AOM caused by *H. influenzae* and 19% in AOM caused by *S. pneumoniae*) and relative susceptibility of even resistant strains to antibiotic concentrations achieved in the middle ear and sinuses may explain this inconsistency.[11]

With the rise in single parent households in the US (the number of single parents increased from 6.9 million in 1980 to 11.4 million in 1994)[61] and with the shift of mothers to the workplace (72% in 1990),[62] remaining home to care for a sick child may be difficult for a family to arrange and to afford. Further, the success of medical treatment since the 1950s against illnesses like pneumonia has largely been attributed to the use of antibiotics. These factors encourage parents' belief that antimicrobials (and often a specific agent) will hasten their child's recovery from any infectious disease, including viral syndromes – permitting a return to daycare and/or school and their own return to work.[33]

Despite parental expectations for antibiotics and physicians' impressions that parents want these agents, when they are inappropriate clinicians should educate parents about the consequences of improper use of an antibiotic. Explanations from the clinician contribute more to patient (and parent) satisfaction than receipt of an antimicrobial prescription.[63] Possible consequences of improper antibiotic use can include an unnecessary risk of adverse reaction and allergy, unnecessary healthcare expense, and promotion of bacterial resistance.

Clinicians need to remain mindful of the appropriate indications for antimicrobial use to preserve the efficacy of our defences against common bacterial infections. Simple measures include resisting the temptation to prescribe an antibiotic for viral syndromes, saving newer agents for treatment failures or for when diagnostic testing proves a definitive susceptibility, and implementation of shorter treatment courses once guidelines have been developed. Physicians can make better-educated choices by consulting susceptibility profiles of community-acquired organisms produced by local

academic centres. When the physician is challenged by recurrent or chronic infections, obtaining a culture will allow definitive therapy. In the case of AOM, tympanocentesis will yield appropriate material for culture. Use of alternative and adjunctive therapies may also help in reducing the emergence of bacterial resistance.

7. Alternatives and Adjuncts to Antimicrobial Therapy

There are a number of potential alternatives and adjuncts to antimicrobial treatment, including vaccination, control of environmental risk factors, surgical techniques and alternative medical therapies. As demonstrated by the dramatic efficacy of childhood immunisations in reducing illness associated with bacterial pathogens like *Corynebacterium diphtheriae* and *H. influenzae*, new vaccines under development may reduce and prevent common outpatient paediatric infectious diseases. Since respiratory tract viruses like respiratory syncytial virus (RSV), rhinovirus, influenza and adenovirus have been implicated in predisposing development of AOM, vaccination to prevent these viral infections may have an indirect impact on the occurrence of AOM and acute sinusitis.[64] In the future, new vaccine combinations with as many as 6 components and new methods of administration (e.g. mucosal surface intranasal spray, single injection of a slow release microsphere vaccine, simple ingestion of transgenic plants) will reduce the susceptibility of children to common bacterial and viral pathogens.

Several risk features (table II) have been associated with an increased prevalence of AOM. It is likely that improving infection control measures in daycare, restricting exposure to environmental pollutants (like wood burning stoves and second-hand cigarette smoke), advocating breast feeding for at least 3 months, and similar measures to modify a child's environment will reduce the frequency of many childhood illnesses.

Surgical procedures can help to control some paediatric infectious diseases. For example, insertion of a tympanostomy tube for long term ventilation and/or drainage has been recommended for chronic otitis media with effusion (unresponsive to medical management) and recurrent AOM (especially antimicrobial prophylaxis failures).[65] This procedure is at least as effective as amoxicillin prophylaxis for recurrent AOM, but carries the risks of anaesthetic complications, persistent perforation (in about 4% of patients), tympanosclerosis and cholesteatoma.[66]

Parents commonly seek healthcare for their children outside of conventional medicine. Homeopathic medicine provides patients with a mixture of microdoses of various substances, which are theorised to stimulate the body's inherent recuperative processes. Spinal manipulation seeks to correct biomechanical defects contributing to infection susceptibility. Acupressure (including acupuncture) and massage stimulate and relax various parts of the body to enhance integrated functions. Botanical medicine and nutrition therapy seek to relieve pain and inflammation, and stimulate immune function.

What therapies do practitioners of alternative medicine advise for common outpatient paediatric infectious diseases? Homeopathic remedies like *Pulsatilla*, acupuncture to alleviate external pathogenic wind and internal heat, clinical nutrition with bioflavonoids, ginger and various vitamins and minerals, and other treatments have been used to care for children with AOM.[67] Parents rarely volunteer that they are providing their children with alternative medicine therapies. By inquiring about these treatments, clinicians may be able to identify promising therapies, as well as protect a child from potentially unsafe ones. There is certainly a need for randomised clinical trials to compare these alternative therapies with conventional medicine, as we seek alternatives to antibiotic therapy.

8. Conclusions

There is a remarkable number of antimicrobial agents available to treat common paediatric infectious diseases. They differ significantly with respect to dosage regimen, cost, taste and predominant adverse effects. Each of these factors affects patient compliance and needs to be accounted for

when selecting a specific antimicrobial agent. Effective physician-parent communication and relatively simple interventions, like dispensing marked syringes and written instructions, will further enhance compliance with treatment courses.

Bacterial resistance to antimicrobial agents has climbed relentlessly in the past decade, particularly with respect to *S. pneumoniae*, which is the leading aetiological bacterial agent in AOM, sinusitis, pneumonia and meningitis. Although current bacterial resistance has had little impact on outpatient management of paediatric infectious diseases, there is concern that if resistance continues to grow, outpatient treatment will become more complicated. Physicians can slow and perhaps reverse the emergence of this problem by being more careful about when they prescribe antimicrobial agents and which ones they select.

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