BYLINES

A Midyear Progress Report

With the arrival of summer, it's time for much-needed vacations and lazy poolside naps—a brief respite from the hectic schedules and heavy workloads typical of spring, fall, and winter. It's also a good time for the editorial team of *The Consultant Pharmacist* to take stock in the accomplishments of the previous six months and progress toward year-end objectives. In that vein, I want to report a few important developments in our ongoing efforts to make the journal the preeminent forum for original research in geriatric pharmacotherapy, senior care news, and valuable insights from pharmacy practictioners.

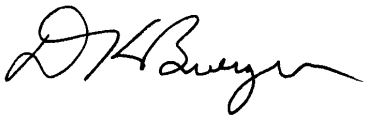
First, I want to call readers' attention to a few newly added lines of text on the journal masthead (see page 687) noting that peer-reviewed articles published in the journal are currently indexed by both International Pharmaceutical Abstracts and the Cumulative Index of Nursing and Allied Health. As you may be aware, over the years the journal's editors have submitted several applications to the National Library of Medicine requesting that the peer-reviewed content of *The Consultant Pharmacist* be included in NLM's Index Medicus database. Each time, the NLM's expert review panel has given the journal a higher priority rating for indexing. We're gearing up for yet another (hopefully successful) run at MEDLINE indexing in the near future, but it's important for current and prospective authors to know that their work is readily accessible right now to an enormous audience of pharmacists and allied health professionals through these prominent indexing services.

Next, I'm delighted to announce that Keith Swann, a seasoned communications specialist with a long background in biomedical publishing, joined the journal staff as senior editor in late May. Keith comes aboard after nearly two years as assistant director of communications for the American Association of Physician Assistants and, prior to that, nearly five years as a writer and editor with St. Anthony's Publishing, a leading medical communications company. Keith has already proven to be a major asset to the journal's editorial team, and I'm sure he'll be contacting many of you personally for interviews, insights, and story ideas in the months ahead.

Lastly, I want to enlist your help in reviving an important part of the journal that has languished in recent months. Over the years, the "Commentary" section of *The Consultant Pharmacist* has provided a high-visibility vehicle for readers to share their views on patient care, practice management, and reimbursement challenges—or simply vent their frustration—with other senior care pharmacists and the broader long-term care community. In recent months, however, submitted commentaries have been few and far between. We've already taken steps to generate more insightful commentaries from members of the journal's Editorial Review Board and Editorial Advisory Board, as well as the Society's elected and appointed leaders, including members of the Board of Directors, Policy Council, VIP / Core Curriculum Work Group, Education Advisory Committee, Government Affairs Committee, and ASCP-PAC Board of Trustees. In addition, we'd like to see many more contributed commentaries from the "rank and file" of consultant pharmacy, those who wrestle with all manner of patient care, policy, and reimbursment challenges every day in their practices.

Do you have some fresh insights on an article published in the journal? Or do you just want to gripe about a thorny patient care dilemma or reimbursement challenge? If so, commentary submissions, always welcome, can be forwarded to me at ASCP's Alexandria, Virginia offices (dbuerger@ascp.com).

Well, that brings me to the end of this midyear progress report. With the addition of a new senior editor, and with your help and commentary columns, we hope to continue raising the journal to even greater heights of excellence and prestige in the months ahead.



David K. Buerger
Managing Editor

CORRECTION

The "Consultant Pharmacist Forum" item on zinc therapy in the May issue of the journal (Consult Pharm 2000;15:556–60) did not identify the author, Richard W. Druckenbrod, PharmD, BCPS, Assistant Professor of Pharmacy Practice, Campbell University School of Pharmacy, Buies Creek, North Carolina. Our apologies to Dr. Druckenbrod for the oversight and to our readers for any confusion this error may have caused.

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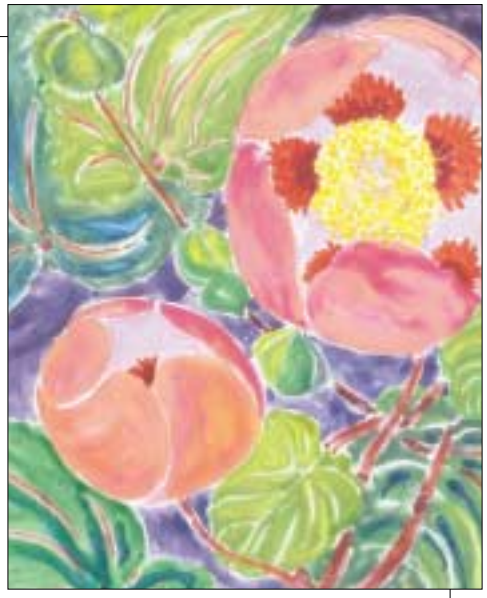
July 2000/Vol. 15, No. 7



About the artist: This month's beautiful cover art, "Desert Bloom," was done in watercolor by Jane Gill, a resident of Leisure World in Silver Spring, Maryland.

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The official journal of the American Society of Consultant Pharmacists

The Consultant Pharmacist

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The Consultant Pharmacist® is indexed by the Cumulative Index of Nursing and Allied Health, and by International Pharmaceutical Abstracts.

The Consultant Pharmacist® is published 13 times a year by the American Society of Consultant Pharmacists (ASCP).

Subscriptions and Change of Address
Paid subscriptions are available for $50 per year in the United States and its possessions and $80 elsewhere. Single copies, both current and back issues, are offered for sale subject to availability for $8 each. Change of address requests should be sent at least six weeks in advance to ASCP, 1321 Duke Street, Alexandria, VA 22314-3563; include the present mailing label with each request.

The Consultant Pharmacist® (ISSN 0888-5109) is published 13 times a year and is a registered trademark of the American Society of Consultant Pharmacists (ASCP). Membership rates in the association are $185 annually, of which $18 is applied to the cost of the journal. Periodicals Postage Paid at Alexandria, VA and additional mailing offices. POSTMASTER: Send address changes to *The Consultant Pharmacist*®, 1321 Duke Street, Alexandria, VA 22314-3563.

HEALTH TRENDS

POSITIVE AFFECT MAY PREDICT FUNCTIONAL INDEPENDENCE

A high degree of emotional well-being appears to be independently associated with improved survival and better functional ability, according to a recent report in the *Journal of the American Geriatrics Society* (J Am Geriatr Soc 2000;48:473–8).

To explore the relationships of positive affect, survival, and functional ability, a team of investigators from the University of Texas Medical Branch, Galveston, conducted a two-year, prospective cohort study of a population-based sample of 2,282 elderly Mexican Americans (aged 65–99 years) who reported no functional limitations at baseline interview.

At two-year follow-up, subjects with high baseline scores for positive affect on a modified version of the Center for Epidemiologic Studies Depression Scale (CES-D) were about half as likely as those with low CES-D scores to have become disabled in activities of daily living (ADLs), and two-thirds as likely to exhibit slow walking speed. Moreover, mortality from all causes during the study period was twofold lower among subjects with high positive affect. The observed associations persisted after controlling for variables such as functional status, sociodemographic variables, major chronic conditions, body mass index, smoking status, alcohol consumption, and negative affect at baseline.

"It is important to note that the effect of positive affect on ADL [status], mobility, and mortality was independent of depressive symptomatology," the investigators commented in their published report. In addition, they said, the results support the concept that positive affect, or emotional well-being, involves not just the absence of depression or negative affect, but "the presence of a positive quality" that enhances health status independent of negative affect.

In their report, the researchers acknowledged that their findings may not be generalizable to other populations ("Older Mexican Americans may differ from other ethnic groups in the relationship of positive affect to subsequent health"), also noting that the observed association of positive affect and better health "is not necessarily causal," but may be due to "some unmeasured correlate of both."

In an editorial published in the same issue of the journal, gerontologist Brenda W.J.H. Penninx, PhD, of Wake Forest University School of Medicine, put forth two broad hypotheses regarding the apparent health benefits of emotional well-being.

It's possible that positive emotions may exert a direct effect through physiologic mediation, Penninx speculated. "If emotionally vital older persons are better able to cope with environmental or physical stressors, these stressors may have less damaging effects on neuroendocrine and immunological regulatory systems, making these persons better able to maintain physiologic homeostasis."

Alternatively, Penninx said, positive affect might exert indirect effects via intermediate outcomes. For example, a high degree of emotional well-being may positively influence motivation for self-care and adherence to treatment regimens, both of which contribute to maintenance of good health.

Penninx urged additional research into the pathways by which positive affect might protect against physical decline. "Instead of focusing only on the more commonly investigated emotional dysfunctions in old age, a broader research perspective that includes positive emotions is strongly warranted."

BLOOD PRESSURE CONTROL MAY CURB ATHEROSCLEROSIS

New research findings suggest that proper treatment of hypertension (HT) can reverse HT-associated atherosclerosis, thereby reducing the risk of stroke and other life-threatening cardiac events.

The encouraging findings emerged from analysis of data on more than 10,000 men and women aged 45–64 years participating in the Atherosclerosis Risk in Communities Study, an ongoing prospective study of clinical and subclinical atherosclerotic vascular disease. Roughly half the subjects had high-normal blood pressure (130–139/85–89 mm Hg) or stage I hypertension (greater than 140/90 mm Hg).

Using an ultrasound radio frequency device, investigators monitored expansion and contraction of the walls of subjects' carotid arteries; reduced arterial contractility indicates increased arterial stiffness. They found that subjects with diastolic and systolic hypertension exhibited significantly smaller changes in arterial diameter than normotensive subjects (Am J Hypertens 2000;13: 317–23).

"The narrower the artery, the harder the heart has to work as it pumps blood,

and, eventually, the greater the risk of strokes or heart disease," journal editor Michael Weber, MD, commented in a news release announcing the study findings. "The results of this study are important because they raise the possibility that treating hypertension could reduce stiffening of vital arteries like the carotids that supply blood to the brain."

Clinical Alert on Alpha-Blocker Use in Hypertension

The American College of Cardiology (ACC) recently issued a "Clinical Alert" urging physicians to reassess use of alpha-adrenergic blockers for treatment of hypertension.

Issuance of the ACC alert follows the recent announcement of data from a large study indicating that the alpha-blocker doxazosin was less effective than the diuretic chlorthalidone in reducing the risk of certain types of cardiovascular disease among patients with elevated blood pressure.

That study, the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), was halted in March when data showed that subjects receiving doxazosin were experiencing 25% more cardiovascular events and were twice as likely to be hospitalized for heart failure than those receiving chlorthalidone.

About one million of the roughly 24 million Americans receiving drug therapy for hypertension receive an alpha blocker.

"The ACC encourages physicians who treat hypertensive patients to review the new data with their colleagues to ensure the rapid dissemination of this important information," Robert Cody, chair of the ACC Hypertensive Diseases Committee, commented in announcing the clinical alert in the college's publication *Cardiology*. Cody emphasized, however, that hypertensive patients currently receiving an alpha-blocking drug should not discontinue its use before consulting a physician.

Is It Sunburn . . . or Something More Serious?

Prolonged, sunburn-like facial redness after outdoor activities may be the first sign of rosacea, a chronic skin condition that affects an estimated 13 million older Americans and can become increasingly severe and conspicuous without medical treatment.

"Rosacea symptoms are often worse in the spring and summer because of the many environmental and lifestyle factors that can aggravate the condition during this time of year," Larry Millikan, chairman of dermatology at Tulane University School of Medicine, commented in a news release from the National Rosacea Society. In addition to sun exposure, the factor most likely to trigger a rosacea flare-up, contributors may include hot weather, wind exposure, strenuous exercise, and ingestion of alcohol or spicy foods.

"Because rosacea's early symptoms are often mistaken for something else, such as sunburn or acne, many people assume it's a temporary complexion problem that will eventually go away by itself," Millikan said.

Without early detection and treatment, rosacea typically progresses from transient redness on the cheeks, nose, chin, or forehead to persistent bumps and pimples. In advanced cases, visible blood vessels may appear, and the nose may become swollen. With proper medical management—initial treatment with fast-acting oral and topical antibiotics followed by long-term maintenance therapy—most cases of rosacea can be effectively controlled, Millikan emphasized. Lifestyle modification is also a key component of rosacea management (see sidebar).

More information and patient education materials can be obtained from the National Rosacea Society at 888-662-5874 (www.rosacea.org).

David K. Buerger
Managing Editor

Tips on Avoiding Rosacea Triggers

- Minimize midday (10:00 a.m.–4:00 p.m.) sun exposure during summer months.
- Wear a broad-rimmed hat when outdoors.
- Use sunscreen with a sun-protection factor (SPF) of 15 or higher year-round.
- Stay in a cool, air-conditioned environment on hot, humid days.
- Sip cold drinks and avoid overexertion.
- When overheated, chew ice chips or spray the face with cool water.

Source: National Rosacea Society.

A PRACTICE-BASED RESEARCH PRIMER, PART II:

Institutional Review and Ethical Considerations

The foundation of solid research results is laid well before the investigation begins, with sound institutional review protocols, appropriate recruitment and informed consent, and careful consideration of other issues in research ethics and study design.

Jeannette Y. Wick
Guido R. Zanni

For consultant pharmacists working with long-term care populations, understanding research requires more than a firm understanding of methodology and statistics. Review of administrative processes employed before research projects even begin contributes to better research proposals and often identifies design flaws or limitations in others' work. Administrative processes and ethical concerns spotlight protection. For older research subjects, protection assumes a meaning that is vastly different than that needed by younger subjects.

The Institutional Review Board

The concept of human rights protection for research subjects was initially developed by the Nuremberg Military Tribunal, which developed the Nuremberg Code to judge human experimentation conducted in Nazi Germany and Nazi-occupied territories. The code's first provision states that "voluntary consent of the human subject is absolutely essential." Other world organizations quickly followed suit, establishing guidelines to protect human rights and differentiate between therapeutic and non-therapeutic research. The most important subsequent declaration was the 1964 Declaration of Helsinki, which in its revised state is now used as the standard by more than 500 biomedical journals. While both of these documents emphasize voluntariness, they do not preclude

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altruism. Subjects may participate in research entailing considerable risk if they are fully informed.[1–3]

In the United States, regulations protecting human rights were first enacted in 1974. These regulations established the institutional review board (IRB) as the primary mechanism to ensure protection. The U.S. Department of Health and Human Services, in both its research and review functions, has adopted the Federal Policy for the Protection of Human Subjects as regulation. Dubbed the "Common Rule," these regulations are promulgated by all federal agencies that conduct, support, or regulate human subject research, as well as the Food and Drug Administration.[1–3] Extensive information about IRB function and composition is available in the *Institutional Review Board Guidebook* published by the National Institutes of Health and available on the Internet (http://grants.nih.gov/grants/oprr/irb_guidebook.htm).

How IRBs Function

Each institution's IRB is challenged with review of all research that involves human subjects. Their function is twofold: to determine where the boundary between research and therapy lies, and to ensure that research conforms with ethical principles.

For the most part, the boundary between practice and research is quite clear. Practice includes interventions designed to improve or enhance well-being with a reasonable expectation of success; diagnosis, preventive treatment, or therapy are considered practice. Research includes activities designed to test a hypothesis leading to conclusions that establish or contribute to a body of knowledge; these are expressed as theories, principles, or statements of relationships. Research itself is not therapeutic and, indeed, is often not immediately beneficial.

Sometimes the line between practice and research becomes blurred. When questions are raised, the more conservative approach is used to protect rights. The safety and efficacy of any action that could be classified as experimental should be reviewed early. Open, collaborative channels of communication between the IRB and the facility's other committees and administration are essential. This ensures that all medical staff members are constantly vigilant about human rights protection, identifying and correcting infractions immediately.

