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Principles of Appropriate Antibiotic Use for Treatment of Uncomplicated Acute Bronchitis

ABSTRACT & COMMENTARY

Synopsis: *The evaluation of immunocompetent adults with an acute cough or a presumptive diagnosis of uncomplicated acute bronchitis should focus on ruling out serious illness, particularly pneumonia. Routine antibiotic treatment of uncomplicated acute bronchitis is not recommended, regardless of duration of cough. Patient satisfaction with care for acute bronchitis depends mostly on physician-patient communication rather than on antibiotic treatment. These guidelines are for adults with acute bronchitis without comorbid conditions, such as chronic lung or heart disease.*

Source: Gonzales R, et al. *Ann Intern Med.* 2001;134:521-529.

The term “acute bronchitis” usually designates an acute respiratory tract infection in which cough, with or without phlegm, is a predominant feature. In the United States, about 5% of adults self-report an episode of acute bronchitis each year, and up to 90% of these persons seek medical attention. In 1997, adults in the United States made more than 10 million office visits for bronchitis. As a result, acute bronchitis consistently ranks among the 10 most common conditions leading to outpatient physician visits.

Evaluation of Acute Cough

A wide variety of infections and inflammatory disorders can lead to an acute cough illness. The American College of Chest Physicians defines acute cough illness as lasting less than 3 weeks.¹ Acute upper respiratory tract infections account for approximately 70% of primary diagnoses, with asthma (6%) and pneumonia (5%) being the next most common. Previously undiagnosed asthma is a consideration in patients presenting with an acute cough. The diagnosis of asthma is difficult to establish because many patients with acute bronchitis will have transient bronchial hyperresponsiveness. The primary objective in a healthy adult with uncomplicated acute cough is to exclude the presence of pneumonia. An evidence-based review concluded that absence of abnormalities in vital signs (heart rate > 100 beats/min, respiratory rate > 24 breaths/min, or oral tem-

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perature > 38°) and chest examination (rales, egophony, or fremitus) sufficiently reduces the likelihood of pneumonia to the point where further diagnostic testing is usually not necessary.²

Microbiology of Acute Uncomplicated Bronchitis

As in community-acquired pneumonia, microbiological studies of uncomplicated acute bronchitis identify a pathogen in the minority of cases, ranging from 16-40%. Specific viruses most frequently associated with acute bronchitis are influenza B, influenza A, parainfluenza 3, respiratory syncytial virus, corona virus, adenovirus, and rhinovirus. To date, only *Bordetella pertussis*, *Mycoplasma pneumoniae*, and *C pneumoniae* (TWAR) have been established as nonviral causes of uncomplicated acute bronchitis in adults.

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Treatment of Uncomplicated Acute Bronchitis

Routine antibiotic treatment of uncomplicated acute bronchitis is not recommended, regardless of the duration of cough. The one uncommon circumstance for which evidence supports antibiotic treatment of patients with uncomplicated acute bronchitis is suspicion of pertussis.

Influenza is the most common pathogen isolated in patients with uncomplicated acute bronchitis. The neuraminidase inhibitors zanamivir and oseltamivir have demonstrated some efficacy in reducing illness duration in adults with naturally acquired influenza A and B if treatment begins within 48 hours of symptom onset.³

In most cases, cough is the major symptom for which patients seek relief. Randomized, controlled trials have demonstrated a consistent benefit of therapy with albuterol vs. placebo in reducing the duration and severity of cough.⁴ Preparations containing dextromethorphan or codeine probably have a modest effect on severity and duration of cough. Cough of more than 3 weeks duration, cough associated with underlying lung disease, or experimentally induced cough have been shown to respond to dextromethorphan or codeine. Elimination of environmental cough triggers such as dust and dander, as well as the use of vaporized air treatments in low-humidity environments, such as high altitude, are also reasonable options.

