

5. Bukantz SC, Lockey RF. Adverse effects and fatalities associated with allergen immunotherapy. In: Bukantz SC, Lockey RF, editors. Allergen immunotherapy. New York: Marcel Dekker, 1991:233-63.
6. Levine MI. Systemic reactions to immunotherapy. [abstract]. J Allergy Clin Immunol 1979;63:209.
7. Rawlins MD, Wood S. Hazards with desensitizing vaccines. In: Arbeiten aus dem Paul Ehrlich Institut (Bundesamt für Sera und Impfstoffe). Stuttgart: Gustav Fischer Verlag, 1988; 82:147-51.
8. Rieckenberg MR, Kahn RH, Day JH. Physician reported patient response to immunotherapy: a retrospective study of factors affecting the response. Ann Allergy 1990;64:364-7.
9. Vervloet D, Khairallah E, Arnaud A, Charpin J. A prospective national study of the safety of immunotherapy. Clin Allergy 1980;10:59-64.
10. Osterballe O. Side effects during immunotherapy with purified grass pollen extracts. Allergy 1982;37:553-62.
11. Nelson BL, Dupont LA, Reid MJ. Prospective survey of local and systemic reactions to immunotherapy with pollen extracts. Ann Allergy 1986;56:331-4.
12. Greenberg MA, Kaufman CR, Gonzalez GE, Rosenblatt CD, Smith LJ, Summers RJ. Late and immediate systemic-allergic reactions to inhalant allergen immunotherapy. J Allergy Clin Immunol 1986;77:865-70.
13. Hepner MJ, Ownby DR, MacKechnie H, Rowe M, Anderson JA. The safety of immunotherapy: a prospective study [abstract]. J Allergy Clin Immunol 1987;79:133.
14. Hejjaoui A, Dhivert H, Michael FB, Bousquet J. Immunotherapy with a standardized *D. pteronyssinus* extract: IV. systemic reactions according to the immunotherapy schedule. J Allergy Clin Immunol 1990;85:473-9.
15. DuBuske LM, Ling CJ, Sheffer AL. Special problems regarding allergen immunotherapy. Immunol Allergy Clin North Am 1992;12:145-75.
16. Lamson RW. Sudden death associated with injection of foreign substances. JAMA 1924;82:1090-8.
17. Lamson RW. So-called fatal anaphylaxis in man. JAMA 1929;93:1975-8.
18. Vance BM, Strassman G. Sudden death following injection of foreign protein. Arch Pathol 1942;34:849-65.
19. James LP, Austen KF. Fatal systemic anaphylaxis in man. N Engl J Med 1964;270:597-603.
20. Rands DA. Anaphylactic reaction to desensitization for allergic rhinitis and asthma. Br Med J 1980;281:854.
21. Committee on the Safety of Medicine. CSM update: desensitizing vaccines. Br Med J 1986;293:948.
22. World Health Organization International Union of Immunologic Societies. Current status of allergen immunotherapy. Working Group Report abridgment. Lancet 1989;1:259-61.
23. Reid MJ, Lockey RF, Turkeltaub PC, Platts-Mills TAE. Survey of fatalities from skin testing and immunotherapy 1985-1989. J Allergy Clin Immunol 1993;92:6-15.
24. Matloff SM, Bailit IW, Parks P, Madden N, Greineder DK. Systemic reactions to immunotherapy. Allergy Proc 1993; 14:347-50.

## Legal issues in allergy and clinical immunology

Allan Gibofsky, MD, JD *New York, N.Y.*

*Clinical risk management for the allergist focuses primarily on concerns regarding adverse occurrences and the possibility of civil litigation as a result of negligence or professional liability. Risk is substantially reduced with an understanding of such predictable drug reactions as overdosage, side effects, secondary effects, and drug interactions. In addition, all clinicians who prescribe have a duty to disclose to their patients the possibility of unpredictable reactions, including intolerance, idiosyncrasy, and allergy or hypersensitivity. This disclosure should be part of a comprehensive discussion of the risks and benefits of, and alternatives to, therapeutic agents and procedures they recommend. The process of informed consent becomes even more critical with the increasing influence of hospital and managed care formularies on prescribing decisions. Although cost effectiveness is an important factor in prescribing*

From the Cornell University Medical College and Fordham University School of Law.