Composition of IRBs

Federal requirements govern the composition of those IRBs that function in institutions receiving funding from the federal government to conduct research with human subjects. Other facilities are wise to review the guidelines and consider the strength of their recommendations even if their research is not federally funded. Certain points deserve special attention:

- An IRB must have at least five members. The IRB should not, however, be so large that management becomes difficult. It is member expertise that makes the IRB a valuable review tool. IRBs often include bioethicists and researchers, and they always provide advice beyond ethics.
- IRB members should represent diverse backgrounds. Their purpose is not solely scientific; they must be able to examine proposals with consideration for diverse cultural backgrounds. The IRB should not consist entirely of men or of women, or of people of the same ethnicity or age.
- If the IRB reviews research conducted in vulnerable populations with any regularity, it must consider including one member who is knowledgeable about or experienced with the population. Thus, an IRB that reviews research in the elderly might include gerontology clinicians. Some facilities include their ombudsman or patient advocate to meet this guideline's intent.
- One member should be unaffiliated with the institution, and should be drawn from and knowledgeable about the local community.
- The IRB can invite specialists or experts as non-voting members as deemed necessary.

IRB members must be trained in regulations and commitments applicable to their own practice locale, as well as professional standards of practice. They must understand the principles of fairness and impartiality and be able to apply them consistently.

The IRB Review Process

Of late, many review groups have expressed concern about the IRB process. Allegations of bias, weighting researcher convenience over subject rights, and expediency are among their concerns. For example, in 1997 U.S. Health and Human Services Secretary Donna Shalala said that the usual requirement for patient consent for disclosure of medical records must be discarded and replaced with "our public responsibility to support national priorities — public health, research, quality care, and our fight against health care fraud and abuse."[5] In essence, this was an endorsement of broad access to confidential medical information. People protested in support of patients' human and civil rights, endorsing the IRB's role as the protective device for patients.

Institutions that engage in research can establish one or more IRBs or designate another institution's IRB to review its research. For small facilities, or those unaccustomed to research, the latter arrangement is often the most efficient. Stephen Feldman, RPh, president and CEO of The ICPS Group, Boston, conducts research in the elderly. He indicates that when research involves several facilities, if one among them has an established IRB, his group submits proposals to that IRB if possible. If no IRB is available, they may retain an outside IRB. In the latter case, they consider cost and timeliness. Regardless, certain processes must be followed.

First, the IRB approves, rejects, or modifies research proposals. In doing so, IRB members must keep immaculate records of their decisions. Meeting minutes require significant detail to guarantee that discussion and recommendations are recorded; these should be maintained for three years after the research is complete.

Second, all IRBs must have written procedures, and these must be adhered to precisely. The individual who proposes research is wise to review these procedures and comply exactly. This prevents proposal rejection based on technicalities and saves time in the long run. Facilities that conduct a great deal of research usually present training to new employees during orientation or conduct periodic training sessions to ensure that all staff is knowledgeable.

Third, the IRB reviews all research using identical criteria. Exhibit 1 describes basic questions concerning the appropriateness and ethics of proposed studies suggested by the NIH. As research proposals are written, investigators should play devil's advocate, testing their own proposal for compliance (or possible noncompliance) with these requirements.

Ethical Considerations

Ethical issues abound when conducting research. Apart from the obvious issue of protecting an individual's privacy and data confidentiality, there is the issue of informed consent. Prior to giving their consent, people must be fully informed of the research's purpose, risks, and expected benefits. Participation must be free of coercion. While subject dropout may not be random and potentially affect results, termination of involvement is a participant right. The principle of informed consent, originally developed for research applications, has transformed and matured over time. Research subjects must provide written informed consent. Today, informed consent is also considered a right for research subjects, as well as patients who receive any type of treatment. Its eight element are described in Exhibit 2.

At times, subjects may not fully understand risks, or risks may even be unknown to the researcher. Consider, for example, FDA-approved medications for treatment of HIV disease; in many cases, their toxicity and side effects may still be under review. Alternatively, there is the ethical issue surrounding those patients who agree to participate because they believe it is their only treatment option. These patients must be properly counseled by someone who is not associated with the research. Similarly, there may be ethical issues surrounding withholding of treatment. Weighing a study's risks and benefits should always be done with consultation and approval from an IRB.

Informed Consent and the Elderly

With elderly populations, informed consent can be complicated by

numerous concerns. Informed consent should be subject-centered, i.e., the rights of the individual should not be weakened by scientific pressures. Ideally, the subject should agree fully to participate in the research project and identify with the possible research findings.[6,7]

The latter statement raises interesting issues when the potential candidate is cognitively impaired or for some reason requires proxy or surrogate consent. In some cases, qualified independent professionals are asked to review the situation; these individuals assess the subject's decision-making capabilities, especially if the proposed research entails more than minimal risk. They offer disinterested opinions, with protection of the subject as their sole concern.

Recruitment Issues

Recruitment of subjects for research is not a straightforward process. The ethics surrounding procedures to identify potential subjects and the interpretation of "undue influence" have been extensively debated. This is particularly true for the recruitment of subjects with a specific disease entity. The IRB must scrutinize all recruitment procedures, including use of motivating incentives—monetary or other.[7]

Subjects with specific conditions are usually identified by reviewing automated systems or medical records. Most IRBs approve such reviews, provided the researcher agrees to abide by the institution's

Exhibit 1. IRB Protocol Review Standards

Guiding principles of institutional review and suggested questions for IRB discussion:

1. The proposed research design is scientifically sound and will not unnecessarily expose subjects to risk.
- Is the hypothesis clear? Is it clearly stated?
- Is the study design appropriate to prove the hypothesis?
- Will the research contribute to a body of knowledge and is it worth exposing subjects to risk?

2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of knowledge that may reasonably be expected to result.
- What does the IRB consider the level of risk to be?
- What does the principal investigator consider the level of risk/discomfort/inconvenience to be?
- Is there prospect of direct benefit to subjects?

3. Subject selection is equitable.
- Who is to be enrolled? Men? Women? Ethnic minorities? Children (rationale for inclusion/exclusion addressed)? Seriously ill persons? Healthy volunteers?
- Are these subjects appropriate for the protocol?

4. Additional safeguards required for subjects likely to be vulnerable to coercion or undue influence.
- Are appropriate protections in place for vulnerable subjects (e.g., pregnant women, fetuses, socially or economically disadvantaged, people with impaired decision-making abilities)?

5. Informed consent is obtained from research subjects or their legally authorized representative(s).
- Does the informed consent document include the required elements?
- Is the consent document understandable to subjects?
- Who will obtain informed consent (principal investigator, nurse, other?); in what setting?
- If appropriate, is there a children's assent?
- Is the IRB requested to waive or alter any informed consent requirement?

6. Subject safety is maximized.
- Does the research design minimize risks to subjects?
- Would use of a data and safety monitoring board or other research oversight process enhance subject safety?

7. Subject privacy and confidentiality are maximized.
- Will personally identifiable research data be protected to the extent possible from access or use?
- Are any special privacy and confidentiality issues properly addressed (e.g., use of genetic information)?

Sources: Adapted from Shuster E[2] and National Institutes of Health.[4]

EXHIBIT 2. ELEMENTS OF INFORMED CONSENT

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental

2. A description of any reasonably foreseeable risks or discomforts to the subject

3. A description of any benefits to the subject or to others that may reasonably be expected from the research

4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject

5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained

6. For research involving more than minimal risk, an explanation as to whether any compensation or medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained

7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject

8. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled

Source: Adapted from Shuster E.[2]

policy on confidentiality and protection of the patient's privacy is clearly understood and accepted by the researcher.

Record review to identify potential subjects is not without controversy. Feldman notes that access to pharmacy records for research purposes requires patients' consent; most IRBs concur. He indicates that data collected for the purpose of dispensing cannot automatically be used for research. For example, some patients would not want any outside person to review records that may contain information on abortion history, HIV infection status, or use of psychiatric medications. To address ethical and process concerns (a researcher would have to contact hundreds of patients for permission to review records), many facilities present a consent form at admission indicating that the medical record may be screened for research. Such forms typically describe precautions to protect patient privacy and data confidentiality.

When pharmacists have questions about whether or not a project is considered research, they should let the IRB decide, Feldman recommends. Clearly, medication use evaluation or any continuous quality improvement exercise used solely to improve care for residents of the facility is not research. If data extraction will be used for any other purpose, the IRB is the body that should determine if the project constitutes research. If the board determines it

The Institutional Review Process: A Case Study

Institutional review boards consider many ethical challenges. For example, when testing a new antiviral medication for its effects on HIV disease in the elderly, the independent variables are administration of the medication and the presence of HIV infection. The operational definition of HIV infection would be the presence of the HIV antibody and a specified viral load, (e.g., 10,000–12,000 HIV RNA copies). The dependent variable would be the change in viral load after a defined treatment period (e.g., eight weeks).

Research such as this often employs a *quasi-experimental* study design. With this design, the researcher selects participants who possess one of the independent variables. Continuing with the example of HIV research, study participants would be selected based upon their HIV status (e.g., viral load). The researcher would manipulate the second independent variable, the antiviral medication. Possible research subjects could be selected using record review in many long-term care facilities.

The IRB might anticipate the problems surrounding sample selection. Is patient privacy violated by this type of record review? Is the sample characteristic of all HIV patients? Suppose the sample were weighted with individuals with histories of addiction and poor diets. How would these characteristics affect the medication efficacy?

This study illustrates another approach to medical research in which there may not be a "pure" control group. The ideal situation would allow medication administration to a control group of HIV-negative individuals. This approach, however, raises serious ethical issues. It is known that many antivirals cause serious side effects such as neuropathy, and it might be deemed unethical to subject people to this risk.

In this case, the investigator might designate study participants to serve as their own control group: a group of HIV-positive patients with the predefined viral load will be given placebo. The IRB, however, firmly believes that the new medication is truly beneficial and that patients receiving the placebo would only decline without it. This raises the ethical issue of placing our hypothetical control group at an increased health risk by withholding treatment. They modify the proposal.

To avoid these ethical concerns, one could employ a *pre-post* design, under which all participants receive treatment and individual improvement is measured against their own baseline data.

Institutional Review and Ethical Considerations

is not, it can grant exempt status to the project.

Once patients are identified as eligible to participate in the study, patient contact can be thorny. For hospital patients, most IRBs require approval from the primary care physician before contact. The concern is the patient's emotional and physical well-being. For example, if the researcher is studying post-mastectomy depression, the physician may believe that the patient will become angry and emotionally distraught to learn that "strange researchers" know about her cancer.

Recruitment in an institutional setting also raises the issue of undue influence. Recruitment in correctional, psychiatric, and long-term care facilities must be carefully structured. Residents must not feel coerced in any way or feel that care will be affected by their refusal to participate. Albeit a judgment call, the manner in which a patient is informed about the study is just as important as the patient's understanding of risks and benefits. For example, if a physician suggests that participation in a clinical trial is worthwhile, by virtue of position, he may be exerting subtle, undue influence.[8]

There are special problems in recruiting patients after discharge, since most IRBs require approval from the patient's physician before the patient is contacted. Some researchers send a letter to the patient explaining the study purpose and asking the individual to consider participation. If the study topic is sensitive (e.g., colon cancer), patients may be offended and feel that the hospital has violated their privacy. Alternatively, the patient's physician could send the letter on behalf of the researcher. While potential participants generally prefer this approach, it also raises the potential for undue influence.

Some researchers advertise for subjects. Advertisements must include a summary of the research project, eligibility criteria, the name of clinical investigator, the location of the research program, the name of a contact person, and a clear description of incentives for participation (e.g., payment, free treatment). Furthermore, the advertisement should state whether the study involves experimental treatments. Advertising claims should not allude to perceived effectiveness of the treatment to be studied.[9]

IRBs are particularly sensitive to the use of incentives for participation, sometimes perceiving them as undue influence. Thus, the appropriateness of studies offering large amounts of money for indigent patients would be questioned. Likewise, subjects should not be led to believe that participation is the only access to treatment. Payment and other incentives should not be contingent upon completing the full study, since this could influence a subject's decision to terminate participation.[9] NIH recommends that incentives reflect risk level, inconvenience, and discomfort associated with participation.[2]

Most medical research relies on volunteers. This presents potential problems, as studies demonstrate that people who volunteer differ from those who do not. Volunteers are generally better educated, have a higher occupational status, are more intelligent, and have a greater need for the approval of others. These characteristics can influence research findings, complicating efforts to generalize findings.

Some researchers who experience difficulty recruiting elderly research subjects are trying a process called *experienced consent*.[10] This procedure allows the individual to participate in the research for a short period (possibly a week or two) before committing fully. The subject can review study obligations, then make an experience-based decision. This approach may allay fear, and gives the subject greater control. Some researchers find that subjects are more likely to join the research and stay enrolled once they experience the protocol requirements.

Feldman indicates that many long-term care facilities are reluctant to allow research. Their concerns range from the public's negative perception that they are "doing experiments on old people," to staff time involved in research-related activities, to concerns about licensing. To overcome fear, he promulgates clear communication with all concerned

parties, including the licensing authority. In Massachusetts, Feldman has worked with the licensing authority to develop a license that recognizes research is being conducted. His firm also reimburses facilities for staff time.

Comorbidity

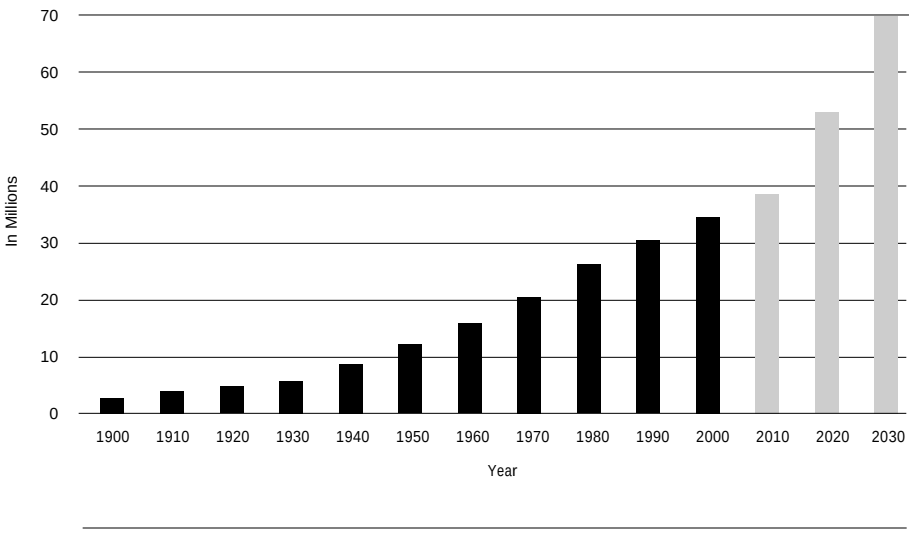
With comorbidity common in the elderly, careful consideration of potential or probable comorbid conditions is essential. FDA guidelines for testing and labeling of drugs that are likely to be used in elderly populations address these concerns, requesting attention to renal and hepatic impairment, and specific interaction research. At the least, interaction information should include digoxin, drugs affecting hepatic metabolism, protein-bound entities, and drugs with a high likelihood of concurrent use.

Quality of Life and Life Expectancy

Quality-of-life issues are difficult to measure and vary from group to group and individual to individual. Society is concerned with both the quantity of life and its quality, as years are added to life expectancy. Often, there is a discrepancy between the resident's perception of quality of life and the researcher's. The best way to ensure that quality-of-life issues are understood is to disclose possible risks completely. Exchange of information is important; potential research subjects should be allowed to express opinions and ask questions. If the researcher notices even a hint of hesitation on the resident's part, it should be explored.

As our population ages, it's in our best interest to make added years as healthy and productive as possible. Aging people are at an ever-increasing risk of disability and dying. With people living longer, medicine and research are undergoing a paradigm shift with respect to the elderly. Historically, disease management was emphasized; today, more emphasis is placed on disease avoidance. Medications are used with increasing frequency to avoid or ameliorate illness onset. Preventive interventions, once reserved for children and young adults, have taken center stage in elder treatment. Exhibit 3 projects the number of Americans who will exceed age 65 over the next 20 years, emphasizing the importance of quality of life in later years.

Exhibit 3. Growth in Number of People Over 65



Source: U.S. Census Bureau.[11]

Placebo-Controlled Studies

Ideally, most clinical research tests the effects of new drugs using a placebo-controlled design. This

approach assigns subjects randomly to groups; half are given the experimental drug and half are given an inert substance generally resembling the experimental drug in size and shape. A double-blind approach is generally used; subjects and the researcher measuring the effects of the drug are unaware of group assignment.