Clinicians should be encouraged to discuss the lack of benefit of antibiotic treatment for treatment for uncomplicated acute bronchitis and stop prescribing antibiotics for this condition as a standard of practice. Mounting evidence indicates that patient satisfaction with the office encounter does not depend on receipt of antibiotic therapy but instead is related to the patient-centered quality of the encounter.⁵

■ COMMENT BY DAVID OST, MD, FACP, & NAJMA USMANI, MD

Most cases of acute bronchitis occur in otherwise healthy adults, in whom this acute cough illness can be called "uncomplicated acute bronchitis." The principles in this guideline are intended to apply to such patients, and do not necessarily apply to patients with chronic lung diseases such as chronic obstructive pulmonary disease.

The recommendations given in this article for discussing the management of acute bronchitis with patients include the following steps:

1. Provide realistic expectations of the duration of the patient's cough, which will typically last for 10-14 days after the office visit.
2. Refer to the cough illness as a "chest cold" rather than bronchitis.⁶
3. Personalize the risk of unnecessary antibiotic use.
4. Explain to patients why we need to be more selective in treating only those conditions for which a major

clinical benefit of antibiotics has been proven. Alert them to the current epidemic in antibiotic resistance among community bacterial pathogens and explain the public health concern. (Dr. Usmani is an Internal Medicine Fellow, Northshore University Hospital, Manhasset, NY.) ❖

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Welding-Related Parkinsonism

ABSTRACT & COMMENTARY

Synopsis: *The search for environmental agents that are responsible for PD has been unsuccessful, until this report.*

Source: Racette BA, et al. *Neurology*. 2001;56:8-13.

A variety of toxins can produce acute parkinsonism, including MPTP, organophosphate pesticides, carbon monoxide, carbon disulfide, cyanide, and methanol. Although all of these agents induce a parkinsonian state, MPTP produces an illness that is clinically indistinguishable from Parkinson's disease (PD). Patients with MPTP-induced parkinsonism are similar to PD in their response to levodopa and their propensity to develop motor fluctuations and dyskinesias. However, MPTP-induced parkinsonism differs from PD in several important ways. First, the parkinsonism is acute, evolving over hours to days to produce a typically severe akinetic-rigid state. Second, the pathology of MPTP parkinsonism is different from PD, as there are no Lewy bodies in the nigra. While the discovery of MPTP produced an explosion of interest in possible environmental triggers of PD, MPTP is clearly not responsible for sporadic PD. The search for environmental agents that are responsible for PD has been unsuccessful, until this report.

In their seminal paper, Racette and colleagues report 15 career welders who developed a parkinsonian state indistinguishable from PD. In their professional life, welders are exposed to particulate fumes and gases with high concentrations of F, Mn, Zn, Pb, As, S, Cr, Ni, CO,

CO₂, F, and HF. All 15 welders in this series were men, with an average occupational exposure of 47,144 welding hours. They developed symptoms of parkinsonism at an average age of 46 years, and were evaluated 8.5 years into the course of their illness.

Parkinsonian welders were clinically indistinguishable from patients with sporadic PD. The incidence of asymmetry, bradykinesia, tremor, rigidity, and postural instability were the same. Thirteen of 15 welders treated with levodopa improved, and younger patients developed motor fluctuations and dyskinesias. Two patients underwent 18-fluoro-dopa PET scanning, which measures the nigro-striatal dopaminergic projection. The scans showed selective reductions of dopaminergic innervation in the posterior putamen, a pattern indistinguishable from that seen in idiopathic PD.

Racette et al compared the clinical features of their 15 welders to a group of 100 sequential patients diagnosed with idiopathic PD, and to 6 patients that were age- and gender-matched to each welder. There were no differences between the welders and PD patients in any clinical features, with the exception that welders developed their first symptoms of parkinsonism an average of 17 years before sporadic PD patients.

■ COMMENT BY STEVEN FRUCHT, MD

This is the first report to directly link an environmental exposure to an illness that is indistinguishable with PD. What is the likely mechanism to explain the development of parkinsonism in welders? Racette et al speculate that a certain population of welders may be at higher risk for the development of PD. Given an adequate exposure to inhaled welding gases, a certain proportion of welders will likely develop PD. This report adds strong support to the argument that sporadic PD may result from exposure to low levels of environmental toxins in susceptible patients.

