Letters

Preventive Care Guidelines

To the Editors: The preventive care guidelines (1) reached our desks the same week that the President of the United States was hospitalized for atrial fibrillation. The guidelines contain a recommendation against routine screening for thyroid disease in persons over 65 years of age. In such patients, however, hyperthyroidism may not present in the classical manner.

The President's atrial fibrillation was found to be secondary to Graves disease in the absence of a palpable goiter. Although President Bush had had a “complete” physical examination only 6 weeks before this episode, thyroid function had not been tested. His doctor felt that “other tests” would almost surely have signaled trouble if there had been a serious problem (2). If routine thyroid testing had been done at the President's annual physical, this anxious period for the country might have been averted.

The American Thyroid Association has recently recommended that all patients over 60 years of age have a free thyroxine assay and highly sensitive thyroid-stimulating hormone determination as part of routine follow-up (3). The guidelines for preventive care as outlined in Annals (1) conflict with the American Thyroid Association recommendations. We suggest that the guidelines be modified to conform to the American Thyroid Association's recommendations.

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References


To the Editors: The article by Hayward and colleagues (1) contains an astonishing omission. The use of spirometry in the early identification of and intervention for smoking-related diseases is not even mentioned! Spirometric abnormalities are potent predictors of premature mortality from ischemic heart disease (2, 3), lung cancer (4), and chronic obstructive pulmonary disease (5). Together, these major health problems are responsible for most of the 400,000 smoking-related deaths each year that are due to tobacco abuse and addiction. Because the article speaks forcefully of opportunities to practice prevention in internal medicine . . . and states that “... physicians would be aided further by new tools to facilitate the assessment and documentation of health risks in the tailoring of preventative programs to individual patients,” why omit spirometry?

At least two studies suggest that smoking cessation can be encouraged when spirometric abnormalities are known (5). Another study clearly shows a reduction in the decline in airflow abnormalities with stopping smoking in the course of emerging airflow obstruction (6). A survival benefit was achieved upon stopping smoking, even in patients who stopped smoking relatively late in the course of chronic obstructive pulmonary disease.

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References


In response: The purpose of our paper (1) was not to develop new practice guidelines but to comprehensively outline existing practice guidelines relevant to screening asymptomatic patients. Drs. Tibaldi and Lorber draw attention to a recent article (2) and suggest that it advocates screening for thyroid disorders with a free thyroxine assay and a highly sensitive thyroid-stimulating hormone assay. The article to which Drs. Tibaldi and Lorber refer, however, focuses on optimal selection of thyroid tests when thyroid disease is suspected, rather than on screening for thyroid disease in asymptomatic patients.

The article did not address the topic we addressed, namely screening, and hence was not relevant to our review of preventive practice guidelines. Both the Canadian Task Force and the American College of Physicians, in contrast, explicitly recommend against screening for thyroid disorders in asymptomatic adults.

Drs. Tibaldi and Lorber also raise the question of whether there are particular patients, such as the President, or groups of patients, such as airline pilots, with whom the consequences of failing to detect asymptomatic disease might be greater than with other persons. We agree that this is possible, and that such consequences should be compared with the benefits and costs of early detection and treatment of disease and with the clinical and financial costs associated with false-positive results. If the President's physician had treated Bush for hyper...
thorothyroidism in the setting of increased free thyroxine but no symptoms, an argument could be made for screening the President with thyroid function tests.

In response to Dr. Petty’s letter, we omitted spirometry from our review because no major organization has systematically reviewed the costs and benefits of spirometry in screening asymptomatic persons. A physician need not use spirometry to select which patients should be advised to stop smoking. All smokers should be advised to stop smoking (3). Dr. Petty also raises the question of whether abnormal spirometry results would encourage a smoker to comply with a physician’s advice to stop smoking. Whether spirometry can be used to help change smokers’ behavior, rather than to screen for pulmonary disease, could be evaluated further (4). We encourage Dr. Petty and other physicians to communicate with their professional organizations about which interventions should be assessed.

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References

Theophylline or Physician Toxicity?