Use of placebo allows the researcher to assess the impact of psychological expectations on study results. Specifically, placebo use lessens the possibility that the researcher's outcome expectations will bias evaluation of subjects. The unequivocal IRB guideline on the use of placebo is straightforward: placebo use is unacceptable if there is an effective therapy that subjects could receive to treat their conditions. Physicians have an ethical obligation to help patients or, at least, to "do no harm." Thus, an IRB would never approve the use of placebo in testing the effectiveness of a new medication to treat serious infection if infected patients could benefit from standard antibiotics.

Terminally ill patients who have exhausted treatment options may qualify for a placebo-controlled study under these conditions; IRBs will still be sensitive to subjecting patients to invasive or potentially discomforting procedures. Placebo use highlights the contrast between a well-designed study and an ethically designed study.

Use of Automated Data

Sometimes, recruiting efforts fail and information on drug use in a specific population is inadequate. Large computerized databases from managed care organizations, pharmaceutical marketing companies or government beneficiary populations frequently provide valuable information on outcomes of medication use. These databases have some limitations: they usually do not concentrate on the elderly or may exclude the elderly; they may omit nonprescription, alternative, or complementary medications; or they may lack integrated information on patients' clinical comorbidities or level of functioning. Any research conducted using large databases must acknowledge such limitations.

Research using Internet response is growing quickly. Any research conducted using this avenue must address certain basic concerns. First, appropriate safeguards must be established to maintain confidentiality of all electronic communication. This is especially important if e-mail is used. Second, use of the Internet itself may bias participation: older, typically less computer-literate subjects may be less likely to participate.

Finally, legal issues surrounding use of automated patient databases should be examined. If data has been collected from multiple facilities, the researcher must be sure that the collecting entity has agreements with each facility that allow sharing of data. Many facilities specifically prohibit transfer of patient-specific or blinded information to others without express written consent.

Investigator Responsibilities

Investigator responsibilities begin with honesty and impartiality. It can be difficult to maintain impartiality when testing a hypothesis and, in fact, some researchers are unable to do so. Obviously, in performing the study, the researcher is obligated to fully comply with the protocol approved by the IRB. This obligation incudes appropriate maintainence of data and keeping essential documents on file for as long as necessary. In addition, researchers must recognize and address any doubt about its status as research, beginning with submission of the research proposal to the IRB if there is even minimal doubt. Researchers must always conform to the requirements of informed consent. Principal investigators are responsible for ensuring inter-rater reliability among the project's members and helping the team identify the study's limitations. Ideally, research teams always release their results—whether positive or negative—and never suppress findings. In actuality, however, the release or suppression of study findings hinges on who owns the data, their motivation for conducting the research, and the level of community interest in the study results.

Institutional Review and Ethical Considerations

Sponsor Responsibilities

Clinical trials are funded privately or through federal grants. Private funding is available through non-profit foundations and endowments (Consult Pharm 2000;15:603–20). Investigators should always divulge any relationships with sponsors before discussing the research project or findings. Federal agencies generally do not experience a conflict of interest in monitoring research, but conflict issues arise when pharmaceutical companies monitor research involving their products.

Companies sponsoring research should not be involved in the collection and analysis of data. In particular, companies that offer unrestricted grants must be completely detached from the research process. IRBs will review the role of the sponsor and individual investigators for potential conflicts of interest. Payment to investigators or consultants for their expertise cannot be perceived as a form of manipulation.

Sponsoring research does not necessarily give the company a right to records or patient information. Sponsors are obligated to accept the study's findings without censorship. The integrity of the scientific process must not be compromised by manipulation of statistical values or subject selection. Negative findings must not be suppressed, but released to the scientific community in the same manner as positive findings. In short, sponsors must not influence the process in any manner.

Conclusion

Many research projects involve a team of specialists. This approach allows division of labor and sharing of insights that invariably leads to superior products. This introduction to research might stimulate novices with research ideas to collaborate with others. The number of colleagues willing to join their effort may be surprising. After all, to be human is to be curious, and there is a scientist in all of us.

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Gianna Bryan, Caren McHenry Martin

QUALITY-FOCUSED REGULATORY INITIATIVES AND COST-DRIVEN REIMBURSEMENT TRENDS OVER THE PAST FOUR DECADES HAVE REDEFINED THE LONG-TERM CARE MARKETPLACE, CREATING NEW PATIENT POPULATIONS, A HEIGHTENED DEMAND FOR HIGH-LEVEL MEDICATION MANAGEMENT—AND EXPANDED OPPORTUNITIES FOR PHARMACISTS AT EACH STEP ALONG THE WAY.

The Changing Face of LONG-TERM CARE

Since the 1950s, when George F. Archambault first coined the phrase "consultant pharmacist" to refer to pharmacists providing comprehensive pharmacy services to nursing facilities, our profession has undergone many dramatic changes. Pioneers of consultant pharmacy laid the groundwork for building our profession from its humble beginnings to today's high standard of practice.

As the long-term care environment has evolved over the years, so has consultant pharmacy. Among other major changes, the profession has been challenged to develop innovative practice strategies and adopt new paradigms to keep up with the rapidly evolving long-term care marketplace.

Regulatory Changes

The long-term care environment is highly regulated, with pharmacy playing a major role in achieving and maintaining full regulatory compliance. It was 1974 when regulations were published by the government requiring pharmacists complete monthly drug regimen reviews for residents of skilled nursing facilities. Survey indicators for assessment of drug regimen review came into play in 1980, followed by the 1985 release of the Survey Procedures for Pharmaceutical Services in Long-term Care Facilities. Mandates that pharmacists perform drug regimen reviews in intermediate care facility (ICF) nursing beds became reality in 1987, with subsequent regulations specific to ICFs for the mentally retarded (ICF-MR) and developmentally disabled (ICF-DD) issued in 1988.

The Omnibus Reconciliation act of 1987 (OBRA '87) brought sweeping changes to both the delivery and outcomes of care in areas including residents' privacy rights, physical and chemical restraints, resident assessments, nurse aide training and nursing services. In 1999, updates to these regulations incorporating new medication quality indicators (QIs) based

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on unnecessary use criteria developed by Mark Beers, MD—the so-called "Beers criteria"—became a reality.

Focus on Psychotropics

In today's practice environment, it's difficult to imagine a time when the use and misuse of psychoactive medications was not a major focus of pharmacist's drug regimen assessments. Yet before regulations to discourage such practices went into effect, some pharmacists performed their drug regimen reviews off site and with little attention to these drugs. OBRA '87 specifically addressed the unnecessary use of psychotropic medications, focusing on the use of sedatives, antipsychotics, and anxiolytics as chemical restraints in the elderly resident. With years of work on this issue behind us, "We have come a long way," notes Tricia Cash, Pharm.D, consultant pharmacist for Vitalink, Stanley, North Carolina. "The antipsychotic problem is not nearly as monumental as it was in the past."

Unfortunately, notes Cash, it took many citations during Medicare and Medicaid certification surveys to drive home the importance of proper management of these issues to some facilities. While it is now uncommon to see gross abuse of these medications in most nursing homes, Cash remembers a facility she serviced many years ago in which approximately 40% of the population were on antipsychotics and, despite her recommendations, no changes were made. It took citations during the survey process to help effect a change, but the needed changes did come. Indeed, a review of the effects of the OBRA '87 act showed that in one facility, antipsychotics were stopped in 45% of residents with "dementia only" diagnoses. (Consult Pharm 1999; 14: 179-88).

With the advent of the QI-driven survey process in 1999, facility administrators and nursing staff became acutely aware of the potential liabilities of the misuse of psychotropic medications. Many facilities now use data from Section O of the Minimum Data Set (MDS) to drive internal quality assurance tools for monitoring medication usage patterns. Facilities are encouraging their staff to become educated on the nuances of the regulations affecting these medications, and nonpharmacologic approaches to management of problem behaviors are now in vogue.

Assisted Living

Unfortunately, the strides we have made towards proper management of psychoactive medications in the nursing facility have not yet pervaded the assisted living market. These facilities desperately need the skills of the clinical consultant pharmacist to help them make sense of their patients' complicated drug regimens. Armon Neel, RPh, president of Institutional Pharmacy Consultants

"THE PPS CREATED A NEED FOR EVERYONE TO ADD A FINANCIAL RATIONALE TO ALL DECISIONS," SAYS ASCP PAST PRESIDENT JAN ALLEN.

of Griffin, Georgia, remembers a situation he faced in which all the patients in one assisted living facility he serviced were on antipsychotic drugs, including some on multiple agents. Many of the antipsychotics were being used as tranquilizers or for other inappropriate reasons. "Almost all the patients were lethargic," Neel recalls. Regulatory controls may be coming to the assisted living market, but in the meantime the clinical consultant pharmacist is in a position to build on the experiences of the skilled nursing environment. Opportunities await consultant pharmacists to make meaningful changes in drug management that can positively influence the quality of life and quality of care of the assisted living resident.

Enter the RAI and QIs

The implementation of OBRA '87 in October 1990 also required use of the federal Resident Assessment Instrument (RAI) in the long-term care environment. Ongoing care planning with current and accurate assessments of resident status was mandated, with the MDS at the core of this assessment.

While the role of the consultant pharmacist in the care planning process varies in different facilities, the basic process has become a pivotal practice area since the July 1999 changes in the HCFA nursing facility survey process. These changes incorporated the use of 24 QIs that surveyors use to select a sample of residents for the Phase I survey. Many progressive consultant pharmacists have found that the QIs can also help them provide better service to their facilities. "These indicators help the pharmacist be both objective and proactive in trying to help the facility with potential problems before they become a reality," notes Mike List, RPh, clinical manager for Neil Medical Group in North Carolina. "They highlight potential survey issues," he points out, "making it easier for the pharmacist to tease out what is important to focus on when conducting drug regimen review and nursing in-services, and when participating in the various quality improvement committees within the facility." In addition, knowledge of the MDS process helps bridge the gap with nurses, List comments. "Suddenly we're all speaking the same language. That's when positive changes begin to happen."

PPS Brings More Changes

With the recent advent of the Medicare nursing facility prospective payment system (PPS), long-term pharmacy underwent further dramatic changes. "The PPS created a need for everyone to add a financial rationale to all decisions," says ASCP Past-president Jan Allen, whose term as the Society's president coincided with PPS implementation in July

1998. "Clinical pharmacists suddenly had to filter all of their medication management recommendations through a 'financial filter,' while dispensing pharmacists had to become more proactive in their review of new medication orders. Stricter formulary controls became necessary. Residents were screened much more closely prior to admission to the long-term care facility, and in some instances services previously offered by facilities (e.g., I.V. services) were discontinued due to cost constraints."

By influencing how facilities screened new admissions, the PPS has also changed the types of patients served in many long-term care facilities, and many hospitals are finding their medically complex patients difficult to place.

A Changing Patient Population

In addition to the changing regulatory focus in long-term care facilities, many of the changes in this environment center around the changing patient population serviced by long-term care facilities. While "long-term care" formerly was synonymous with nursing home care, today's long-term care environments encompass an entire continuum of care, from home-like settings to the skilled nursing facility. The elderly population is growing dramatically, with the greatest impact projected during the period 2010–30, when those on the leading edge of the "baby boom" generation begin to reach age 65. By 2030, there will be about 70 million elderly persons in the United States, more than twice their number in 1998. This year, people 65 and over will represent approximately 13% of the population, but that figure is likely to exceed 20% by the year 2030.[1]

Although the number of elderly persons is projected to grow dramatically over the next few decades, growth in the number of nursing home beds is not expected to keep pace. Alternative care models, such as the assisted living model, specialized Alzheimer's care units, and board and care homes are claiming and will continue to claim a large number of patients who once resided in nursing facilities. While the precise number of U.S. assisted living facilities is difficult to ascertain, a recent study estimated that there currently are upwards of 11,000 assisted living facilities, with a total of over 600,000 beds and more than 500,000 residents.[2] Accounting for 75% of new housing for seniors in 1998, the assisted living industry is the fastest-growing segment of the senior housing industry, with 50,667 new assisted living units constructed during that year.[3]

While the impact of the baby-boomer population shift has yet to be fully realized, consultant pharmacists are already seeing many changes in the long-term care industry. "Quicker and sicker" is the phrase often used to describe the typical admission to today's nursing home, referring to the fact that these patients tend to be discharged from the hospital sooner than in the past and often present to the nursing facility with a greater number of comorbidities and a more complicated medical regimen. Consultant pharmacists who once practiced in a process-oriented environment driven primarily by regulations now find themselves in an environment that demands a high caliber of clinical skills and participation in an interdisciplinary care team.

"When I started as a consultant pharmacist 30-plus years ago, the skilled nursing facility patient was not as sick as the ICF patient is today," notes Neel. "Patients requiring tube feeding or respiratory therapy were in the hospital. Now I have homes with respirators, hyperalimentation, and all types of therapies that were formerly reserved for hospitalized patients. The patients who used to be our nursing facility patients are now residing in the assisted living facilities.

Comments Cash, "I remember in the late 1980s going into facilities and having only one or two new admissions from the previous month. Now an entire wing of a facility will be new patients due to Medicare patients and increased acuity levels." These increases in patient complexity have meant some changes in the way consultant pharmacists do their drug regimen reviews, with many seasoned consultant pharmacists such as Neel and Cash reporting the need to spend more time in their facilities, exploring the intricacies of compli-

"I REMEMBER IN THE LATE 1980s GOING INTO FACILITIES AND HAVING ONLY ONE OR TWO NEW ADMISSIONS FROM THE PREVIOUS MONTH. NOW AN ENTIRE WING OF A FACILITY WILL BE NEW PATIENTS DUE TO MEDICARE PATIENTS AND INCREASED ACUITY LEVELS."

cated medication regimens. Some consultants have found it necessary to decrease their bed loads in order to be able to provide appropriate care to their nursing facility patients. In addition, the recent focus on the HCFA quality indicators has added a new dimension to consultant pharmacy practice. "It's important for consultant pharmacists to possess a working knowledge of the MDS process," notes List. "Just checking for accuracy in Section O of the MDS could save the facility from a deficiency. Further investigation with the Resident Assessment Instrument provides potential for reducing falls, negative behaviors, pain, infections, weight loss, pressure sores, and myriad other concerns that effect the day-to-day life of the patients we serve."

A Fast-Moving Target

This increased involvement in the patient's overall care has necessitated that many consultant pharmacists participate in committees within the facility, helping to assess potential medication-related causes and solutions for falls, wounds, negative behaviors, and other patient problems.

The practice of consultant pharmacy has evolved from the dreams of visionaries into a diverse, valuable, and respected palette of services provided across an expanding long-term care continuum. To paraphrase Robert Frost, we have miles to go before we sleep, but oh, what a marvelous journey!

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This article is recommended by the Commission for Certification in Geriatric Pharmacy as a certification examination study resource.