It is not known which element in welding vapor is responsible for the development of parkinsonism, although manganese is a likely culprit. Occupational exposure to manganese produces a syndrome called manganism, characterized by extrapyramidal signs of parkinsonism and dystonia. However, the response of manganism to levodopa is only partial and often transient, and such patients often have neuropsychiatric features that were not seen in PD welders. Nevertheless, the possibility exists that long-term, low-level manganese exposure in a susceptible patient population produces a syndrome that is indistinguishable from sporadic PD. (Dr. Frucht is Assistant Professor of Neurology, New York Presbyterian Hospital-Cornell Campus, New York, NY.) ❖

Long-term Changes in Lifestyle Favorably Influence Plasma Levels of Leptin

ABSTRACT & COMMENTARY

Synopsis: *Decreased intake of dietary fat and increased physical activity reduced plasma leptin concentrations beyond the reduction expected as a result of changes in fat mass.*

Source: Reseland JE, et al. *Am J Clin Nutr.* 2001;73:240-245.

Leptin is a peptide hormone expressed and secreted in proportion to adipocyte size and number and circulates in plasma in a concentration highly correlated with body fat mass. Administration of leptin to animals has indicated that it participates in the regulation of food intake and energy expenditure. Because there is a large variation in leptin concentration in individuals with similar body composition, Reseland and colleagues and Considine and colleagues¹ believe that factors other than fat cell mass and number must be important in determining plasma leptin concentrations.

The objective of this study was to determine whether changes in dietary energy sources and exercise-mediated energy expenditure, alone or in combination, affect plasma leptin concentrations. In a randomized trial, 1186 men with metabolic syndrome (insulin resistance) were divided into 4 groups: diet, exercise, combination of diet and exercise, and control. Data on dietary intake, physical fitness, and demographics were collected, and plasma leptin concentrations were measured before and after a 1-year intervention period.

Plasma leptin concentrations, body mass index, and fat mass decreased in association with long-term reductions in food intake as well as increased physical activity. By adjusting for either body mass index or fat mass, they observed a highly significant reduction in plasma leptin concentration after both the diet and exercise interventions. There was no interaction between interventions, suggesting a direct and additive effect of changes in diet and physical activity on plasma leptin concentrations. Reseland et al concluded that decreased intake of dietary fat and increased physical activity reduced plasma leptin concentrations beyond the reduction expected as a result of changes in fat mass.

■ COMMENT BY RALPH R. HALL, MD, FACP

Obese individuals have increased concentrations of

serum leptin and a concomitant decreased sensitivity to leptin. This is similar to the findings with serum insulin levels in obesity. As with insulin, administration of leptin may result in increased signaling to the central nervous system and pituitary. Thereby, reductions in food intake, body fat mass, and body weight in obese patients may result from treatment with recombinant leptin.

Leptin treatment of a young obese girl with a mutated *ob* gene with congenital leptin deficiency produced a reduction in body fat and a dramatic reduction in appetite, food seeking behavior, food intake, and body weight.² Additional trials in obese adults have also been encouraging.³

There are other effects of leptin, such as Heptulla and colleagues' study on the effects on pituitary growth hormone release and other studies noting the relationship to LH, FSH, ACTH, and cortisol levels which will merit following.⁴ However, in the meantime, the studies of Reseland et al demonstrate that just as with insulin resistance, exercise and diet can increase the sensitivity to serum leptin. This seems to be a more desirable approach than the administration of recombinant leptin which is likely to be an extremely expensive effort. ❖

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Alternative Medicine Use in Older Americans

ABSTRACT & COMMENTARY

Synopsis: *Alternative medicine is used by 30% of English-speaking Americans older than age 65. Those who made the most visits to medical physicians were more likely to use alternative medicines, and 57% did not tell their doctors about it.*

Source: Foster DF, et al. *J Am Geriatr Soc.* 2000;48:1560-1565.

A national survey from the center for Alternative Medicine and Research at Beth Israel Deaconess Medical Center in Boston, Mass, was conducted in 1997-98 to assess the prevalence and patterns of alternate therapies in the United States. They found 42% of

all Americans reporting use in the previous year.¹ This current study further analyzes that data for persons aged 65 and older.