To the Editors: Schiff and colleagues’ report (1) on preventable factors in inpatient theophylline toxicity documents the many circumstances that may contribute to the development of theophylline toxicity. Also documented are the negligence or incompetence of the responsible physicians at Cook County Hospital. Being a “busy physician” is no excuse for (1) ordering a drug level but failing to check the result; (2) failing to consider factors predisposing to theophylline toxicity (for example, heart failure, liver disease, or coadministration of drugs known to decrease theophylline clearance) when determining dosage; (3) failing to consider drug toxicity in a patient developing theophylline toxicity and finding (for example, heart failure, liver disease, or coadministration of drugs known to decrease theophylline clearance) when determining dosage; (4) neglecting the past medical history (review of medical records revealed recurrent theophylline toxicity in 25% of the patients); (5) giving a potentially toxic medication without documentation or, at least, historical evidence of subtherapeutic blood levels; (6) simultaneously giving full theophylline dosages both parenterally and orally; or (7) discharging a patient on the same dose of theophylline that previously caused toxicity.

There is no a priori reason to believe the authors’ results can be generalized. The authors state, “Although we have no data on the generalizability of our findings, we suspect the problems are not isolated because our institution’s overall quality of care is rated highly.” The Chicago Tribune (the reference for this statement [2]) is not widely known as a forum for scientific discussion.

The authors obviously did an excellent job of researching their data. Further, their data provide truly useful information, reminding us of some of the circumstances that predispose patients to theophylline toxicity and of the importance of carefully considering all relevant factors before prescribing any medication. In addition to the authors’ conclusions, I believe that some physicians at large public hospitals are practicing a brand of medicine that is not in the best interests of their patients. Identifying circumstances leading to theophylline toxicity allowed the authors to implement measures that will decrease the incidence of this problem; however, until the root of the problem, suboptimal physician performance, is attacked, it is sure to appear in other aspects of patient care.

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References

To the Editors: In their excellent review of inpatient theophylline toxicity, Schiff and coworkers (1) listed corrective measures for preventing recurrent management errors. We wholeheartedly agree with most of these measures, but we feel that the most appropriate solution to prevent excessive dosing in the emergency department is to stop using theophylline there. Making faster analysis for theophylline levels available in the emergency department is not the answer.

Rosing and colleagues (2) first showed in 1980 that intravenous aminophylline was a significantly less potent bronchodilator than frequently used aerosolized or subcutaneous agents. Since then, many controlled clinical trials have shown that theophyllines give no further benefit in acute airways obstruction but frequently add to the toxicity when added to optimal beta-agonist therapy in the emergency department (3). Theophylline use in hospitalized patients is somewhat less clear and requires further study (4).

The authors (1) correctly point out that the risk:benefit ratio for theophylline use may be significantly greater outside the setting of the controlled clinical trial. The lack of benefit for using theophylline in the emergency department treatment of acute airways obstruction has been established; the risk does not appear to be worth taking. This attitude is consistent with the recommendations recently released by the National Heart, Lung and Blood Institute, National Asthma Education Program Expert Panel Report on the diagnosis and management of asthma. They have excluded theophylline from the treatment recommendations for the emergency department management of acute asthma exacerbations in children and adults (5).

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References

In response: One of the beauties of the Japanese continuous quality improvement paradigm is that it permits us to examine familiar problems from a new perspective. The blur of irresponsible, negligent, and incompetent physicians and hospitals can be re-examined as processes begging for improvement. Dr.
Henry views these problems and sees the blur; we see the processes.

With fail-safe mechanisms in place for rapid toxic drug level reporting and action; standardized concentrations for aminophylline administration; protocols for withholding the drug in the emergency room until a nontoxic level is available; protocols to reserve theophylline for use as a third-line (after β-agonists and steroids) rather than first-line agent, any hospital will be less likely to encounter the problems we documented before our implementation of these corrective measures.