TREATMENT STRATEGIES FOR THE MANAGEMENT OF CONSTIPATION IN LONG-TERM CARE PATIENTS

Kevin T. Landers
David P. Elliott

Objective: To provide a review of current therapies available for constipation along with recommendations by consultant pharmacists for the proper treatment of constipation.
Data Sources: A MEDLINE search of English language reports published during the period 1966–99, and a manual search of bibliographies of relevant papers. Tertiary references were also used as data sources.
Study Selection: Several clinical trials were reviewed. These trials were selected based on their content regarding the therapy of constipation. Trials were chosen to review the efficacy of agents currently used for constipation.
Data Extraction: Data were selected based on pertinence to the objective of the review.
Data Synthesis: Few controlled clinical trials comparing laxatives or other agents used to treat constipation have been published. Treatment of constipation is usually based on clinical opinions of prescribers. Although very little data are available on many agents, there is some data that supports the use of certain agents for constipation. Diet therapy and increased fluid intake are the mainstays for the treatment of constipation. If diet therapy alone fails, adding a bulking agent or hyperosmolar agent is a reasonable recommendation for drug therapy. Emollient-type laxatives should be used for prevention and not for treatment of constipation. Mineral oil should rarely be used for treating constipation due to risk of pneumonia. Saline products and stimulants should be used as needed for acute constipation. Senna has been used for the treatment of opioid-induced constipation. It appears to be relatively safe and efficacious, although adverse colonic effects do occur with chronic stimulant laxative use. Newer prokinetic agents may prove to be beneficial for treating constipation, but studies need to be performed to determine the long-term effects. A newer agent similar to polyethylene glycol (PEG)-3350 (GoLYTELY, Braintree Laboratories, Braintree, Massachusetts) is Braintree formula 851 (MiraLax), which may prove efficacious for the treatment of constipation in acute situations (less than two weeks).
Conclusion: Optimal therapy of constipation has not been established due to lack of clinical trials on many of the agents used for treatment. Proper treatment must be based on clinical experience and opinions of practitioners. Consultant pharmacists can recommend some agents that have been proven effective in clinical trials.
Key Words: Constipation, Elderly, Laxative, Diet therapy, Bulk former, Emollients, Lubricants, Saline products, Stimulants, Hyperosmolar agents, Prokinetic agents, Misoprostol, Opioid-induced.
Abbreviations: PEG = polyethylene glycol; NSAID = nonsteroidal anti-inflammatory drug; NANC = nonadrenergic, noncholinergic.
Consult Pharm 2000;15:725–33.

Chronic constipation is a problem affecting nearly 26% of elderly men and 34% of elderly women.[1] Constipation has been defined as defecating less than three times per week.[2] An estimated $400 million per year is spent on laxatives.[3] It is important to remember that what may be "regular" to someone may be constipation to someone else. For example, a patient with a bowel habit of four times weekly may be considered regular, whereas less than twice a day may be constipation for another patient. Constipation is a symptom caused by varying etiologies, including the following: dietary, gastrointestinal, metabolic and endocrine, pregnancy related, neurogenic, psychogenic, and drug induced.[4] Inactivity, strictures, and neoplasms can also result in constipation.[2] If at all possible, proper diagnosis and determination of the cause is a necessity. However, for the majority of patients with constipation, no etiology can be identified.[2] Whether or not an etiology is determined, proper therapy must begin.

With the aforementioned considerations in mind, a general review of the current literature on the treatment of constipation, both drug (old and new) and nondrug, is presented. Several clinical trials are also presented, along with various pharmacoeconomic data. Unfortunately, there are insufficient supportive data published for many of the agents used to treat constipation, so consultant pharmacists must use clinical knowledge and judgment to determine the appropriate therapy required for treatment of individual patients.

A consultant pharmacist should know when to treat constipation and when not to treat constipation (e.g., refer a patient to identify an underlying cause), as well as know how to treat a constipated patient appropriately, thus improving the patient's quality of life. Treatment should begin when constipation affects the patient's physical and psychological well-being. However, proper diagnosis of the potential etiology must be determined before any treatment begins.

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TABLE 1. AGENTS THAT CAUSE CONSTIPATION

Analgesic drugs (narcotics, NSAIDs)
Antacids (aluminum- and calcium-containing)
Anticholinergic drugs
Antihistamines
Phenothiazines
Anticonvulsant drugs
Antidepressant drugs (TCAs)
Antihypertensive drugs (CCBs, clonidine, diuretics)
Antiarrhythmic drugs (disopyramide)
Metals (bismuth and iron)
Sympathomimetic drugs (pseudoephedrine)
Anti-Parkinson drugs (benztropine, trihexyphenidyl)

TCA = tricyclic antidepressant; CCB = calcium channel blocker;
NSAID = nonsteroidal anti-inflammatory drug,
Sources: Longe RL, DiPiro JT[4];Floch MH, Wald A[10]; Schaefer DC, Cheskin LJ.[11]

CLINICAL PRESENTATION

Subjectively, patients with constipation often complain of increased difficulty defecating and hard stools. Patients may also feel full or bloated, with a sense of incomplete evacuation upon defecation.[2] Objectively, patients may have smaller amounts of stool and decreased frequencies of bowel movements relative to baseline bowel function.

PATHOPHYSIOLOGY

Acute distension of the rectum initiates the defecation process. This leads to partial relaxation of the internal anal sphincter. Pressure within the rectum increases as rectal and sigmoid contractions increase.[2] This results in the sensation to defecate.

Poor dietary habits are a primary cause of constipation. The elderly population may be at increased risk for developing constipation.[5] This is due in part to the relatively sedentary lifestyle of some elderly.[6] In the elderly, adequate intake of dietary fiber is a necessity to maintain normal bowel functioning. Adequate intake of fluids, such as water and juices, can improve bowel habits.[7] In addition to poor dietary habits, there are several physiological conditions that may result in constipation.

Gastrointestinal problems cause constipation. Two common gastrointestinal disorders that can lead to the development of constipation are diverticulitis and irritable bowel syndrome. Irritable bowel syndrome may also present with diarrhea or even a mixed diarrhea/constipation picture.[4]

Metabolic and endocrine disorders also predispose to the development of constipation.[4] Diabetes is a relatively common state in the elderly that can increase a patient's risk of developing constipation due to changes in the gastrointestinal tract.[4] Hypothyroidism is very common in the elderly and is a cause of constipation.[4] Thus, thyroid function tests should be considered in patients whose symptom complex includes chronic constipation.

Disorders of the central and peripheral nervous systems can predispose patients to the development of constipation.[4] Common central nervous system etiologies of constipation consist of multiple sclerosis, Parkinson's disease, and cerebrovascular accidents.[4]

Of all the etiologies of constipation, drug-induced constipation is an area where pharmacists can be most beneficial to the patient. Different classes of pharmacologic agents induce constipation by various methods. For centuries, opioids have been known to cause constipation. They prolong transit time by inducing spastic intestinal contractions and, possibly, by increasing electrolyte absorption.[8,9] Moreover, there are many miscellaneous agents that can produce constipation as an adverse effect (see Table 1).[4,10,11] Oral calcium supplements have been thought to cause constipation.[12] Saunders et al. conducted a study comparing the effect on fecal output of calcium carbonate and aluminum hydroxide.[13] The eight patients enrolled in the study ate a controlled diet and received each therapy for a period of three weeks. The study revealed that calcium carbonate actually increased fecal output in patients receiving it (as measured by daily stool weights). The lack of substantiated evidence of calcium as a constipation-inducing agent and the results of the study by Saunders et al. may lead one to believe that calcium does not usually

cause constipation. A larger and long-term study should be performed to definitively determine if calcium does or does not induce constipation.

A long-term care pharmacist should reduce the inappropriate use of therapeutic agents causing or contributing to constipation. However, if the use of agents is necessary, pharmacologic therapy may be necessary to improve symptoms and quality of life.

EVALUATION OF CONSTIPATION

An individual patient's complaints of constipation must be addressed by his or her health care providers. One must remember that bowel habits may vary tremendously from one patient to the next. It is the responsibility of the health care provider to ask the proper questions to assess the patient's constipation. Questions should include whether the patient complains of painful defecation, smaller stools, harder stools, less frequent stools, a feeling of fullness, and/or a sense of incomplete evacuation.[2] Once these items are identified, and correctable causes of constipation are ruled out, proper treatment may begin.

Once treatment is begun, the patient's stool frequency, quantity, and other symptoms should be monitored to determine the efficacy of therapy. This can be recorded by caregivers if patients are not cognitively able to perform these functions alone. If at all possible, assessment of the patient's own perception of the effectiveness of therapy should also be ascertained.

THERAPY OF CONSTIPATION

INCREASED ACTIVITY AND BOWEL TRAINING

Increasing an individual's activities decreases the need for laxative products in the elderly, even if the activity increase is minimal.[7] Bowel training can be used to overcome the inhibition of the gastrocolic reflex. By allowing the patient to attempt a bowel movement at an appointed time or times every day, constipation may be relieved. If a bowel movement does not occur, an agent (suppository or

TABLE 2. AGENTS FOR THE TREATMENT OF CONSTIPATION

Agent	Dosage forms	Time of action	Cost*
Bulk formers			
Methyl-cellulose	P†	12–72 hours	3
Polycarbophil	T	12–72 hours	1
Psyllium	P†	12–72 hours	1
Emollients			
Docusate calcium	C	12–72 hours	1
Docusate potassium	C	12–72 hours	1
Docusate sodium	C, L, T	12–72 hours	1
Saline products			
Magnesium citrate	L	0.5–3.0 hours	2
Magnesium hydroxide	L	0.5–3.0 hours	1
Magnesium sulfate	G	0.5–3.0 hours	1
Sodium phosphate	L†	2 min–3 hours	3
Stimulants			
Bisacodyl	S, T	15 min–12 hours	1
Cascara sagrada	L, T	6–12 hours	1
Casanthrol	C††	6–12 hours	
Senna	G, L, S, T	6–12 hours	2
Hyperosmolar			
Glycerin	S	0.25–1.0 hour	1
Lactulose	L	12–48 hours	3
Sorbitol	L	12–48 hours	2
PEG-3350 (GoLYTELY)	P	0.5 hours–4.0 days	3
Braintree Formula 851 (MiraLax)	P	Variable	3
Prokinetic agents			
Erythromycin	L, T	1 hour–2 days	2

C = capsule; G = granule; L = liquid, solution, suspension, or syrup; P = powder; S = suppository; T = tablet.
* As per long-term care dispensing pharmacy for one month of therapy (1 = $0.0–$15.0, 2 = $15.0–$30.0, 3 = $30.0 or more).
† Available sugar-free.
†† Only available in combination products.
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enema) is used to induce a bowel movement. After several days of this scheduled toileting, the bowel movement usually occurs without the aid of an agent.[7] In the elderly, bowel-training techniques have been shown to be very effective.[14]

DIET THERAPY

As mentioned earlier, dietary therapy and adequate fluid intake should be the first steps in relieving chronic constipation.[7,15] Hull et al. performed a study using dietary therapy alone to alleviate constipation in a 300-bed long-term care facility.[16] Dietary fiber content of patients' daily diet was increased from 25% to 40% by adding bran to each patient's breakfast cereal. The use of laxatives was eliminated in 162 of 270 residents who remained on the diet therapy at the end of one year. The addition of a prune juice/bran/applesauce mixture was added to the above combination in 108 residents due to the ineffectiveness of the bran/cereal mixture alone. A decrease in expenditures on laxatives for that same year resulted in a cost savings of $44,000. Although the first week or two of this specific dietary therapy may be difficult for the patient and facility staff due to erratic bowel movements, long-term treatment will result in more regular bowel movements. Dietary fiber is a necessity for the treatment of constipation, as revealed by Hull et al.[16]

One dietary agent that is commonly used is prune juice. Hubacher and Doernberg believe that the laxative effect is a result of magnesium in prune juice.[17] No matter how prune juice actually works—it does.

Consultant pharmacists should stress the role of dietary therapy for the long-term relief of constipation along with dieticians, who can create a broader insight into dietary treatment. When dietary therapy alone cannot help, the next step is pharmacological therapy.

PHARMACOLOGICAL THERAPY

Agents used to treat constipation can be categorized into the following seven categories: bulk formers, emollients, lubricants, saline products, stimulants, hyperosmolar products, and prokinetic agents.

Bulk formers. Bulk-forming products include polycarbophil, psyllium, methylcellulose, carboxymethylcellulose, malt soup extract, and plantago seeds. Their action may be mediated via water retention, leading to an increased volume of luminal contents, thus reducing colonic transit time.[18,19] These agents are similarly effective, with the most significant difference among them being the various dosage forms in which they are available. Some products are sugar-free (see Table 2) and, therefore, beneficial to diabetic patients.[15] Long-term use of these agents has been validated. McRorie et al. conducted a randomized, double-blind, parallel-design study in 170 patients (age range 20–74 years) with chronic constipation.[20] The study compared docusate sodium 100 mg twice a day (with psyllium placebo) versus psyllium 5.1 gm twice a day (with docusate placebo). Psyllium significantly increased the water content of stool (psyllium 2.33% vs. docusate 0.01%) and water weight (psyllium 84 gm vs. docusate 71.4 gm), as compared to baseline. The researchers demonstrated that psyllium was superior to docusate sodium for stool softening and for increasing water content of stool. With the above in mind, however, adverse effects can occur with bulk-forming agents. These effects are primarily diarrhea and abdominal cramps.[19] Patients who may benefit most from bulk formers are patients with well-formed, small, hard stools. With the addition of a bulk-forming agent, the stools will increase in weight and be softer due to the increased water content. These agents should be administered with eight ounces of water or juice to reduce the risk of obstruction, which may occur if these agents are not consumed with adequate fluids. A consultant pharmacist may not want to recommend these agents in patients who have swallowing or esophageal problems that may increase the risk of obstruction.[6] Patients who do not have adequate fluid intake or are unable to express their thirst may also be poor candidates for bulk formers due to the risk of obstruction.

Emollients. Emollients are surfactants that promote the blending of aqueous and fatty substances in the gastrointestinal tract to soften the stool.[18] Docusate sodium and docusate calcium are two examples of emollient-type laxatives.[18] These agents have been proven to be no more effective than placebo for the treatment of constipation in the elderly.[21] Castle et al. conducted a randomized, double-blind, crossover study comparing docusate calcium and placebo over a 10-week period in 22 elderly patients. There was no statistically significant difference between the two groups in any variables measured (e.g., stool frequency, consistency, volume).

Emollients are best suited to prevent constipation in patients who may have other health-related issues that may be exacerbated by constipation and its effects, such as abdominal hernias, hypertension, myocardial infarction, previous anorectal surgeries, or hemorrhoids. Stool softeners should not be used to treat a patient's constipation due to their lack of effectiveness. Moreover, stool softeners should not be used in patients receiving mineral oil, as emollients may increase systemic absorption of mineral oil.[15]

Lubricants. These agents work by coating fecal matter, thereby inhibiting colonic absorption of water, allowing for easier elimination.[4] Mineral oil is a commonly used agent in this category but should not be. Aspiration of mineral oil is a potential problem, predisposing elderly bedridden patients to lipoid pneumonia.[22] Moreover, mineral oil may reduce the absorption of fat-soluble vitamins such as vitamins A, D, E, and K.[18] A consultant pharmacist should minimize the use of mineral oil in the elderly because the risk of developing lipoid pneumonia outweighs the benefit of this particular laxative.[6]

Saline products. Saline products exert their pharmacologic effect via an osmotic effect that increases gastrointestinal volume, leading to increased motility.[15] Examples of saline laxatives are magnesium citrate, magnesium hydroxide, magnesium sulfate, and sodium phosphate. These agents are recommended for the treatment of acute constipation only.[23] Chronic use of products that contain magnesium may lead to hypermagnesemia in patient with impaired renal function.[24] Saline agents that contain phosphate (e.g., Fleet Enema, Fleet Phospho-Soda) may induce hyperphosphatemia and hypocalcemia, especially in patients with impaired renal function.[25] Phosphate-containing enemas can also damage the rectum and rectal mucosa due to their hypertonicity.[24,26] Sodium-containing enemas may be toxic to patients with edema, congestive heart failure, or renal failure.[15] In certain situations, such as bowel preparation for a barium enema, these agents may be recommended.[6,15] A consultant pharmacist may see that magnesium hydroxide is often used daily in patients. There is no documented data on the safety of using this agent three or four times per week, but there are safer agents to use routinely in patients with impaired renal function. If these agents are used, the potential benefits must be weighed against the risks of their use. Unfortunately, the lack of clinical trials to determine long-term effects of chronic daily use of these agents leaves the prescriber and consultant pharmacist to decide on the use of these agents by clinical judgment alone.