In the telephone survey, which was limited to English speakers, random-digit dialing was used to identify households and financial incentives were used to ensure adequate participation. The data were then weighted to adjust for geographic variation in cooperation. Out of 2049 total respondents, 311 were aged 65 or older. Demographically this group corresponded to US Census Bureau descriptors for older Americans compared to younger ones, such as lower incomes, less well educated, less racial diversity, and more women.

The survey first asked about the respondent's medical conditions, and then about their use of 20 alternate medicine therapies, which were defined as interventions not taught in medical schools and not widely available in US hospitals. Herbal and vitamin use was clearly defined to exclude daily vitamin use or vitamins prescribed by a medical doctor (MD or DO). All users of alternate therapies who acknowledged seeing a medical doctor in the past year were also asked if they had discussed their use with their medical doctor.

Compared to respondents younger than 65, the older persons used alternative medicine less often (30% compared to 46% for < 65 years). The most popular choices were chiropractic (11%) and herbal remedies (8%) for the older group, compared to relaxation/massage and herbal choices in younger persons. The other top choices for older persons were high-dose vitamins, relaxation techniques, and religious healing by others.

The use of alternative medicine declined with advancing age, starting at a high of 33% in ages 65-74, 28% in ages 75-84, and 17% for those age 85 and older. In contrast, the age group 36-55 reported 50% usage of alternative medicine.

Arthritis and back pain were the most common reported conditions for which alternative medicine was used. One in 9 of the older group reported using chiropractic in the past year. Alternative medicine use was correlated with visits to conventional physicians, with users ranging from 22% of those making 1-2 annual visits to 44% of those who had 7 or more visits. Only 7% of older persons who made no visits to medical physicians used alternative therapies.

■ COMMENT BY MARY ELINA FERRIS, MD

This is the first study showing that older Americans are following national trends of increasing alternative medicine use, although their choice of therapies may be somewhat different from younger persons. A previous survey from Great Britain suggested that 15% of older

persons used alternatives there, but this number may be greater today.²

The fact that users of alternative medicine also subscribed to conventional medicine (indicated by the correlation between medical visits and alternative visits) suggests that users are not necessarily rejecting or abandoning traditional care, a view that is supported by other research.³ It may be that they are overusers, but a more likely explanation is that they are combining all available therapies when faced with illness and discomfort. Surveys have shown most alternative users are very satisfied with the care they receive, even if they did not find improvement in their presenting complaint.⁴

Safety issues and drug interactions are a concern if our patients are not telling us about the alternate treatments they are receiving. Many published reviews have reminded us that not all herbal remedies are harmless, and older persons with joint deformities may not tolerate vigorous physical manipulations.

Although this study had a small sample size and was probably culturally limited, it gives us useful information to guide our history taking. No longer should we assume that older persons are immune from the rush to alternative medicines, nor that they would tell us if they were seeking alternate treatments. Only by directly asking can we hope to obtain a complete picture of the various treatments our older patients are using. ❖

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Pharmacology Update

Formoterol—A New Long-acting Beta Agonist Inhaler

By William T. Elliott, MD, FACP
and James Chan, PharmD, PhD

The fda recently approved formoterol inhalation powder, a long-acting, inhaled selective beta-2 adrenergic agonist. The drug is the second long-acting beta agonist on the market along with salmeterol (Serevent). Formoterol is approved for the maintenance

treatment of asthma and the prevention of exercise-induced bronchospasm. Formoterol, which has been available in Europe, is marketed as Foradil by Novartis Pharmaceuticals.

Indications

Formoterol is indicated for the long-term maintenance of asthma and the prevention of bronchospasm in adults and children 5 years of age and older. It is also indicated for the acute prevention of exercise-induced bronchospasm in adults and children 12 years of age and older.¹

Dosage

For the long-term maintenance of asthma, the usual dose is inhalation of the contents of 1 capsule (12 mcg) every 12 hours. The total daily dose should not exceed 2 capsules per day. For the prevention of exercise-induced bronchospasm the dose is 1 capsule (12 mcg) at least 15 minutes before exercise.

Formoterol is available as 12 mcg capsules and is administered with the Aerolizer Inhaler.