Reprint requests: Allan Gibofsky, MD, JD, Departments of Medicine and Public Health, Cornell University Medical College, Hospital for Special Surgery, 1300 York Ave., New York, NY 10021.

J Allergy Clin Immunol 1996;98:334-8

Copyright © 1996 by Mosby-Year Book, Inc.

0091-6749/96 \$5.00 + 0 1/0/77333

*decisions, the possibility of adverse effects, treatment failure, noncompliance, and other negative considerations must also be weighed. (J Allergy Clin Immunol 1996;98:S334-8.)*

**Key words:** Risk management, liability, allergy, adverse reactions, asthma, antihistamines, corticosteroids, informed consent

The American legal system has three major branches: criminal law, civil law, and administrative or regulatory law.<sup>1,2</sup> Criminal law, which varies from state to state, defines society's plan to punish people who do not comply with appropriate codes of conduct, known as the penal codes. Civil law is the body of rules that govern the resolution of disputes between parties who cannot resolve them without outside intervention. There is no element of punishment inherent in civil law. Administrative or regulatory law is created by a legislature in its attempt to regulate a highly technical area. Agencies created by the legislature are empowered to promulgate rules and regulations, examine whether they are carried out, and enforce compliance.

Risk management in the clinical setting focuses primarily on concerns regarding adverse occurrences and the possibility of resultant civil litigation. There are three major branches of civil law: contract, property, and tort.<sup>2</sup> Tort law is most relevant to clinical risk management; in general, it deals with private disputes that do not involve contract interpretation or ownership rights. In clinical settings, the tort of primary concern is that of negligence or professional liability. Failure to deliver care in accordance with the standard required is an essential element of professional liability.

## ASPECTS OF PROFESSIONAL LIABILITY

The tort of professional liability has four major elements: duty, breach, causation, and damages.<sup>3</sup> Duty is defined as the obligation to do or refrain from doing. In law, where a professional has no duty, there can be no liability for the outcome. When one contracts for a duty, assumes a duty, or is a party in certain relationships with legally recognized inherent duty (as in the physician-patient relationship), the first element of professional liability is satisfied.

Breach, the second element of medical malpractice, is the converse of duty: something is done that should not have been done, or something is not done that should have been. Fundamentally, breach refers to errors of commission or omission.

The third element of professional liability, causation, refers to a situation in which the purported breach of duty results in the patient's complaint. The law recognizes two types of causation: actual (direct) and proximate (indirect).<sup>4</sup> Actual causation refers to the direct responsibility of the physician for the injury suffered by the patient and may be claimed when a physician performs a procedure during which something deleterious occurs. In contrast, proximate causation refers to situations in which physicians may not have been directly involved, but by their actions may have set into play a chain of events that resulted in the injury.

Proximate causation is proven by the "but for" test: "but for" something that someone did or did not do, the injury would not have occurred.<sup>4</sup>

In proximate causation liability, a physician need not be present during the procedure in which the injury occurs. The procedure need only be ordered by the physician. If injury results, both the person who performed the procedure and the physician who ordered it may be responsible, the physician by proximate causation. In reviews of litigation against physicians in the United States, it is commonly found that some physicians are identified as having caused the alleged injury directly, whereas others are named as defendants with only indirect involvement.

Damages, the last element of the tort of professional liability, may be both economic and noneconomic. Economic damages refer to paid or compensable monetary losses resulting from an injury or complaint, such as lost wages and medical costs. Economic damages, however, may be only a small proportion of total damages. What distinguishes the American legal system from other legal systems is recognition and awarding of significant noneconomic damages for "pain and suffering."<sup>5</sup>

## RISK MANAGEMENT AND THE LAW IN CLINICAL DECISION MAKING

As part of their professional responsibility, allergists and clinical immunologists must know the indications, contraindications, risks and benefits, adverse reactions, and toxicities of the Food and Drug Administration-approved drugs they prescribe. An understanding of the various types of drug reactions should result in significant reduction or elimination of liability concerns.