Stimulants. Stimulants are another class of laxatives that should generally be used only as needed. These agents include bisacodyl, cascara sagrada, castor oil, casanthrol, and senna. They exert their mechanism of action via production of contractions in the colon to facilitate bowel movements.[23] They may also stimulate water and electrolyte secretion in the intestines.[27] Adverse effects of these agents are usually limited to cramps, but patients may develop *cathartic colon* if they receive these agents on a regular basis for several years.[28,29] Cathartic colon is a condition of impaired motor function of the colon due to chronic stimulant laxative use. Stimulants should be avoided for chronic, daily use if at all possible. However, in an acute situation to relieve constipation (approximately one week), stimulants are relatively safe. Therapy with

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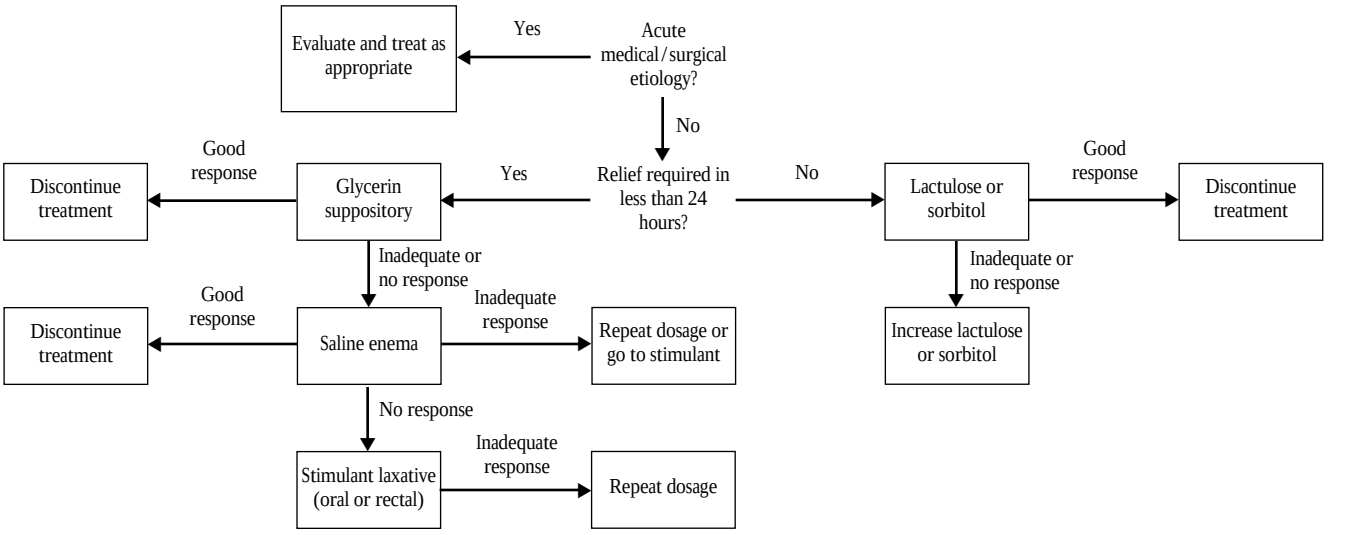
another agent, such as a bulk former or an osmotic agent, should be started concurrently with the stimulant, so the stimulant may be stopped after the acute constipation has been treated. Moreover, in situations such as opioid-induced constipation, the risk-benefit ratio must be examined, and a patient's quality of life must be maintained. Use of stimulants for opioid-induced constipation appears to be one appropriate niche for chronic stimulant laxative use.

Hyperosmolar agents. Hyperosmolar agents used for constipation include lactulose, sorbitol, and glycerin. These agents work by increasing water absorption into the gastrointestinal tract leading to increased luminal pressure, thus stimulating peristalsis.[18] Glycerin should be used only on a short-term basis and may cause local irritation.[23] It is very safe for acute constipation and works very rapidly.

Both lactulose and sorbitol are commonly prescribed for daily use. Lactulose may cause cramps and flatulence.[19] Both sorbitol and lactulose may cause nausea, vomiting, and diarrhea, which may lead to dehydration.[19] Health care providers should exercise caution while using lactulose in patients with diabetes due to the small amount of absorbable sugar content.[30] Closer monitoring of blood glucose should be performed to determine the effects of these agents on an individual patient's diabetes. Lederle et al. conducted a randomized, double-blind, crossover study comparing lactulose and sorbitol in the elderly.[31] Patients received either lactulose or sorbitol (up to 60 mL per day) for four weeks, with a two-week washout period. They were then switched to the opposite medication and treated for four more weeks. The average number of bowel movements per week was 6.71 and 7.02 in the sorbitol and lactulose groups, respectively, a statistically insignificant difference. This study concluded that there is no significant difference between lactulose and sorbitol regarding their effect on constipation.

Sorbitol is a nonprescription medication that is much less expensive than lactulose but is not usually included in drug benefit plans, including Medicaid. Using sorbitol may be less expensive to the patient or nursing facility if patients are paying privately or if the nursing facility receives capitated reimbursement (e.g., Medicare) for their care. However, many long-term care residents are covered by Medicaid, which will pay

FIGURE 1. ALGORITHM FOR MANAGEMENT OF ACUTE CONSTIPATION



for lactulose but not sorbitol. Therefore, payment status may be a consideration when deciding which product to use.

Prokinetic agents. The newest class of agents used in constipation are the prokinetic agents, such as cisapride, prucalopride, erythromycin, and misoprostol. These agents work by enhancing gastric motility via cholinergic activity, thus accelerating gastric emptying.[18] Cisapride enhances gastric motility but does not accelerate colonic transit time. Cisapride may be effective at relieving constipation, but it can cause Q–T interval prolongation and life-threatening cardiac arrhythmias.[18] Cisapride interacts with macrolide antibiotics and triazole antifungals via the cytochrome P450 3A4 pathway.[18] Both interactions increase cisapride level, leading to prolonged Q–T intervals, potentially resulting in torsades de pointes.[18] For these reasons, this product was withdrawn from the market by its manufacturer in mid-2000.

Prucalopride is an investigational agent that

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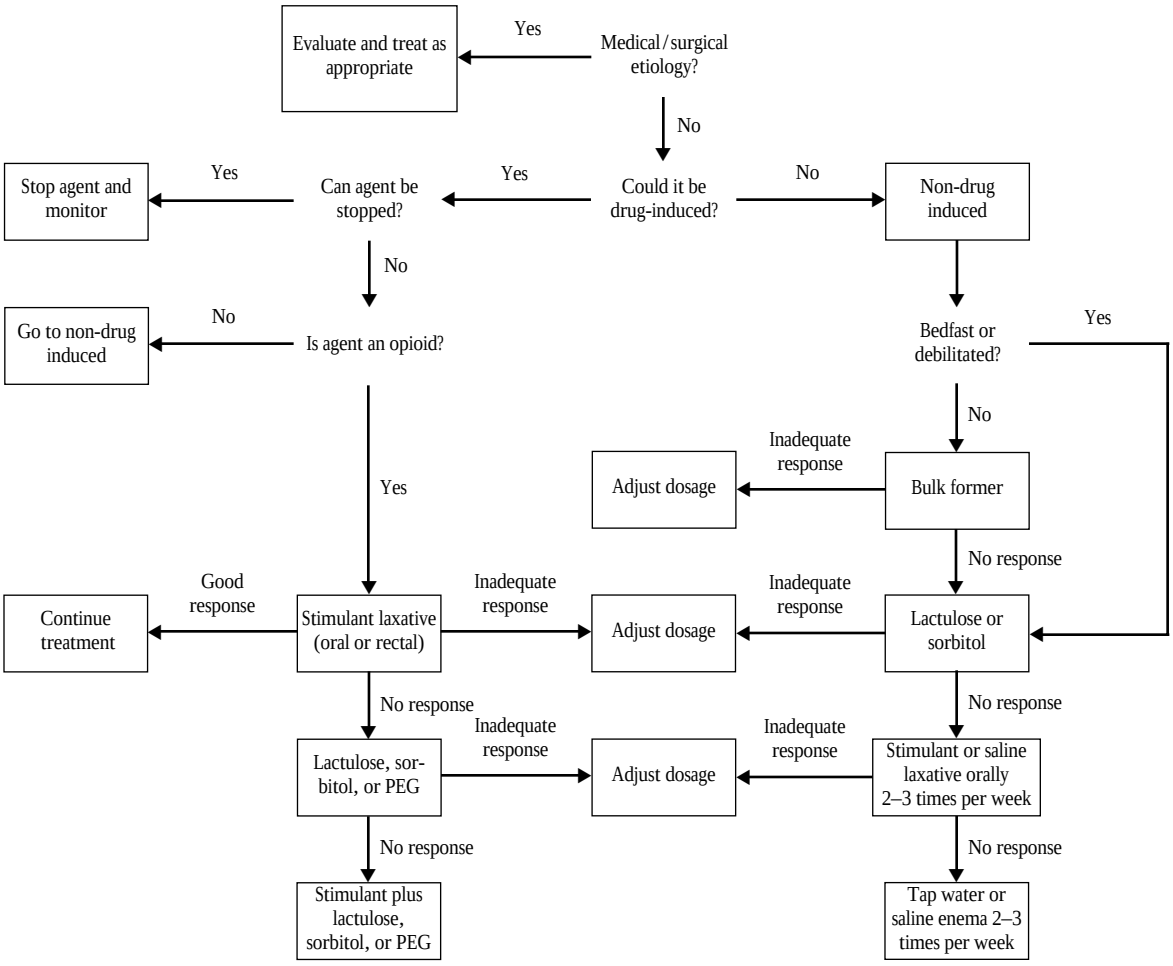
FIGURE 2. ALGORITHM FOR MANAGEMENT OF CHRONIC CONSTIPATION



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not only enhances cholinergic activity, but also increases nonadrenergic, noncholinergic (NANC) activity.[32,33] NANC activity enhances colonic activity specifically.[32,33] NANC activity may be very beneficial in the treatment of constipation, but more clinical trials must be performed to determine the effects of use of this agent. Prucalopride's specificity for the colon, as compared to cisapride's nonspecific effects, may create a niche for this agent. If it does become available, long-term studies will be needed to determine its proper place in constipation therapy.

Another agent that has prokinetic effects on the gastrointestinal tract is erythromycin. It most likely works by acting as a motilin-receptor agonist.[34–36] Erythromycin is primarily used to treat infections, but due to its effects on the gastrointestinal tract, it has been studied for the treatment of constipation.[37] Eleven patients ranging in age from 25 to 65 years with idiopathic constipation (defined as less than three stools per week, symptoms greater than six months, and normal colon on barium enema and/or colonoscopy) were included. Patients received oral erythromycin 1 g daily in four divided doses for 14 days. The dose was then reduced to 500 mg daily for 14 more days. Colonic transit time shortened from the baseline mean of 86.2 hours to a mean of 44.8 hours after one week of therapy. Stool frequency also increased, from a mean of 2.3 times per week at baseline to 6.7 times per week at the end of therapy. Erythromycin does appear to work, but larger and longer clinical trials are needed before its use can be recommended in the management of constipation.

Misoprostol is another agent that has been studied recently for the treatment of constipation. The reason for using this agent is that an adverse effect of misoprostol is diarrhea, due to its stimulating effect on intestinal smooth muscle and fluid and electrolyte secretion.[4] Roarty et al. performed a trial with misoprostol for the treatment of chronic refractory constipation.[38] The trial was composed of only 18 patients who had had two or fewer bowel movements per week for at least two years. Twelve patients completed at least four weeks of treatment with misoprostol in doses ranging from 600–2,400 mcg per day (six patients dropped out due to abdominal cramping). Of these 12 patients who completed the four weeks, the mean interval between bowel movements was decreased from 11.25 to 4.8 days. However, 10 of the 12 patients used other medications (docusate sodium, bisacodyl, mineral oil, cisapride, and unspecified enemas) to treat constipation along with misoprostol, which makes it difficult to determine how effective misoprostol would be when used alone. Due to misoprostol's expense, adverse effects, and the apparent need for concurrent medications in the treatment of constipation, it should not be recommended as a first-line therapy for constipation. If a patient cannot tolerate or has adverse reactions to other constipation modalities, then misoprostol may be recommended.

Treatment objectives. The primary goal of constipation therapy is to relieve constipation in a timely manner with an agent that will have minimal adverse effects on the patient. Unfortunately, constipation is a difficult symptom to treat due to varying etiologies, definitions, and various potential therapies. The algorithms that follow may be helpful in choosing the proper treatment for constipation in various situations (Algorithms 1 and 2). Algorithm 1 begins with the determination of the etiology of constipation. If there is no acute, medical etiology, and relief is required within a 24-hour period, glycerin suppositories may be used. The algorithm then guides one through the other potential therapies for acute constipation. We recommend using this algorithm for treating individuals with constipation symptoms lasting no more than several days. Algorithm 2 also begins with the determination of the etiology of constipation. After the cause is determined, patients should be treated adequately. Use of oral agents is often the preferred route for chronic treatment of constipation. If enemas are required, saline or

tap water enemas should be used. Soap enemas should not be used due to their potential to adversely effect the rectal mucosa.[39–41]

OPIOID-INDUCED CONSTIPATION

Opioid-induced constipation is very difficult to treat. Stimulant laxatives are the most frequently used agents for this type of constipation.[42] Izard and Ellerson conducted a study in 100 patients with drug-induced constipation over a six-month period.[43] Patients were chosen from various hospital services without regard to gender or service; patients less than 15 years of age were excluded. There were three groups: 33 received no treatment, 33 received 30 mL of magnesium hydroxide with or without mineral oil, and 34 received senna 450 mg on day one, 900 mg on day two, up to 1,350 mg on day three (senna-treated patients had their dose increased daily if therapy was ineffective). Treatment was considered a success if a bowel movement occurred during the treatment period of three days. There was one success in the untreated control group, 12 successes in the magnesium hydroxide group, and 32 successes in the senna group. In the senna group, 26 of 34 patients had narcotic-induced constipation; of these, 24 were successfully treated.

Freedman et al. studied the use of polyethylene glycol (PEG)-3350 (GoLYTELY, Braintree Laboratories, Braintree, Massachusetts) solution and lactulose in a double-blind, placebo-controlled trial for relieving opioid-induced constipation.[44] Patients were receiving methadone at a drug-dependency hospital. Methadone is thought to cause greater constipation than other opioids. Patients received either 240 mL of water, 30 mL of lactulose (diluted with water to reach 240 mL), or PEG-3350 solution (240 mL), all of which where identically flavored. Three periods of two weeks of the above-mentioned treatments were performed. Both lactulose- and PEG-3350–treated patients had fewer hard stools, as recorded in a personal daily diary. Patients receiving lactulose experienced more adverse effects (abdominal cramps) than the other treatment groups, but the PEG-3350 treatment group had more episodes of diarrhea. Although patients may experience some adverse effects, both lactulose and PEG-3350 are beneficial agents for the treatment of opioid-induced constipation. Since both lactulose and sorbitol work by a similar mechanism, it is reasonable to consider using sorbitol for opioid-induced constipation.

Another product composed of PEG-3350, Braintree formula 851 (MiraLax, Braintree Laboratories), has recently been marketed for the treatment of constipation. This product has been shown to be effective in the treatment of constipation for short periods (less than two weeks).[45] There are no published long-term studies on this agent to date, but it appears to be safe for short-term usage.

A safety and efficacy study was performed by the manufacturer in 151 healthy patients with constipation (defined as two bowel movements or less per week).[46] Patients received either 17 g of Braintree formula 851 or dextrose placebo in water for 14 days. Patients kept a diary of stool frequency, stool consistency, ease of passage, cramps, and flatus. By the end of the two-week period, there was a statistically significant difference between the two groups. The placebo group had 2.7 bowel movements per week, as opposed to 4.5 bowel movements per week in the treatment group.

CONCLUSION

Constipation is a common symptom in the elderly population. As stated earlier, proper diagnosis and determination of the cause is a necessity. Adequate hydration and diet therapy are the first steps in treating chronic constipation, along with ample exercise and, possibly, bowel training. Adjuvant pharmacologic agents can be added on an as-needed basis to help a patient through the acute situation. In our opinion, if an agent is required daily for the treatment of constipation, bulk-forming agents or hyperosmolar agents (lactulose or sorbitol) should be recommended, depending on the individual patient's needs and tolerance of the agents. The aforementioned algorithm may help to guide consultant pharmacists in recommending agents for the treatment of constipation. No matter what agent or agents are selected for use, they should be chosen to provide the relief of symptoms as quickly and as safely as possible.