Dr. Henry is incorrect in implying that the problems uncovered are isolated to one hospital or type of hospital. Recent studies show that 14% to 28% of deaths and other adverse events in hospitalized patients are attributable to “negligence” or other preventable iatrogenic errors (1-3). Such studies consistently show medication complications heading the list of iatrogenic problems. In 1990, a record number of adverse reactions to theophylline (88, including 4 deaths) were reported to the Food and Drug Administration (FDA) Adverse Drug Reaction Spontaneous Reporting System (Dr. J. Bacsanyi, FDA Division of Epidemiology. Personal communication).

Public hospitals, the nation’s safety-net hospitals, are straining under expanding demands. They remain, nonetheless, centers of innovation and excellence (4). The Chicago Tribune article was cited for its discussion of the excellent performance of Cook County Hospital on the Health Care Financing Administration’s Medicare mortality data release. The hospital continues to show a remarkably low mortality rate in each subsequent release (5).

We concur with Drs. Kelly and Murphy that the risks of theophylline in the emergency department might outweigh its benefits. Based on the literature Kelly and Murphy cite and on recent studies done by our emergency department, we now avoid routine use of the drug in this setting.

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References


To the Editors: We commend Schiff and colleagues for their study (1). We want to emphasize the authors’ statement that “the drug’s clinical indications have been questioned.” Two very recent investigations have extended emergency department-based conclusions about the treatment of asthma with theophylline into the hospital setting (2, 3). Double-blind, randomized, placebo-controlled studies in both adults (2) and children (3) have failed to show a significant added benefit of theophylline when added to frequent inhaled albuterol and high-dose glucocorticoid therapies. Although further studies are needed to determine if some subgroups of patients could benefit from theophylline in the hospital treatment of asthma, the considerable risk for overdose that is found by Schiff and colleagues and numerous other authors, must be weighed very carefully. We suggest, therefore, that in Table 3 of the article the last “corrective action” should be greatly emphasized for most patients in future drug use evaluations in hospitals. That is, do not use theophylline unless aggressive inhaled albuterol and systemic glucocorticoid therapy have failed.

Schiff and coworkers make another excellent point that is frequently overlooked by academicians. Theophylline toxicity in carefully controlled studies probably occurs much less commonly than in routine patient management. In our opinion, this finding is particularly true when the drug is prescribed by clinicians who are not familiar with its dosing and the factors that modify its clearance.

Although routine theophylline use should be discouraged in acute care settings, it is still useful for treating selected ambulatory patients, especially those with nocturnal asthma or chronic obstructive pulmonary disease. First-line therapy in ambulatory asthma, however, should be anti-inflammatory medications with inhaled steroids or cromolyn (4). Optimal doses of anti-inflammatory drugs also obviate the need for theophylline in the management of most patients with nocturnal asthma. Most patients with chronic obstructive pulmonary disease respond well to inhaled beta agonists and ipratropium and do not need theophylline; exceptions are patients with chronic respiratory insufficiency, hypercapnia or cor pulmonale (5). As pointed out by Schiff and colleagues, outpatient theophylline toxicity continues to be reported. More selective use of this agent in both outpatient and inpatient settings is needed.

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Diuretic Resistance versus Adaptation

To the Editors: Ellison (1), in his excellent study of diuretic resistance, does not consider its most common occurrence—the absence of diuresis with continued administration of a diuretic to a person with heart disease but whose heart failure has been dissipated. In the treatment of heart failure, continued daily administration of a diuretic is common practice to prevent recurrence of edema, attainment of dry weight notwithstanding. In such a circumstance, the body is resistant to the diuretic. The diuretic drug becomes paradoxically not only a salt-retaining agent, but also a stimulator of potentially noxious neurohormones. With subsidence or control of precipitating factors of heart failure, daily administration of a diuretic may be unnecessary to maintain dry weight. For these reasons, intermittent use, in a dose size and interval designed to keep the patient edema-free, is preferable and may avoid diuretic resistance and its undesired effects (2).