Some drug reactions are allergic. Drug allergy or hypersensitivity is an immunologically mediated event in which humoral or cellular processes (or both) can result in adverse effects for the patient. One example is the broad spectrum of penicillin allergic reactions, which can range from mild rash to anaphylaxis and death. To develop a logical diagnostic and therapeutic strategy for assessing an allergic person, the allergist must understand the mechanisms of allergic reactions, including (1) IgE mast-cell-mediated anaphylactic and urticarial responses; (2) antibody-mediated cytotoxic reactions such as hemolytic anemias; (3) immune-complex-mediated reactions such as IgG antibody-associated vasculitic syndromes; and (4) cell-mediated reactions, including contact dermatitis.

An intracutaneous prick test to exclude IgE-mediated reaction induced by an antibiotic agent, for example, may show that the drug can be administered without risk of anaphylactic response; however, a negative skin-test result may not exclude IgG-mediated vasculitic syndromes. Sim-

**TABLE I.** Classification of drug reactions

---

|                             |
|-----------------------------|
| Predictable reactions       |
| Overdosage                  |
| Side effects                |
| Secondary effects           |
| Unpredictable reactions     |
| Intolerance                 |
| Idiosyncrasy                |
| Allergy or hypersensitivity |
| Drug interactions           |

---

ilarly, although a negative patch-test result may exclude contact sensitivity to an agent, it may not predict an antibody-mediated cytotoxic response with oral administration. Thus, each diagnostic test is specifically predictive only for certain aspects of a patient's potential responses.

Drug reactions can be classified into those that are predictable and those that are unpredictable<sup>6</sup> (Table I). The first of the predictable reactions is overdosage. In this situation, the untoward effects observed are directly related to absolute overaccumulation that prevents breakdown or excretion of the drug at a normal rate. Physicians in emergency departments often see patients who have an overaccumulation of agents such as barbiturates or benzodiazepines.<sup>7</sup> Of particular concern to the allergist, however, are patients who may have forgotten that they have already taken their medication and therefore take another dose. Also of concern is the anxious patient with asthma who may take repeated doses of medication in an effort to alleviate an acute asthmatic attack.

The recent reports of death consequent to repeated doses of salmeterol by patients having asthma attacks<sup>8</sup> illustrate the risk of improper use of medication by patients with asthma. Salmeterol, a safe and effective drug when administered twice daily as a bronchodilator<sup>9</sup> and as a prophylactic agent that protects against selective bronchospastic stimuli,<sup>10</sup> has a relatively prolonged onset of action. Repeated dosing by an anxious patient for the treatment of acute bronchospasm may result in accidental overdose and cardiac toxicity before any beneficial effects on pulmonary physiologic function.<sup>11</sup> Therefore, patients who use salmeterol should also have available a short-acting bronchodilator such as albuterol, terbutaline, pirbuterol, or metaproterenol as acute rescue medication if bronchospasm occurs.<sup>12</sup> Because overdosage can occur with virtually any medication, the allergist must be able to recognize the signs and symptoms of overdosage and the toxic effects of prescribed medications.

Side effects are predictable, undesirable, but sometimes pharmacologically unavoidable effects of a medication. For example, some antihistamines cause sedation; therefore, when they are prescribed, the patient should be counseled not to operate machinery or perform tasks that require mental acuity. In situations demanding optimal mental agility, the allergist may be compelled to prescribe an antihistamine with a low incidence of somnolence.

Secondary effects, which also may be predictable, are the indirect consequences of the primary action of a drug. For

instance, a vaginal yeast infection may develop in a woman treated with a broad-spectrum antibiotic agent.