CLINICAL NOTE

This article is recommended by the Commission for Certification in Geriatric Pharmacy as a certification examination study resource.

INAPPROPRIATE USE OF METFORMIN IN ELDERLY LONG-TERM CARE RESIDENTS

Samuel L. Gurevitz

Objective: To identify the inappropriate use of metformin among elderly long-term care residents.
Design: Retrospective chart review of long-term residents receiving metformin.
Setting: Ten long-term care facilities in northwest Indiana.
Subjects: Twenty three of 917 long-term residents over the age of 65 receiving metformin during the period October–December 1999.
Interventions: No prospective intervention was employed.
Main Outcome Measures: Use of metformin in long-term care residents at risk for developing lactic acidosis. Use of metformin in residents with a diagnosis of heart failure requiring pharmacotherapy, serum creatinine > 1.4 mg/dL for females and >1.5 mg/dL for males, a calculated creatinine clearance below 60 mL/min, or > 65 years of age without documented renal function assessment prior to initiation of metformin therapy was considered inappropriate.
Results: Eighteen of the 23 residents (78%) receiving metformin had a diagnosis of either heart failure requiring pharmacotherapy, renal dysfunction, or an estimated creatinine clearance of less than 60 mL/min.
Conclusion: Eighteen of the 23 (78%) long-term care residents who were receiving metformin therapy were treated inappropriately, putting them at risk for development of lactic acidosis. Consultant pharmacists should be monitoring patients receiving metformin and working with physicians concerning the appropriate use of metformin therapy.
Key Words: Acidosis, Biguanide, Elderly, Geriatrics, Lactic acidosis, Metformin.
Abbreviations: FDA = Food and Drug Administration; HF = heart failure; SrCr = serum creatinine.
Consult Pharm 2000;15:734–7.

Metformin hydrochloride, a biguanide antidiabetic, received Food and Drug Administration (FDA) approval for the treatment of type 2 diabetes in the United States in 1995. It is indicated for use in monotherapy or in combination with a sulfonylurea. Metformin improves glycemic control by decreasing hepatic glucose production, increasing peripheral glucose uptake, and, to a lesser extent, by decreasing intestinal absorption of glucose. Metformin provides glycemic control comparable to that provided by sulfonylureas but does not cause hypoglycemia when used as monotherapy. Metformin reduces plasma total cholesterol, low-density lipoproteins, and triglyceride levels, and slightly increases high-density lipoproteins. Unlike sulfonylureas, metformin may cause weight loss. Decreased platelet aggregation is another potential benefit of metformin use.[1–3]

The most common adverse reactions associated with metformin are gastrointestinal effects (30%), such as diarrhea, nausea, epigastric pain, and anorexia.[3] Long-term metformin therapy (three to six years) is associated with vitamin B_{12} deficiency,[1,2] and annual screening is recommended.[2]

The major clinical concern with metformin is lactic acidosis.[1–3] Although lactic acidosis is rare (0.03 cases per 1,000 patient years), it is fatal in about half the cases.[3] It is largely avoidable by strict adherence to the contraindications and precautions to therapy (Table 1).[1]

From May 1995 through June 1996, the FDA received 66 reports of lactic acidosis in patients being treated with metformin.[4] The diagnosis was confirmed in 47 patients; of those, 43 patients had at least one risk factor for lactic acidosis. In addition, 30 patient (64%) had cardiovascular disease, of whom 18 had heart failure (HF) and 13 (28%) had pre-existing renal insufficiency. Other reports describing lactic acidosis associated with metformin use have also been published.[5–7]

Metformin may cause lactic acidosis by modifying the normal production and removal of lactate.[2] Metformin causes a shift in the redox

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ACKNOWLEDGMENTS: The author would like to acknowledge Elizabeth Auble, RPh, and Edward Casko, PharmD, of Care Pharmaceutical Services, Inc. for help with this project.

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potential from aerobic to anaerobic metabolism, which promotes anaerobic gylcolysis, with the generation of lactate by the intestinal mucosa.[1,2,9] Metformin also decreases lactate metabolism in the liver by suppressing pyruvate carboxylase, causing lactate levels to accumulate, resulting in acidosis.[2] Lactic acidosis is associated with lactate levels greater than 5 mmol/L and blood pH of less than 7.25.[2,3,6] The onset of lactic acidosis is often insidious and associated with nonspecific symptoms, including nausea, vomiting, somnolence, epigastric pain, thirst, and increased respiratory rate.[2,3]

Numerous risk factors for lactic acidosis have been identified,[1,3,9] the most notable being renal impairment.[1,9,10] Metformin is primarily eliminated by the kidney.[1,2,9] When the drug is given to patients with impaired renal function, metformin plasma levels will increase. If the levels of metformin increase to greater than 5 ug/mL, lactic acidosis may occur.[3,9]

Metformin should be avoided in patients with HF requiring pharmacotherapy.[3,4,9] HF is associated with decreased cardiac output and reduced perfusion of the kidneys; this, in turn, causes a reduction in glomerular filtration rate that may result in increased metformin concentrations. In addition, many patients with type 2 diabetes are also receiving digoxin and furosemide, two agents with the potential to increase metformin concentrations.[3] Concomitant use of cimetidine and nifedipine has also been reported to increase metformin levels.[2,3]

Because of comorbid illnesses, concomitant medical therapy, and age-related pharmacokinetic changes (e.g., decreased renal function), elderly patients in general are at higher risk for adverse events. As many as 28% of hospital admissions of the elderly are a result of medication-related problems, and up to 70% may be attributable to adverse drug reactions.[11]

Ensuring the appropriate use of metformin or any drug therapy in elderly long-term care residents is paramount. The purpose of this study was to evaluate whether metformin was being appropriately prescribed to elderly long-term care residents.

METHODS

During the period October–December 1999, 26 of 917 elderly residents (aged 65 years and older) in 10 long-term care facilities were identified as receiving metformin therapy from a computer-generated list derived from pharmacy records. The facilities are located in four counties in Indiana (Jasper, Lake, LaPorte, Stark) and range in size from 46 to 200 beds. Only the information available in the nursing home charts was used for this study.

According to a review by Cusi and Defronzo,[9] impaired renal function, HF requiring pharmacologic treatment, and advanced age (> 80 years) are the most important contraindications to metformin therapy. The manufacturer, in the product labeling, recommends assessment of renal function in the elderly before initiation of metformin therapy and annually thereafter. Therefore, residents were included in the study if they were 65 and older with a documented diagnosis of HF requiring pharmacotherapy, serum creatinine (SrCr) > 1.4 mg/dL for females and >1.5 mg/dL for males, an abnormal creatinine clearance (defined as below 60 mL/min, as suggested by Morely[8]), or age > 65 years of age without documented assessment of renal function prior to initiation of metformin therapy.

For the purposes of this study, therapy with metformin was considered inappropriate if metformin was given to elderly residents with HF requiring pharmacotherapy, with renal dysfunction, or a calculated creatinine clearance below 60 mL/min; or if given to residents > 65 years old in the absence of renal function monitoring before initiation of metformin therapy.

RESULTS

Upon review of the medical charts of the 26 residents receiving metformin, 23 met the inclusion criteria. Twelve residents were less than 80 years of age, and 11 were 80 years of age or older, with a mean age of 79 ± 13 years. The majority of residents were females (18 of 23).

Based on the study definition of inappropriate use of metformin therapy in the elderly long-term resident, 18 of 23 residents (78%) were

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TABLE 1. RESIDENTS INAPPROPRIATELY RECEIVING METFORMIN

Criterion	Number of residents
HF	8
Renal dysfunction	4
Abnormal CrCl (< 60 mL/min)	5
≥ 65 years of age no renal data before initiation of metformin therapy (without other contraindications or precautions)	1
HF and renal dysfunction	1
HF and abnormal CrCl (< 60 mL/min)	2
HF and no renal data	3
Renal dysfunction and abnormal CrCl	4
HF and renal dysfunction and abnormal CrCl	3
CrCl <60 mL/min with a SrCr < 1.4 mg/dL	6 (2 with HF)
< 80 years of age	1

HF = heart failure; CrCl = calculated creatinine clearance (Cockcroft and Gault); SrCr = serum creatinine. Abnormal CrCl = < 60 mL/min.

receiving metformin therapy inappropriately (Table 1). There were eight residents (35%) with a diagnosis of HF requiring treatment, of whom three also had renal impairment. Four residents (17%) with renal dysfunction and five residents (22%) with a calculated creatinine clearance of less than 60 mL/min were also receiving metformin; and renal function assessment data was lacking on one resident > 65 years of age before initiation of metformin therapy. Renal data was lacking in three patients with HF.

DISCUSSION

Lactic acidosis is a serious medical condition with a high mortality rate. With careful attention to precautions and contraindications, (Table 2), the rare occurrence of lactic acidosis in patients with type 2 diabetes can be further minimized. This has been demonstrated in Canada, where no cases of lactic acidosis were reported during 56,000 patient-years of metformin treatment during the period 1972–82.[12]

This study found, however, that the metformin prescribing guidelines were not being adhered to in a sample population of elderly long-term care residents with type 2 diabetes. In a similar study, Rheney et al.[13] evaluated whether metformin was temporarily withheld or discontinued in patients with renal dysfunction during hospitalization or in patients at risk for developing acute renal dysfunction (i.e., those receiving radiologic parenteral iodinated contrast dye or undergoing surgical procedures). They found that metformin was not discontinued in five of 10 patients (50%) who actually developed renal dysfunction in the hospital. Moreover, metformin was not discontinued in three patients (14%) prior to receiving iodinated contrast dye and in five patients (12%) prior to surgery.

Metformin labeling suggests that SrCr and creatinine clearance should be determined before initiation of metformin in the elderly and at least annually thereafter. It should be noted, however, that serum creatinine alone does not accurately predict renal impairment in some patients. This was evident in this study, as seven

residents had a serum creatinine less than 1.4 mg/dL but estimated creatinine clearance less than 60 mL/min.

Although this study identified eight residents receiving metformin who had heart failure requiring pharmacotherapy, two of eight (25%) had normal renal function, based on a creatinine clearance estimate. It is debatable whether any patients with an estimated CrCl of less than 60 mL/min should be prescribed metformin. Hart and Walker[14] suggest that the risk of metformin-associated lactic acidosis is negligible in patients with chronic stable heart failure and normal renal function (as assessed by SrCr). Metformin is a valuable drug in the management of type 2 diabetes, and its use in HF patients with normal renal function should be further evaluated.

One limitation of this study was its dependence on chart reviews: deficiencies in medical records could have led to a higher reported percentage of inappropriate use of metformin therapy if medical laboratory tests were not available.

Despite this possible limitation, this study found that when metformin was prescribed in elderly long-term care residents with type 2 diabetes, its use was deemed inappropriate use in 78% of cases.

To help ensure appropriate metformin therapy in the elderly long-term care resident, the consultant pharmacist must take an active role, carefully assessing patients and monitoring renal function prior to and during use of metformin. They also should take the initiative to consult the prescribing physician to discuss the appropriateness of metformin therapy.

TABLE 2. PRECAUTIONS AND CONTRAINDICATIONS TO THE USE OF METFORMIN

Renal disease or renal dysfunction, defined as a SrCr of 1.4 mg/dL or more for females and 1.5mg/dL or more for males
Heart failure requiring pharmacotherapy
Chronic liver disease (abnormal liver function tests)
Abnormal creatinine clearance (< 60 mL/min)
Alcohol abuse with binge drinking
Use of intravenous radiographic contrast agents (metformin should be temporarily discontinued)
Hypoxic conditions associated with cardiovascular collapse

Sources: Adapted from references 3 and 8.

Consultant Pharmacist

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1. Jones GA, Smith LE, Webster RT et al. Interaction of phenytoin with nutrients. Clin Pharm 1986;5:118–23.

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Caffeine and Medications: Not Always a Good Combination

Oftentimes we think of our morning cup of coffee without regard to how it may interact with the medications that we are taking. To most of us, that morning cup of coffee, tea, or caffeinated soft drink is usually the beginning of a day filled with caffeine consumption.

In America, a coffee break or meeting with someone over coffee is a way of life. Many new coffeehouses and bookstores have made it very popular to enjoy a cup of cappuccino or delightfully flavored coffee while relaxing with a book, reading the newspaper, or chatting with a friend or colleague. Whatever our beverage, it is easy to find a caffeine "fix."

For many of the patients we treat, the caffeine encountered throughout the day may be hazardous to their health. There has been increasing concern in recent years over the undesirable effects of caffeine, which has led to a general decline in consumption. However, many of us claim that caffeine increases our mental and/or athletic performance.

Caffeine is a xanthine derivative stimulant that occurs naturally in coffee beans, tea leaves, cocoa beans, and kola nuts. It is commonly found in dietary sources such as coffee, tea, soft drinks, and chocolate products. A strong cup of coffee contains more caffeine than other products commonly consumed (see Table 1). Caffeine is also used in many nonprescription medications such as analgesics, cold remedies, and weight loss products.

TABLE 1. CAFFEINE CONTENT OF SELECTED BEVERAGES AND FOODS

Beverage/Food	Serving Size	Caffeine Content (mg)
Soft drink	12 oz	
Mountain Dew		55.0
Coca-Cola		45.6
Diet Coke		45.6
Pepsi Cola		37.2
Diet Pepsi		35.4
Coffee	7 oz	
Drip		115–175
Brewed		80–135
Instant		65–100
Espresso	1.5–2 oz	100
Tea	12 oz	
Iced		70
Brewed		40–60
Instant		30
Miscellaneous		
Hot cocoa mix	1 envelope	5
Chocolate bar	1 bar	15–30
Chocolate milk	8 oz	8

Source: Aruna A. Caffeine fact & fallacy handbook. New Orleans, LA: Global Publishing Network; 2000.

CAFFEINE'S EFFECTS

Claims have been made that caffeine is the most widely used psychoactive substance in the world.[1] The most recognized effects of caffeine include increased alertness, energy, and ability to concentrate; these effects occur after low to moderate doses of 50–300 mg. Typical caffeine content may range from 70-220 mg per 5 oz of coffee, 30-50 mg per 5 oz of tea, 32-70 mg per 11 oz of a caffeinated soft drink, and 4 mg per 5 oz of cocoa.

Caffeine is a central nervous system (CNS) stimulant, a cardiac muscle stimulant, and acts on the kidneys to produce diuresis. As doses are increased, signs of progressive CNS stimulation occur, which may include anxiety, restlessness, insomnia, and tremors. In toxic doses, tachycardia, arrhythmia, and hypertension are observed.[2] Caffeine has been linked to an increased risk of spontaneous abortion and intrauterine growth retardation. Caffeine also decreases the ability to absorb calcium, potentially contributing to the development of osteoporosis. It may also cause ulcerogenic effects due

to secretion of both pepsin and gastric acid from parietal cells of the stomach.[3]

Interaction Risks

Caffeine has been added to both prescription and nonprescription drugs since the early 1900s. In low to moderate doses, the combination of caffeine with aspirin and acetaminophen has been found to enhance the efficacy and absorption of these drugs in treating headache.[3] Caffeine enhances the action of ergotomine for treatment of migraine or cluster headaches. The debate continues about caffeine being a trigger of migraine headaches. Caffeine has also been combined with aspirin and other analgesics for the treatment of headaches, but there is little data to substantiate its efficacy for that use.[3] Caffeine is also used in combination with antihistamines to overcome the drowsiness associated with antihistamine use.[3] In addition, weight loss products may include caffeine, as it suppresses appetite and may elevate blood glucose levels.[3]

Although caffeine has been used with success in numerous products, there are serious side effects and adverse reactions that must be considered. These side effects and adverse reactions become increasingly important when a patient is taking a prescribed medication and uses dietary sources of caffeine or nonprescription medication containing caffeine.

Theophylline is also a xanthine derivative and is chemically related to caffeine. Figure 1 shows the chemical structures of the methylxanthine derivatives.[3] Caffeine is a trimethylxanthine, while theophylline and theobromine are dimethylxanthines with two methyl groups. The less commonly discussed theobromine is the principle alkaloid of the cocoa bean, cola nuts, and tea. While the methylxanthines have different biochemical effects, they are very similar, differing chemically only in the position of the methyl groups in their structure.