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References

In response: Dr. Zatuchni suggests that diuretic resistance frequently develops when effective treatment of congestive heart failure reduces extracellular fluid volume. Because “diuretic resistance” was defined as the failure to achieve a desired reduction in extracellular fluid volume (1), the example cited is appropriately termed “diuretic adaptation.” This phenomenon occurs whenever diuretics are given as long-term therapy and is not unique to the treatment of congestive heart failure (1). I agree, nevertheless, that physicians should consider reducing diuretic therapy once the underlying disease has been controlled. The reduction would avoid unnecessary side effects and maintain diuretic responsiveness.

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References


Disopyramide and Inducible Arrhythmias

To the Editors: Singh (1), in a recent review article on ventricular arrhythmias, lists as unknown the efficacy of disopyramide in suppressing ventricular tachycardia and ventricular fibrillation at programmed electrical stimulation. At least 14 studies have addressed this question. The largest study was done by Lerman and colleagues (2), who studied 50 patients with inducible sustained ventricular tachycardia or ventricular fibrillation. These investigators found that disopyramide rendered 34% of the patients noninducible. Studies involving crossover drug testing have shown disopyramide to be equivalent to quinidine (3) and superior to mexiletine (4) for rendering ventricular tachyarrhythmias noninducible.

Singh also stated that the role of class I antiarrhythmic agents will likely diminish because of proarrhythmia and that the use of class III drugs will increase. This statement may be misleading. The incidence of serious proarrhythmia with the class III agent amiodarone is greater than with any class IA or IB antiarrhythmic (5).

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References


In response: In retrospect, we were sorry we did not assign a figure for disopyramide in preventing inducible ventricular tachycardia. We could not confidently do this, because the drug has a high propensity to induce heart failure in patients having electrophysiologic testing (12 of 111 patients, who responded to the drug given orally, developed heart failure in the series of Lerman and coworkers cited by Dr. Stanton). Thus, disopyramide cannot be compared quantitatively with other agents. We were also influenced by the ongoing Electro-physiologic Study Versus Electrocardiographic Monitoring (ESVEM) Trial in which six class I agents and sotalol were selected for study; disopyramide was not included. The figure of 34%, cited by Stanton, is high; Nattel (1) recently cited a composite figure from the reported literature of about 19%.

We are surprised that Dr. Stanton took issue with our perception that “the role of class I antiarrhythmic agents will likely diminish because of proarrhythmia and that the use of class III drugs will increase.” His restatement of our tentative conclusions is misleading. We concluded: “The role of class I agents is likely to diminish because of proarrhythmia, and that of class III agents, especially with associated anti-adrenergic effects, to grow. This is suggested by increasing experience with sotalol and amiodarone. . . . The role of newer class III agents is being investigated.” We believe these statements are a reasonably accurate reflection of current opinion, especially in the wake of the Cardiac Arrhythmia Suppression Trial and meta-analysis of antiarrhythmic trials in survivors of infarction (2). The statements are also consistent with the fact that over 30 class III agents are currently under development worldwide.

We are particularly surprised that Stanton, from his studies, suggested that the incidence of serious proarrhythmia with amiodarone was greater than with any class IA or IB antiarrhythmic. This assertion is not supported by the literature. Scheinman, in his editorial (3) accompanying the Stanton article (4), stated that patients treated with amiodarone may experience tachycardia that usually disappears with further therapy, and the incidence of serious proarrhythmic effects in patients on amiodarone is less than 1%. This mirrors our experience (5). We, of course, agree that such a low incidence of proarrhythmic effects may not be a property of other class III agents.

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References


Lawyer’s Advice

To the Editors: Lo and Steinbrook’s fine article on the Cruzan case (1) suggests troubling issues about physician consultation with hospital attorneys. The authors say “lawyers might advise caregivers . . . to disregard advance directives to withhold artificial feedings unless laws are changed or test cases are decided.” They cite cases in which patients were abusively subjected to other life-sustaining procedures after the physician received legal advice. Physicians should resist legal opinions that undermine their duties to patients, including the duty to respect a patient’s wish not to be subjected to life-sustaining treatment.