Potential Advantages

Formoterol has a faster onset of action than salmeterol.² There have been a few case reports of patients with preferential response to formoterol compared to salmeterol.^{8,9}

Potential Disadvantages

Some may find the inhalation of dry powder difficult, especially if they are accustomed to aerosolized inhalers. Since the delivery system is self actuated, drug delivery is sensitive to the patient's inspiratory flow rate.⁴

Formoterol may have a greater potential to cause side effects such as tremors and effect on Q-T interval compared to salmeterol.³

Comments

Formoterol is the second long-acting selective beta-2 adrenergic agonist approved for the long-term treatment of asthma. It is administered as a dry powder and does not use a CFC propellant. Salmeterol is available both as an aerosol and dry powder.

These drugs appear to be comparable in improving pulmonary function in asthmatics in single-dose trials.^{2,3} The primary difference between formoterol and salmeterol is the faster onset of action of the formoterol which is similar to that of albuterol. With daily twice-daily dosing, the benefit of faster onset may be negligible. Despite its faster onset of action, formoterol is not recommended for rescue use as its long duration of action

may mask signs of more serious asthma.² However, the faster onset of action of formoterol may be advantageous for the prevention of exercise-induced bronchospasm. In contrast to salmeterol, formoterol has not been approved for the maintenance treatment of bronchospasm of chronic obstructive pulmonary disease but appears to be equally effective.^{5,6}

Both drugs are priced similarly with a 30-day cost of about \$70.

Clinical Implications

Long-acting beta agonists such as salmeterol and formoterol are recommended as alternatives to medium-dose inhaled corticosteroids in the long-term management of moderate to persistent asthma.⁷ Formoterol provides a safe and effective alternative to salmeterol. Both are approved for use in adults and children, although salmeterol is approved down to the age of 4 compared to 5 for formoterol. ❖

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CME Questions

32. Which of the following statements are false?

- a. Elevation of plasma leptin is associated with leptin resistance.
- b. Leptin responds to exercise similar to insulin.
- c. Changes in plasma leptin are associated with changes in growth hormone.
- d. Administration of leptin to obese patients is associated with decreases in fat mass.

33. Which age group reports the highest use of alternative medicine?

- a. Age 75-84
- b. Age 65-74
- c. Age 56-64
- d. Age 36-55
- e. Age 18-35

By Louis Kuritzky, MD

Prior Alcohol Consumption and Mortality Following Acute Myocardial Infarction

Population studies have demonstrated a U-shaped distribution of the relationship between alcohol intake and coronary heart disease (CHD), in that persons with the most “moderate” alcohol consumption appear to enjoy lesser CHD than either nondrinkers or heavy drinkers. Whether the alcohol itself exerts a beneficial effect, or moderate alcohol consumption is associated with other lifestyle factors which enhance cardiovascular health remains unknown.

The current study, the first of its kind, examined the relationship of alcohol consumption to mortality in individuals suffering an acute myocardial infarction (AMI). Mukamal and colleagues interviewed men and women (n = 1935) within a few days of having an AMI about their alcohol consumption in the previous year, stratified by grams of ethanol per week into abstainers, light drinkers (< 7 drinks/week), and moderate drinkers (> 7 drinks/week).

Almost half of the patients reported no alcohol intake in the prior year. Higher alcohol intake correlated with higher educational attainment and higher income. AMI mortality was highest among abstainers, and lowest in moderate drinkers. Mukamal et al conclude that in this population, moderate alcohol intake in the year prior to AMI was associated with a more favorable survival outcome than abstention or light alcohol consumption. ❖

Mukamal KJ, et al. *JAMA*. 2001;285:1965-1970.

A Re-evaluation of the Duration of Survival After the Onset of Dementia

Life expectancy among persons with dementia has been reported to be substantially reduced, ranging from 5-9 years on average. Such observations suffer from length bias—persons with rapidly progressive dementia and demise participate less often in studies—which would tend to underestimate the effect of dementia on mortality.

In order to gain a clearer picture of the effect dementia imparts on survival, Wolfson and colleagues used data from a randomly selected large Canadian population (n = 10,263) of persons older than age 65 who were screened for cognitive impairment. In addition to determining the presence of dementia, date of onset for cognitive impairment was noted. Subjects were followed for 5 years.