Theophylline is used to treat conditions such as asthma, chronic bronchitis, and emphysema by opening air passages of the lungs and helping to alleviate wheezing and shortness of breath associated with these conditions. Since both stimulate the CNS, theophylline and caffeine may act synergistically, causing tachycardia and tachypnea.[6] Patients taking xanthine derivatives should be advised to avoid eating or drinking large amounts of foods or beverages containing caffeine and to avoid over-the-counter drugs that contain caffeine.[6]

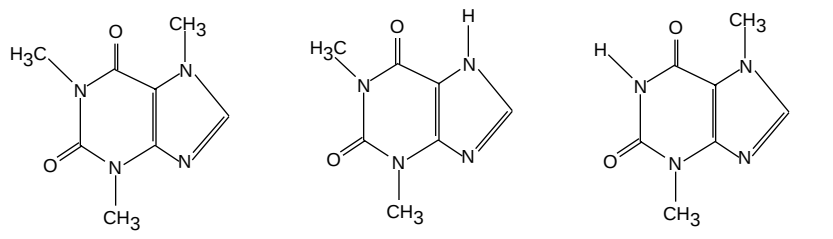
Xanthines such as caffeine and theophylline are involved in the cytochrome P450 1A2 isoenzyme system and may cause drug interactions with other substrates, inducers, and inhibitors of that system. Increased theophylline toxicity has been reported with the combination of caffeine and theophylline.[2] In addition, the fluoroquinolone ciprofloxacin has been shown to significantly increase the half-life of caffeine.[8] Patients need to be counseled about caffeine consumption with medications such as erythromycin and ciprofloxacin.

The combination of diuretics and caffeine has been shown to have detrimental effects on blood pressure.[3] Caffeine produces diuresis in the kidneys and potentiates the action of diuretic drugs, resulting in hypotension. Restricting caffeine intake should be encouraged while taking diuretics.

Patients taking monoamine oxidase (MAO) inhibitors such as isocarboxazid, phenelzine, and tranylcypromine should be cautioned regarding caffeine intake. Ingestion of large amounts of caffeine with concurrent MAO inhibitor use has been reported to cause hypertension and arrhythmias.[5] Even ingesting small amounts of caffeine may cause mild hypertension and tachycardia.

Caffeine may interact with other psychotropic agents such as the selective serotonin reuptake inhibitor (SSRI) fluvoxamine.[7] Fluvoxamine has recently been found to substantially elevate serum caffeine levels. Therefore, individuals who continue their regular caffeine ingestion are at risk for caffeine intoxication.[7]

FIGURE 1. XANTHINE DERIVATIVE METHYLXANTHINES



Source: Goodman AG, Gillman LS.[3]

Role of Health Promotion

Due to increasing awareness of drug interactions, health promotion, and disease prevention, a "caffeine assessment" should be a routine component of the medication history.[2] Since caffeine may affect the action of some drugs, health care providers should be familiar with all drugs being taken by the patient, including both prescription and nonprescription.[6]

Attention should also be given to clients who smoke. Nicotine stimulates the drug-metabolizing enzymes in the liver. This action causes the smoker to consume more caffeine in order to feel its effects. Patients using both tobacco and caffeine are at greater risk for caffeine intoxication.

Conclusion

It is imperative that we assess the quantity of caffeine consumed by our patients when taking a medication history. Sometimes, medication dosage adjustments should be made or closer monitoring provided. Counseling and assistance with selecting decaffeinated alternatives should be provided. Fortunately, many traditional caffeine products are now available in decaffeinated versions, and numerous herbal teas are also marketed. So, next time you do that medication history, consider the caffeine consumption: is it moderate or excessive? For that matter, is your *own* caffeine consumption potentially problematic? Something to think about the next time you have that morning cup of java!

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Rectal Administration of Pain Medication in the Elderly

The elderly patient is at increased risk of undermanagement of pain. It is estimated that 45%–80% of elderly patients residing in nursing homes have pain that contributes to functional impairment and decreased quality of life.[1] The estimated prevalence of pain in people under 60 years of age is 125 per 1,000; in people over 60, the estimated prevalence almost doubles, to 250 per 1,000.[1] In the institutionalized elderly, the incidence of pain may be greater than 70%.[1]

Pain Etiology and Treatment

Musculoskeletal (arthritis) pain is the principal complaint in the elderly. Cancer, herpes zoster, temporal arteritis, polymyalgia rheumatica, and atherosclerotic peripheral vascular disease are examples of other pain syndromes that occur in the elderly.[1]

Undermanagement of pain in the elderly has been a hot topic lately, especially in long-term care facilities. Identified obstacles to adequate pain control in the elderly include attitudes of the elderly toward pain, inadequate pain management skills among health care providers, and inadequate pain assessment methods. A patient who has severe cognitive impairment is at extremely high risk of suffering from uncontrolled pain.

Treatment of pain is based on the severity of symptoms, frequency of symptoms, the patient's tolerability to medications used, and the patient's response to previous attempts at analgesia. Oral administration remains the route of choice for administering pain medications. Oral dosage forms are generally less expensive, with the advantages of more reliable absorption, generally predictable pharmacokinetics, and simple techniques of administration. Although the oral route is preferred, a non-oral route of analgesia administration may be necessary or preferable for a variety of reasons. Persistent nausea and vomiting, absorptive impairment, gastrointestinal obstruction, and mental status changes are all reasons to search for an alternative route.[2]

The Rectal Route

Rectal administration of medications has been the subject of many review articles. Advantages of this route include a limited need for patient and/or family education and training and no need for "high-tech" equipment; in addition, rectally administered pain medication bypasses the gastrointestinal tract and is relatively inexpensive.[2] Analgesics administered rectally are usually the last resort before a decision to use parenterally administered pain medications. The risks associated with parenteral drugs (e.g., increased risk of infection) make researching other alternatives a worthwhile investment of time and money.

In order to be absorbed rectally, a drug must first be soluble in a limited amount of rectal fluid (1–3 mL).[3] Absorption of drugs across the rectal lumen occurs by two routes: transcellular and paracellular.[3] Many factors affect absorption: drug formulation (time to liquefaction), volume of liquid, concentration of drug, length of rectal catheter (site of drug delivery), presence of stool in the rectal vault, pH of the rectal contents, rectal retention of drug(s) administered, and variances in rectosigmoid venous drainage.[4]

Once the drug is absorbed, it is transported via one of three intestinal veins. The superior rectal vein drains into the portal vein and, subsequently, into the liver. The remaining two veins drain into the inferior vena cava, thus bypassing the liver and avoiding hepatic first-pass metabolism. In theory, avoidance of hepatic first-pass metabolism should allow for administration of smaller doses of pain medications to obtain adequate analgesia than would be required by the oral route.

Long-term administration of some medications via the rectum may induce rectal ulceration, resulting in bleeding and pain.[3] Suppository medications containing ergotamine tartrate 0.8 mg, aspirin 500 mg, codeine phosphate 20 mg, caffeine 80 mg, paracetamol 500 mg, and belladonna extract 10 mg have been reported to induce rectal stenosis and ulceration.[3]

Available Options

Several studies have explored the pharmacokinetics and effectiveness of administering narcotic analgesics via the rectal route. Oxycodone is available in the United States in 5 mg tablets, as well as 5 mg/5 mL and 20 mg/mL oral liquid (a suppository form is available in Australia).[2] A study focusing on rectally administered oxy-

codone concluded that only the liquid forms are clinically useful for moderate to severe pain, although multiple daily dosing diminishes the attractiveness of this drug for use in chronic pain syndromes.[2]

Codeine phosphate in alkaline solutions is completely absorbed rectally, but bioavailability is affected by hepatic first-pass metabolism.[3] As noted above, codeine is highly irritating to the rectal mucosa and can cause ulcerations and bleeding when used for long-term pain control.

Morphine given via the rectum in various forms (e.g., starch-containing gel; aqueous microenema with pH of 4.5; hard, fatty suppository) has been studied extensively. These studies have generally concluded that the pharmacokinetic profile of rectally administered morphine is comparable to that of equivalent oral doses.[3]

A study by Kaiko et al. using 30 mg of rectally administered controlled-release morphine tablets concluded that drug absorption over 24 hours was equivalent to that observed with oral administration.[4] Placement in the rectum is important; Kaiko et al. found that 6–10 cm above the anus is the ideal placement site.[4] The frequency of erythema following use of rectal morphine suppositories was numerically greater than that after rectal administration of controlled-release morphine tablets.[4]

A study of 39 patients who were switched from orally to rectally administered MS Contin (morphine sulfate) tablets was performed at Mercy Hospice in Nampa, Idaho. The patients were given rectal doses equivalent to those they had previously received orally. Eleven of the patients required dose adjustments within five days due to increased self-reported drowsiness.[5] Pain control was maintained, with no need for dose increases in any of the patients.[5] These patients were given 30 mg tablets, but MS Contin is available in 60 mg and 100 mg tablets (a higher dose than is available with the suppository form of morphine).

TABLE 1. RECOMMENDATIONS ON ADMINISTERING RECTAL ANALGESICS

- Position patient on the left side with the top leg flexed.
- Moisten dosage form with water or water-soluble lubricant to avoid irritation. If rectum is dry, instill 10 mL warm water prior to inserting dose, with syringe attached to catheter.
- Introduce suppositories rounded end first. Gently insert the drug approximately a finger's length into rectum, angling it toward the umbilicus and placing the medication against the rectal wall.
- After withdrawing your finger, hold the patient's buttocks together until the urge to expel ceases.
- Keep preparation volume of solutions less than 60 mL. Inject with lubricated rubber-tipped syringe or large-bore catheter and balloon. Inflate the balloon to assist retention.
- Don't split suppositories or crush or dissolve oral controlled-release formulations.
- Avoid enteric-coated tablets. They require an acidic environment to release active drugs; colon pH is alkaline.
- Minimize the number of insertions. Enclose a multiple-tablet dose in a single gelatin capsule.
- Avoid repeat administration of solutions and drugs that use alcohols or glycols as delivery vehicles, such as parenteral lorazepam, diazepam, chlordiazepoxide, and phenytoin.
- Treat irritation with lubricants and topical medications, such as cortisone ointment.

Source: Pasero C, McCaffery M.[6]

IMPLICATIONS FOR PHARMACISTS

Proper administration of rectal doses of medications is necessary for maximum effectiveness. To that end, the *American Journal of Nursing* recently issued recommendations on administering rectal analgesics (Table 1).[6]

Consultant pharmacists are in an ideal position to positively affect the pain management of residents of nursing homes. Many hospice organizations also use rectally administered oral dosage forms of medications. The greatest impact that consultant pharmacists can make on pain control in the hospice setting is by teaching the nurs-

ing staff proper administration technique for maximum analgesia. In my experience, some pharmacists have a tendency to shy away from practices that are unconventional or unorthodox relative to their training; many practices of hospice organizations fit those descriptions, and pharmacists should keep an open mind about their appropriateness and effectiveness, even if support in the scientific literature is lacking or minimal.

Regardless of the practice setting, by virtue of their pharmacotherapy expertise and close, ongoing contact with various members of the health care team, pharmacists can play a lead role in promoting the multidisciplinary teamwork—and involvement of residents and families—that holds the key to maximizing pain control outcomes.

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INFORMATION ACCESS

Selected Web Site Reviews

In this department our goal is to provide you with structured evaluations of Internet sites of potential interest to you and the clients you serve. We will also look at other communications technologies and discuss various techniques for getting the most out of those technologies.

Members of the American Society of Consultant Pharmacists— including Editorial Review Board members—and other health care professionals provide the reviews and their respective opinions on the sites presented in this column. Each review contains an overview of the site's intended audience, purpose, most useful content, highlights and special features, limitations, and related sites.

Independent submissions of Web site reviews are welcome. Please e-mail to dbuerger@ascp.com.

AGENET
www.agenet.com

Audience
Aging consumers and their caregivers.

Purpose
AgeNet states that the site was designed to "bridge the distance between aging parents and adult children by providing products and services that allow for long distance caregiving." The site is an Internet-based information and referral network committed to enhancing the quality of life of older adults and their caregivers. Its mission is further defined as "a business designed to help older adults maintain independence, dignity and security."

The site was created in 1995 by David Williams and Doug Hennig, who met while working on the development and marketing of an assisted living company.

Content
Overall, the site is attractive and easy to navigate. Content areas are listed on the left side of each page, and an AgeNet logo is located on every page; clicking the logo returns the user to the site's home page. The content of Agenet.com is divided into major topic areas: health, drugs, legal, insurance, finance, and caregiver support. Health information and resource links specific to older adults can be found in the "Geriatric Health" section. Content includes articles on the benefits of geriatric assessment and case management, Alzheimer's disease, Parkinson's disease, diabetes, and incontinence. A section on geriatric drugs contains drug reviews for Alzheimer's disease, Parkinson's disease, and diabetes; a "Watchful Eye" area with information on new drugs; and an advice column, "Ask a Pharmacist."

Information on estate planning and advance directives can be found in the legal section. In addition, a lawyer search and a section for purchasing legal software for creating living wills is available. Insurance and finance are both discussed in their respective sections and contain an on-line reference library describing different types of insurance and asset protections, as well as information regarding estate planning, living trusts, and document storage.

The caregiver support section contains articles and information to improve communication between caregivers and aging parents. It includes a Web reference library, the "Ask Terri" advice column on how to make a home safe for aging, and links to senior centers and geriatric care managers.

Most of the sections also contain related press releases, book reviews, and links to other pertinent Web sites. For instance, the finance section contains an article on innovative elder care financing strategies, and an article on exercise for better aging can be found in the Geriatric Health section.

Another section on housing/living options includes a variety of different checklists on home safety, nursing home care, assisted living, and home health services. A free search and referral service for senior housing alternatives is also available.

Highlights and Special Features

Agenet offers access to Geriatric Medication Assessment Services for a fee of $45 per review. The review application includes space for five medical conditions or diagnoses and 10 medications. The page states that the review will be completed by an Agenet pharmacist, but the pharmacist's name and/or credentials are not listed—and there is no mention of how long it will take to receive the pharmacist's report.

Site visitors can sign up to be a member of Agenet for free. Members are able to access the chat and message boards, receive e-mail updates specific to a medical condition or special interest, and receive free registration in an on-line "Living Will and Caregiver Notification Registry." The registry provides a listing for each registrant indicating the existence of a living will or other advance directive; last known update; location(s) of the documents with contacts; and the name, address, and phone number of a caregiver or responsible party to be notified upon the registrant's admission to a health care facility. Each registrant will receive an AgeNet registry card and identification number.

Participating hospitals and related professionals will be able to retrieve registrant information by using the AgeNet identification number or, if the registry card cannot be found, by conducting a sex, name, city, and state search of the registry database. If you have a living will or advance directive, the hospital will ascertain the document's location and who to contact to obtain an original copy. Likewise, if a person has registered for caregiver notification, the hospital can find out who to notify upon admission of the registrant.

Geriatricians who visit the site can get a free e-mail address (yourname@geriatrician.com) for becoming a member of Agenet.

Limitations

Geriatricians can sign up for listing on this site. Unfortunately, it does not appear that the geriatrician registration process is monitored, as I was able to register as a geriatrician and get a listing on the site, no questions asked (I am not a geriatrician). Furthermore, I was unable to find a way to contact the site's Webmaster about this problem.

Another drawback is the lack of disclosure of the sources of posted information. For example, the "Drugs to be Used With Caution in the Elderly" article in the Geriatric Drugs section states that Agenet has developed a list of 24 drugs that should be used with caution in the elderly, but it lists no references or information on how the list was created or who participated in its development. In light of that, keep in mind that this site was created and is managed by business people, not health care practitioners, so a certain amount of caution is needed when reviewing clinical topics.

Related Sites

American Association of Retired Persons (AARP) at www.AARP.org.

Reviewer

Lisa F. Han, BS, Insight Therapeutics, LLC, Norfolk, Virginia

MDCHOICE

www.MDChoice.com

Audience

Health care professionals of any practice type; a separate area on the Web site is devoted to consumers.