Hospital lawyers and physicians have fundamentally different loyalties and goals. A lawyer’s duty is to the hospital as a corporate entity. Hospitals might want their lawyers to con-
sider various interests in advising physicians, but hospitals always want lawyers to manage risk. An essential value for physicians—respect for individual patients—is only incidental to risk management. In that the goal of risk management is avoidance of liability, risk management loves rules. Many hospital attorneys treat absence of an authorizing rule as a prohibition: Without a rule that directly approves withholding or withdrawing specific life-sustaining treatment, lawyers often advise continuing treatment or seeking court approval to withhold or withdraw treatment to avoid any liability exposure. Risk management inherently subordinates patients' (and families') interests to institutional interests, and so undermines physicians' responsibility to patients.

Continuing inappropriate treatment is obviously wrong. Going to court for permission to stop such treatment is also wrong. Court action exposes patients and families to emotional suffering and to court for permission to stop such treatment is also wrong. Court action exposes patients and families to emotional suffering and unnecessary, when a physician and patient (or surrogate) concur on a care plan, seems to me to be abandonment.

"Do no harm" means just that. It does not mean: "Do no harm unless a lawyer advises it" (including advice that to do right by a patient might expose the physician to a lawsuit). Physicians suggest that patients who feel uncomfortable with medical advice get a second opinion. When a lawyer advises action that a physician feels is against patient interest, the physician should get a second opinion, too.

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Reference

In response: We agree with Mr. Barnett's cautions against accepting legal advice uncritically. We thank Dr. Grant for correcting several legal citations. As he points out, laws on surrogates make decisions for incapacitated patients (1). Table 1 was provided to help clarify this issue; several citations, however, are inaccurate. The Barber case from California appears at 147 Cal. App. 3d 1006 (1983); the Hamin case (Washington) was decided in 1984. The Virginia statute has been recodified as Va. Code Ann. Sec. 54.1-2896 (1990). In the text, reference 26, Eicher v. Dillon, should read 438 N.Y.S. 2d 266. These changes should save research time and possible frustration.

Although the authors claim that the Cruzan case might not directly affect legally informed practicing physicians, differences in language and interpretation create pitfalls for the unwary. In some states, family surrogates can render health care decisions only for incapacitated adults. In Arkansas, however, the law also includes minors. A patient's incapacity or terminal illness may be certified by the attending physician in Florida, but requires separate opinions from the attending physician and one other physician in Texas. In Oregon, life-sustaining procedures can be withdrawn only after the patient's medical condition is confirmed by a committee of physicians, excluding the attending physician. Statutes often rank family members for appointment as surrogates, that is, spouse or legal guardian. This is usually followed by a mechanism for the patient's parent(s), sibling(s), or other relatives. New Mexico allows withdrawal of treatment only by agreement of all available family members.

The authors also suggest that oral statements made to physicians by patients about life support show serious intent and should be considered clear and convincing evidence. These oral statements, when they occur, are important, but some patients may be unable to hold meaningful discussions with their physicians. Such oral statements did not appear in the cases cited in the paper. They were either not made to the physicians involved or else were not deemed clear and convincing evidence. Instead, personal values, religious beliefs, previous statements made to loving, caring friends and family, attitudes about the impact of illness on others, and other relevant circumstances are the most important factors considered by courts. The lack of consideration of these factors is what makes the Cruzan case and the more recent Wanger case in Minnesota unusual. In the Cruzan case, a hospital seeks to discontinue life support for an 87-year-old woman in a persistent vegetative state despite the ethical and religious objections of her spouse and family (2, 3).

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References

To the Editors: Lo and Steinbrook comment that the Cruzan ruling may increase physicians' legal uncertainties when family surrogates make decisions for incapacitated patients (1). Table 1 was provided to help clarify this issue; several citations, however, are inaccurate. The Barber case from California appears at 147 Cal. App. 3d 1006 (1983); the Hamin case (Washington) was decided in 1984. The Virginia statute has been recodified as Va. Code Ann. Sec. 54.1-2896 (1990). In the text, reference 26, Eicher v. Dillon, should read 438 N.Y.S. 2d 266. These changes should save research time and possible frustration.