In the cognitively impaired subjects (n = 821), most had Alzheimer’s disease, but almost one-fourth had vascular dementia.

Unadjusted median survival for the group, which did not differ significantly between those with probable Alzheimer’s disease, possible Alzheimer’s disease, or vascular dementia, was 6.6 years. When adjusted for length bias, this median survival was reduced to 3.3 years. This survival is substantially less than in previously reported data, and Wolfson et al note that this places dementia in a category with other substantially mortal disor-

ders like congestive heart failure. ❖

Wolfson C, et al. *N Engl J Med*. 2001;344:1111-1116.

Effectiveness of St. John’s Wort in Major Depression

St. john’s wort (sjw) is a widely popular treatment for depression, both in the United States and Europe. Meta-analysis has concluded that SJW is superior to placebo, with approximately equal efficacy to traditional proprietary pharmacologic agents, and often fewer side effects. There has been some criticism of previous study flaws that may have undermined the certainty with which conclusions about SJW efficacy may be drawn. This prospective, randomized, double-blind, placebo-controlled (n = 200) investigation was designed to evaluate the comparative efficacy of 300 mg of SJW over an 8-week period. Study participants had suffered depression for an average of more than 2 years.

Because of the risk of suicide in depressed persons, and since this study contained a placebo arm, any demonstration of suicide risk was a reason for exclusion. Additionally, deterioration from baseline depression scores also resulted in exclusion from the trial.

Despite the use of multiple measurement tools for depression outcome (eg, Beck Depression Inventory, Clinical Global Impression, Hamilton Anxiety Scale), Shelton and colleagues were not able to demonstrate an antidepressant response significantly greater than placebo. ❖

Shelton RC, et al. *JAMA*. 2001;285:1978-1986.

ECG Review

Shifting Sites

By Ken Grauer, MD

Figure. ECG obtained from an asymptomatic 76-year-old woman.

Clinical Scenario: The ECG in the Figure was obtained from an asymptomatic 76-year-old woman. How do you interpret this tracing?

Interpretation: The most interesting part of this 12-lead ECG is the rhythm strip that appears at the bottom of the tracing. The rhythm is clearly irregular. Atrial activity is present, but it does not remain constant throughout the tracing. The obvious question is how to interpret the rhythm?

The easiest approach to arrhythmia interpretation when confronted with changing atrial activity and an irregular ventricular rhythm is to look first for the presence of an *underlying* rhythm. Recognition of the fact that the underlying rhythm in this case is sinus greatly facilitates interpretation of surrounding nonsinus activity. The complexes marked *X* (and possibly also the complex just before the first *X-labeled* beat) all occur at a regular rate (of about 75 beats/minute), and are all preceded by a similar looking upright P wave with a constant PR interval. This presumably reflects an underlying sinus rhythm. Atrial beat morphology subtly changes with the P wave marked *Y*, and beginning with the P wave marked *Z* is seen to take on a taller, more peaked shape for the remainder of the rhythm strip. The site of atrial pacemak-

er activity has therefore shifted from the sinus node to some other atrial site which manifests a similar P wave morphology to that seen at the very beginning of this tracing (ie, prior to the *X-marked* sinus beats).

The rhythm strip findings we have just described suggest a *wandering* atrial pacemaker as the etiology of the rhythm, in which P wave morphology intermittently changes reflecting rotation of the site of atrial pacemaker activity. An alternative explanation might be that the gradual acceleration of peaked P wave complexes toward the end of the rhythm strip reflects a “warm-up” phenomenon of an ectopic atrial tachycardia (EAT) arising from increased automaticity of some ectopic atrial site. Additional rhythm strip monitoring is needed to clarify this possibility.

Apart from the rhythm, nonspecific ST-T wave abnormalities are present in multiple leads on this ECG, but there are no acute changes. This tracing therefore provides a nice illustration of how helpful simultaneously recorded leads may be for assisting in complex rhythm interpretation, since the etiology of this arrhythmia would not be evident from inspection of the 12-lead ECG shown here *without* the accompanying rhythm strip. ❖