Allergists and immunologists who prescribe inhaled corticosteroids, which are currently recommended in the treatment of asthma and other diseases, should be aware of their many possible side effects, including osteoporosis,<sup>13</sup> oral candidiasis,<sup>14</sup> and dysphonia.<sup>15</sup> Side effects to be considered when oral corticosteroids are prescribed are even more significant and include growth suppression,<sup>16</sup> osteoporosis,<sup>13</sup> posterior subcapsular cataracts,<sup>17</sup> hypertension,<sup>18</sup> and hyperglycemia.<sup>18</sup>

In the treatment of allergy, the cardiovascular side effects of some antihistamines require special attention. Although prolongation of the QT<sub>c</sub> interval has been noted with administration of terfenadine,<sup>19</sup> variability of the QT<sub>c</sub> interval is normal, and the variability seen with terfenadine administration may not have an effect on clinically relevant end points. However, terfenadine's cardiac effects may become more pronounced with the concomitant administration of azole antifungal agents<sup>14</sup> or macrolide antibiotic agents.<sup>20</sup> Interactions with cardiovascular consequences have also been seen between astemizole and erythromycin or ketoconazole.<sup>21</sup> Potentially fatal arrhythmias, including torsade de pointes, and cardiac arrests have occurred consequent to interactions between terfenadine<sup>22, 23</sup> or astemizole<sup>24</sup> and macrolides or antifungal agents.

Hypokalemia, which can occur with the use of diuretic agents, and congenital QT prolongation may predispose patients treated with astemizole or terfenadine to arrhythmias.

The implications of polypharmacy are serious. Drug-drug interactions occur when the metabolism of one medication is altered by another. In the treatment of allergic disease, one example is the interaction between cimetidine and theophylline: concurrent administration of cimetidine slows the metabolism of theophylline, thereby prolonging its half-life.<sup>25</sup> Conversely, in the asthmatic person who smokes, theophylline elimination may occur more readily.<sup>26</sup> Because these factors affect dosage or regimen, both the physician and the pharmacist should be aware of potential interactions. Knowledge of other medications the patient is taking, including over-the-counter preparations, is also critical. What the patient eats and whether the patient drinks alcohol or smokes may also be relevant. Failure to elicit this kind of information could result in a drug-drug interaction.

Unpredictable reactions are unlikely to occur but still must be disclosed to the patient. Although systemic allergic reactions to immunotherapy usually represent an unpredictable adverse reaction, the possibility of their occurrence during the course of allergen immunotherapy is always present. Certain factors that may serve as a warning to the physician (and thereby decrease risk) have been identified: unstable asthma, increased signs of systemic allergic symptoms, increased intensity of allergen exposure, and a history of systemic allergic reactions to immunotherapy. In the case of the patient with asthma, monitoring of the patient's peak flow rates before immunotherapy to ensure a stable clinical status would allow continuation of allergen immunotherapy without excess risk of induction of an asthmatic response. In these instances, however, both the physician

and the patient must be aware of the potential adverse allergic reaction that may occur as a consequence of allergen immunotherapy.

Perhaps the most common unpredictable reaction is intolerance: the patient experiences an untoward effect that may simply be an increased normal effect of the drug. Typically, the patient reports, "I can't take this drug; it doesn't agree with me." This statement may be a predictor of poor compliance (which may also increase liability concerns). If the medication is continued, the likelihood of a predictable adverse reaction may increase.

Noncompliance is another important issue to recognize. Significant noncompliance with a drug regimen or unintentional error in taking medication occurs in approximately 50% of all patients.<sup>27</sup> Furthermore, noncompliance has been shown to be a direct result of inadequacy of the information provided to patients regarding their therapy<sup>28</sup> and can contribute or lead directly to poor therapeutic outcome. In a well-meaning effort to overcome noncompliance in the patient with asthma, the prescribing physician may be tempted to prescribe multiple agents. If the patient then complies with all agents prescribed, untoward reactions may result from their simultaneous use and overlapping therapeutic benefits or toxicities.