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Red Man Syndrome after Oral Vancomycin

To the Editors: Vancomycin-induced red-man syndrome is characterized by pruritus, erythema, and, in severe cases, angioedema, hypotension, and cardiovascular collapse (1). The frequency and severity of this phenomenon diminish with repeated administration of the drug (2). This reaction is usually associated with rapid intravenous infusions but may occur after slow administration (2). A recent report suggests that intravenous vancomycin may also cause the red-man syndrome (3). We report an association between oral administration of vancomycin and the red-man syndrome.

A 67-year-old woman developed profuse diarrhea and abdominal pain during treatment with amoxicillin-clavulanic acid for bronchitis. Results of a flexible sigmoidoscopy suggested pseudomembranous colitis. Vancomycin was prescribed (500 mg every 6 hours by nasogastric tube). Other medications included metronidazole, 500 mg, and ranitidine, 50 mg, intravenously every 8 and 12 hours, respectively, as well as phe-
arms. Erythema over her face, neck, thorax, and arms was noted by a blinded investigator. Vital signs were unchanged from baseline. A 25-mg dose of diphenhydramine was administered intravenously, and 50 minutes later the erythema and pruritus had subsided. The patient denied involvement below the midline of her body for both reactions. Mild pruritus was noted by the patient after her oral vancomycin dose the next day despite diphenhydramine pretreatment. Trough and peak (90 minutes after the sixth vancomycin dose) vancomycin concentrations were 3.3 and 4.1 μg/mL, respectively. No further reactions were noted.

The minimum vancomycin concentration required to cause red-man syndrome is unknown. Significant absorption of vancomycin may occur following oral administration (4), which may result in adverse reactions such as rash (5). A small amount of vancomycin may have been absorbed in our patient, sufficient to incite the syndrome.

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References

Hepatitis C from a Needlestick Injury

To the Editors: Transfusion-associated non-A, non-B hepatitis has recently been shown to result usually from infection with the hepatitis C virus (HCV) (1). Although we recognize that non-A, non-B hepatitis can follow small inocula of percutaneous exposure, such as a needlestick injury (2), data implicating HCV in this circumstance are lacking. I report an instance of HCV transmission by a needlestick injury incurred 18 years ago with persistence of circulating anti-HCV to the present.

In 1972, a nurse injured her finger removing a hypodermic needle from a patient's arm. We were then doing a multicenter study to evaluate the protective efficacy of hepatitis B immune globulin (3). Evaluation of the patient showed that he had aplastic anemia for which he had received multiple blood transfusions, and that, at the time of the accident, he had apparent acute non-B hepatitis. We recommended that the nurse receive conventional immune globulin, after which we took frequent blood samples. Six weeks later she developed anicteric hepatitis, and her serum enzymes remained abnormal for almost 1 year. In 1975, the assay for hepatitis A virus became available. We then determined that both the patient and the nurse were seronegative for hepatitis A and B markers. The initial serum from the patient was later used to inoculate and infect chimpanzees, a result repeated regularly over a 6-year period and that identified him as a carrier (4). The patient is now entirely well with the hepatitis C virus in prospectively followed transfusion recipients with acute and chronic non-A, non-B hepatitis. N Engl J Med. 1989;321:1494-500.


"Misconceptions" about AIDS

To the Editors: Why students have misconceptions about the transmission of human immunodeficiency virus (HIV) in health care settings is easy to understand (1). The short, tragic history of the acquired immunodeficiency syndrome (AIDS) epidemic is replete with underappreciation by "the experts" of the potential risks of transmission associated with various body fluids. The number of persons who developed AIDS after receiving a blood transfusion at the start of the epidemic is a case in point.

Granich and Mermin (1) criticize the misconception among medical students that HIV could be transmitted through aerosolization of body fluids. Just this past week, an article in the ACP Observer reported that the possibility of a person becoming infected by inhalation of infectious aerosol is still open to question (2).

Although the risks for such exposure may be low, I think it would be premature to label as a misconception the idea that exposure to any body fluids might transmit HIV infection. To be fair to our future physicians, education about HIV issues should acknowledge those areas of potential transmissibility that are not fully understood.

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References