Purpose

MDChoice.com is a free service that bills itself as "The Ultimate Medical Information Finder." The service was founded by academic physicians with the goal of increasing the efficiency and reliability of medical information searches on the Internet. The group claims to achieve this by incorporating proprietary search software (patent pending) and content partnerships with organizations such as NetMedicine, Physician's Choice, and EMBBS.com. The site lists eight physicians on its editorial board. This group is tasked with evaluating the Web's medical content and publishing opinions via structured Web site reviews.

Content

The health care professionals portion of the site contains three main sections: "Medical Information," "Interactive Education," and "Reading Room." Each of these subsections contain links to search tools or specific content. Free user registration is available to those who wish to use the site customization feature.

The Medical Information section provides external links to sites deemed appropriate by the physician panel. There are two search engines provided: MEDLINE and UltraWeb, which will only search for content selected by their board-certified physicians.

There is a drug information page listing sites that provide drug monographs and drug interaction tools. The site's health news content is licensed from Reuters, which does a good job and is ubiquitous on commercial health-related sites throughout the Web. Clinical calculators are links to applications at a site maintained by the National Center for Emergency Medicine Informatics and a Brazilian site, MedStudents.com. The Interactive Education section contains case studies that use photographs or electrocardiography (EKG) readings to illustrate concepts, as well as links to cardiac life support programs at other sites. The Reading Room lists links to a number of full-text journals and reference books available on the Web.

Highlights and Special Features

"MyChoice" is MDChoice's customized Web page feature, which allows a registered user to choose selected offerings of the site. A database-built page is then served to the users with only the selected items displayed (e.g., Journal, MEDLINE, News, Clinical calculator).

This site's claim to uniqueness is its advanced search engine, UltraWeb, an application that searches only sites that are deemed credible by the MDChoice staff for the desired key words. This allows the user to search multiple sites simultaneously. Searches can be narrowed by type of document desired (e.g., reviews, articles, case presentations) or type of media (e.g., photos, EKGs, scans), or limited to continuing medical education (CME) programs or peer-reviewed documents. Search results are returned in four categories: photo links, CME links, peer-reviewed links, and consumer links. From the list, users may view or "check" desired items for downloading to their personalized MyChoice database. A similar search engine (built by Knowledge Finder) is used for searches of the MEDLINE, Healthstar, Cancerlit, and AIDSLINE databases.

Limitations

Although the site aggregates many services, it provides little original content. The search engine does a good job of limiting searches to a handful of journal or reference sites with content written by health care professionals, such as eMedicine and the Merck Manual Web site. But there is little MDChoice can do to control the timeliness of information displayed by these sites. For example, a search for "congestive heart failure" and selecting only peer-review articles revealed that some of the documents returned were up to six years old. Care should be used to verify that guidelines, articles, and other data are appropriate and consistent with current standards of practice. The Interactive Education feature may prove of little use to pharmacists or physicians. Beyond the unique search feature, the site is nothing more than a "bookmark" file to content on other sites. Clever use of frames make it look like some of the applications belong to MDChoice when they actually do not. The calculators developed by MedStudents.com were found to be particularly useful, yet there is no need to use MDChoice to access them (better to go directly to the desired Web site). The MyChoice feature adds little to the functionality of the site besides allowing users to save UltraWeb search results. MDChoice also falls short in not disclosing what method the panel uses to make decisions regarding the credibility of information. There is also no structured Web site reviews to be found, even though the site claims that this is a monthly occurrence. Finally, a peek at the consumer site shows that there is little difference in offerings at that site and the professionals site except that consumers are offered fewer services.

Conclusion

Use this Web site for what it is: a unique search engine. Its other offerings should be reviewed and their links bookmarked. Consumers are encouraged to simply use the more robust professional section.

Related Web Sites

Medscape.com (http://www.medscape.com/)

Reviewer

Bao-Anh Nguyen-Khoa, PharmD, Center for Health Information, Chesapeake, Virginia

POLICY CURRENTS

Illinois Assisted Living Facility Is First to Gain JCAHO Accreditation

The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) recently announced that King-Bruwaert House in Burr Ridge, Illinois, is the first of an estimated 30,000 U.S. assisted living facilities to be accredited under JCAHO's new assisted living program.

King-Bruwaert House and other assisted living facilities seeking JCAHO accreditation or reaccreditation will be judged in accordance with roughly 180 standards comprising the JCAHO *Accreditation Manual for Assisted Living* (While the new JCAHO assisted living standards became effective last month, the printed manual, including detailed intent statements for each standard, won't be available until this fall). A preview of the standards is posted at JCAHO's Web site (www.jcaho.org).

Many of the new standards relate directly or indirectly to medication use processes. The heart of the medication-related provisions of the JCAHO standards lies in the "Resident Services" section, which specifically addresses drug information, medication storage, and administration (see sidebar). "The intent statement for this standard will recommend that assisted living facilities obtain consultation from a 'qualified medical or health care professional' as they work to develop appropriate medication management processes," notes ASCP Director of Professional Affairs Tom Clark, RPh, MS. "Although the standard doesn't specifically require the involvement of a pharmacist in this process, it certainly provides a clear opening for increased involvement by pharmacists."

Several other JCAHO standards imply additional opportunities for pharmacist involvement.

For example, Standard CC.5.3 ("Continuity of Services") stipulates, "Appropriate resident information is exchanged when the resident is referred, transferred, or moves out"; the intent statement indicates that information on resident medications should be among that information. In the "Resident Education" section, Standard PF.7 calls for education of residents on proper storage of medications "as needed"—another clear opportunity for pharmacists. The intent statement for Standard PS.1 ("Health and Wellness Promotion") mentions "pharmacy drug regimen reviews" and pneumonia/influenza vaccination programs as examples of appropriate preventive care services.

Other JCAHO standards allude to opportunities for pharmacists in the areas of data collection for performance improvement activities, medication documentation and record-keeping, and infection control.

The full text of the assisted living standards can be obtained from JCAHO, One Rennaissance Blvd., Oakbrook Terrace, IL 60181; 630-792-5000 (www.jcaho.org). An "Overview of JCAHO Standards for Assisted Living" prepared by Clark is available in the "Practice Resources" section of ASCP's Web site (www.ascp.com).

KEY MEDICATION-RELATED JCAHO STANDARDS

RS.4: *If the assisted living community offers medication management services, processes are planned to ensure that medication use is safe, secure, and meets each resident's needs.*

RS.4.1: *When medication management is provided, staff have appropriate information in writing about the medications.*

RS.4.2: *If the assisted living community provides medication assistance, the assistance provided is appropriate to the resident's needs.*

RS.4.3: *When medication administration is provided, medications are stored under proper conditions of sanitation, temperature, light, moisture, ventilation, and security.*

RS.4.4: *If medication administration is provided, medications are safely and accurately administered.*

RS.4.5: *If medication administration is provided, the assisted living community responds appropriately to adverse drug events.*

Source: JCAHO.

WHERE DO THE CANDIDATES STAND ON HEALTH ISSUES?

Four months out from the November elections, a fairly clear picture of where the leading

presidential candidates stand on major health care reform issues is taking shape.

"Anyone expecting grand health care reform proposals like [President Clinton's proposed] Health Security Act will be disappointed" in the proposals to date by Republican candidate George W. Bush Jr. and Democratic candidate Al Gore, according to a recent analysis by Web-based medical education company Cyberrounds (cyberrounds.com).

Using information gleaned from Bush's and Gore's own Web sites (www.georgewbush.com, www.algore2000.com) and news reports, the Cyberrounds analysis explores the candidates' stance on three issues central to the ongoing national health care reform debate: Medicare prescription drug coverage, managed care patient rights, and how to insure the estimated 44 million Americans who currently lack any insurance or have inadequate insurance (see sidebar below).

Both candidates' health care reform proposals have drawn criticism from policy experts, Cyberrounds notes. For example, Bush's plan to provide tax credits to help the uninsured purchase insurance on the open market has been criticized because the proposed credit amounts—$1,000 for individuals and $2,000 for families—are considered too low to enable the purchase of adequate coverage. Gore's insurance proposal has been criticized for its heavy reliance on expansion of the Children's Health Insurance Program (CHIP), which has been "plagued by low enrollments" and affords states "considerable discretion to limit eligibility and benefits," the Cyberrounds analysis notes.

The Cyberrounds overview also observes that neither Bush nor Gore have addressed in specific terms the overarching issue of health care price inflation, currently running at 8%–10% annually—far higher than the overall inflation rate. "This is unfortunate," Cyberrounds says, "since rising health care costs are, in part, responsible for people lacking adequate health insurance and being unable to afford prescription drugs, and for employers and other third-party payers pushing people into managed care plans where they may feel their rights are being compromised."

David K. Buerger
Managing Editor

The Candidates' Stance on Key Health Care Issues

Issue	Bush	Gore
Medicare prescription drug coverage	Supports Medicare outpatient prescription drug benefit (specific details not available as of June 1)	Plan would give beneficiaries option to buy insurance covering 50% of prescription drug costs up to $5,000 annually and 100% of costs after out-of-pocket costs exceed $4,000.
Managed care patients rights	Supports patient protections similar to those provided under Texas law, which permits patients to sue managed care plans and holds plans to "reasonable" standard of care.	Supports Democratic version of "Patient Bill of Rights" (H.R.2723), including right to sue managed care plans as permitted under state law.
Lack of health insurance and/or underinsurance	Plan would provide individual and family tax credits to help purchase insurance on open market; ease restrictions on tax-exempt medical savings accounts. Cost: Estimates range from $40 billion over five years to $135 billion over 10 years.	Plan would expand state Children's Health Insurance Program (CHIP) by raising income eligibility threshold and implementing enrollment incentives; provide tax credits for families lacking employer-sponsored insurance. Estimated cost: $150 billion over 10 years.

Source: Cyberrounds. The 2000 Presidential Race: Where the Candidates Stand on Health Care Issues (http://www.cyberrounds.com.cme/). Accessed May 2000.

CALENDAR

AUGUST

60th World Pharmacy Congress
Vienna, Austria
August 26–31
Contact: International Pharmaceutical Federation, P.O. Box 84200
2508 AE The Hague, The Netherlands;
+31-70-302 1970,
Fax +31-70-302 1999

SEPTEMBER

ALFA Fall 2000 National Conference and Expo
Seattle, Washington
September 10–12
Contact: Assisted Living Federation of America, 10300 Eaton Place Suite 400, Fairfax, VA 22030;
703-691-8100,
Fax 703-691-8106

OCTOBER

AMCP 2000 Educational Conference
San Diego, California
October 4–7
Contact: Academy of Managed Care Pharmacy, 100 N. Pitt Street, Alexandria, VA 22314;
703-683-8416,
Fax 703-683-8417

AHCA Annual Meeting
Orlando, Florida
October 15–18
Contact: American Health Care Association 1201 L St., N.W., Washington, DC 20005;
202-842-4444,
Fax 202-842-3860

2000 AAHSA Annual Meeting
Miami Beach, Florida
October 23–26
Contact: American Association of Homes and Services for the Aging, 901 E. Street, N.W., Washington, DC 20004;
202-783-2255,
Fax 202-783-2242

2000 AAPS Annual Meeting
Indianapolis, Indiana
October 29–November 2
Contact: American Association of Pharmaceutical Scientists, 1650 King Street, Suite 200, Alexandria, Virginia 22314;
703-548-3000,
Fax 703-684-7349

NOVEMBER

Senior Care Pharmacy 2000: ASCP's 31st Annual Meeting and Exhibition
Boston, Massachusetts
November 1–4
Contact: American Society of Consultant Pharmacists, 1321 Duke Street, Alexandria, VA 22314;
703-739-1316, ext. 113,
Fax 703-739-1500

2000 ACCP Annual Meeting
Los Angeles, California
November 5–7
Contact: American College of Clinical Pharmacy, 3101 Broadway, Suite 380, Kansas City, Missouri 64111;
816-531-2177,
Fax 816-531-4990

DECEMBER

35th ASHP Midyear Clinical Meeting
Las Vegas, Nevada
December 3–7
Contact: American Society of Health-System Pharmacists, 7272 Wisconsin Avenue, Bethesda, MD 20814;
301-657-3000

MARCH 2001

AMDA Annual Meeting
Atlanta, Georgia
March 15–18
Contact: The American Medical Directors Association, 10480 Little Patuxent Parkway, Suite 760, Columbia, MD 21044;
800-876-2632

APhA Annual Meeting
San Francisco, California
March 17–20
Contact: American Pharmaceutical Association, 2215 Constitution Ave., NW, Washington, DC 20037;
800-237-APhA

CALENDAR POSTINGS
To share information about upcoming events, please send the sponsoring organization's name, telephone number, dates, and location of the event to Will Judy, Associate Editor, ASCP, 1321 Duke Street, Alexandria, VA 22314-353563; Fax 703-739-1500; e-mail *wjudy@ascp.com*. Information should be sent at least three months in advance of the event.

ASCP REPORTS

ASCP Officially Endorses 'SENIORx Gold' Prescription Drug Coverage Plan

ASCP has formally announced its support for "SENIORx Gold," a proposed voluntary state-based program for extending prescription drug coverage to millions of low-income seniors.

According to ASCP Director of Government Affairs Leigh Davitian, the decision to support SENIORx Gold came after in-depth analysis of other competing proposals introduced by members of Congress and the White House. ASCP has endorsed SENIORx Gold because many of its key provisions are in line with the previously adopted position statement by the ASCP Board of Directors, "Principles for Implementing a Senior Prescription Drug Assistance Benefit." Those principles hold that any program of expanded senior access to medication services must include the following components:

- Coverage targeted to low-income seniors and those without supplemental drug coverage
- Access to all Food and Drug Administration–approved drugs
- Payment for pharmacists' patient medication management services
- Payment for specialized dispensing and packaging services

The SENIORx Gold plan calls for expansion of prescription benefits to about 7 million community-dwelling American seniors with incomes below 200% of the federally defined poverty threshold who currently lack drug coverage. Central features of SENIORx Gold include federal funding for expanded efforts to enroll currently eligible seniors in existing Medicaid pharmaceutical assistance programs, and payment for a range of pharmacist-provided medication management services, including disease-specific medication management and patient compliance services. Drug formulary restrictions would be permitted, but only if seniors' access to non-formulary medications preferred by their primary care providers were assured.

The Society's support for SENIORx Gold comes at a time when the political climate is favorable for decisive action by both Congress and President Clinton—perhaps this year, according to ASCP Government Affairs Manager Mary Jo Carden.

The National Association of Chain Drug Stores, along with the American Pharmaceutical Association and the National Consumers League, are supporting SENIORx Gold. "Endorsement of SENIORx Gold by a broad spectrum of pharmacy interests will increase the likelihood of congressional and White House support and prompt program implementation," Carden said.

"In addition to lobbying in support of SENIORx Gold," Davitian said, "ASCP is drafting a legislative proposal specifically addressing the needs of seniors in long-term care settings. Several members of Congress have recognized the need for specialized medication dispensing and packaging services that should be incorporated into any prescription benefit for the elderly."

A large-scale publicly funded outpatient prescription benefit for seniors, whether state or federally administered, will have major ramifications for millions of chronically ill American seniors and "major implications for all of pharmacy, irrespective of your practice activities," ASCP Executive Director Tim Webster, commented. Webster emphasized that along with tough challenges for pharmacists, including potential coverage, access, and formulary restrictions, a senior-focused drug benefit program will also offer "dramatic opportunities for both the profession and the business of pharmacy—opportunities for broader recognition of consultant pharmacists' unique skills." In particular, he predicted, consultant pharmacists' long record of providing high-quality, cost-effective pharmaceutical care to Medicaid recipients "will create opportunities for continued success."

For more information on pending Medicare drug benefit proposals and ASCP's lobbying initiatives, click on the "Government Affairs" link at ASCP's Web site home page, www.ascp.com; or contact Davitian (703-739-1316, ext. 141; ldavitian@ascp.com) or Carden (ext. 170; mcarden@ascp.com).

David K. Buerger
Managing Editor