Idiosyncrasy refers to situations in which the reaction to a drug is qualitatively abnormal and does not correspond to its usual pharmacologic actions. For example, patients in whom acetylation of isoniazid and procainamide is slow have a high incidence of autoimmune-like diseases.<sup>29-32</sup> Clearly, it is the responsibility of the prescriber to recognize this situation as a drug idiosyncrasy and to adjust or discontinue the medication.

## INFORMED CONSENT

Informed consent is not a piece of paper signed before a procedure, nor is it solely the discussion of patient options before a procedure (such as invasive vs noninvasive treatment, lumpectomy vs mastectomy, or chemotherapy vs radiation).

During the process of informed consent, the patient is advised of the risks and benefits of and the alternatives to recommended therapeutic agents and procedures.<sup>33,34</sup> The prescriber has a legal duty to disclose these risks, benefits, and alternatives. It follows that the patient or the patient's representative must be competent to understand the information presented and must voluntarily make a decision about the proposed treatment after understanding the appropriate disclosure of information (Table II).

In the diagnosis and treatment of allergic diseases, informed consent must be obtained before initiating potentially dangerous procedures such as allergen skin testing, inhalation challenges, or double-blind placebo-controlled food challenges. Treatment involving allergen immunotherapy or the use of immunomodulators, including intravenous immunoglobulin, should be undertaken only after informed consent has been obtained and documented in the patient's medical records.

There are legal and moral elements to informed consent. A patient who has been informed of all of the

**TABLE II.** Elements of informed consent

---

|                           |
|---------------------------|
| Disclosure of information |
| Competence                |
| Understanding             |
| Voluntariness             |
| Decision making           |

---

possible risks of a specific therapy would have an extremely difficult time succeeding in "an action" alleging lack of informed consent. However, the physician's goal should not be self-protection but rather the care of a well-informed patient with the knowledge to make the best possible choice regarding treatment.<sup>34</sup>

## COST EFFECTIVENESS AND CLINICAL DECISION MAKING

Cost effectiveness is a widely used but perhaps imprecisely understood term. It is used mainly to replace the idiom, "worth the money," and often equates quality with quantity and cost with value. Cost is easy to calculate, but value is notoriously difficult to assess.

Pharmacologic therapy for allergic and immunologic problems may have economic consequences beyond the initial costs. If a decision to prescribe or dispense is based solely on acquisition costs, and an adverse effect or treatment failure results in noncompliance leading to hospitalization or longer hospital stay, not only is the therapy not cost effective, but there is a real concern regarding liability on the part of the provider and possibly the dispenser for failure to warn and counsel the patient.<sup>35</sup> However, the costs of education, monitoring, errors, failures, speed of effect, and adverse reactions may not be evident immediately. Therefore, the adverse economic consequences of the least expensive drug may not be readily apparent.

As hospital, governmental, and managed care formularies become an increasingly influential sector of the health-care system, greater restrictions on physician prescribing decisions will be seen. These restrictions, based largely on cost containment, may include recommendations for less expensive and possibly less effective generic and therapeutic substitutions. Of particular concern to the allergist may be cost-containment questions related to the use of older antihistamines in place of second-generation antihistamines. This concern is also applicable to asthma care, in which the use of new antiinflammatory therapies may be questioned on the basis of cost containment regardless of the efficacy or toxicity of older regimens.

Clearly, physicians who enter into contracts with managed care organizations should carefully review any language that absolves the managed care organization of responsibility in the event of liability resulting from a formulary-driven prescribing decision. In addition, in the interest of ensuring proper patient care, physicians have a duty to obtain authorization to prescribe nonformulary agents when necessary or to recommend the use of this type of agent despite reimbursement limitations.

## CONCLUSION

Allergists and immunologists are among the more fortunate medical specialists with regard to malpractice because they are involved in fewer potentially litigious high-risk situations. Even these situations can be avoided by adherence to established standards of care. Careful documentation in the patient's medical record to demonstrate that the process of informed consent has been followed is strongly recommended; a simple note (e.g., "Discussed risks and benefits with Mr. Jones. Risks include but are not limited to . . .") with the date of discussion is usually sufficient. As with all other choices in medical care, prophylaxis is superior to malpractice. Appropriate informed consent is one of the best preventative measures available.

## REFERENCES

- Hansen KD. The nature of American law. In: Hirsch HL, editor. *Legal medicine: Legal dynamics of medical encounters*. American College of Legal Medicine textbook. St. Louis (MO): CV Mosby, 1988:3-6.
- Sanbar SS. American law and justice. In: *Medical and hospital law*. Oklahoma City: Law of Medicine Publications, 1982:21-9.
- Brennan TA. Tort law as it applies to medical malpractice litigation. In: Vevania JR, Bone RC, Kassoff E, editors. *Legal aspects of medicine*. New York: Springer-Verlag, 1989:22-5.
- MacDonald MG, Meyer KC, Essig B. The law of medical malpractice. In: MacDonald MG, Meyer KC, Essig B, editors. *Health care law*. New York: Matthew Bender, 1993:11.1-78.
- Hoffman AC, Zimmerly JG, Seifort JB. Torts. In: Hirsch HL, editor. *Legal medicine: Legal dynamics of medical encounters*. American College of Legal Medicine textbook. St. Louis (MO): CV Mosby, 1988:34-46.
- Rosenow EC, Rosenow SE. Legal implications of adverse drug reactions. In: Vevania JR, Bone RC, Kassoff E, editors. *Legal aspects of medicine*. New York: Springer-Verlag, 1989.
- Prince BS, Goetz CM, Rihn TL, Olsky M. Drug-related emergency department visits and hospital admissions. *Am J Hosp Pharm* 1992;49:1696-700.
- Finkelstein FN. Risks of salmeterol? [letter]. *N Engl J Med* 1994;331:1314.
- D'Alonzo GE, Nathan RA, Henschowicz S, Morris RJ, Ratner P, Rennard SI. Salmeterol xinafoate as maintenance therapy compared with albuterol in patients with asthma. *JAMA* 1994;271:1412-6.
- Verberne AA, Hop WC, Bos AB, Kerrebijn KF. Effect of a single dose of inhaled salmeterol on baseline airway caliber and methacholine-induced airway obstruction in asthmatic children. *J Allergy Clin Immunol* 1993;91:127-34.
- Serevent® Inhalation Aerosol. In: *Physician's desk reference*. Montvale (NJ): Medical Economics, 1996:1176-9.
- Lotvall J, Svedmyr N. Salmeterol: an inhaled beta 2-agonist with prolonged duration of action. *Lung* 1993;171:249-64.
- Reid DM, Nicoll JJ, Smith MA, Higgins B, Tothill P, Nuki G. Corticosteroids and bone mass in asthma: comparisons with rheumatoid arthritis and polymyalgia rheumatica. *Br Med J* 1986;293:1463-5.
- Spector SL, Wangaard C, Bardana EJ. The use of cultures and immunologic procedures to predict oropharyngeal candidiasis in patients on steroid aerosols. *Clin Allergy* 1982;12:269-78.
- Williams AJ, Baghat MS, Stableforth DE, Cayton RM, Sheno PM, Skinner C. Dysphonia caused by inhaled steroids: recognition of a characteristic laryngeal abnormality. *Thorax* 1983;38:813-21.
- Reimer LG, Morris HG, Ellis EF. Growth of asthmatic children during treatment with alternate-day steroids. *J Allergy Clin Immunol* 1975;55:224-31.
- Rooklin AR, Lampert SI, Jaeger EA, McGeedy SJ, Mansmann HC. Posterior subcapsular cataracts in steroid-requiring asthmatic children. *J Allergy Clin Immunol* 1979;63:383-6.
- Whitworth JA, Gordon D, Andrews J, Scoggins BA. The hypertensive effect of synthetic glucocorticoids in man: role of sodium and volume. *J Hypertens* 1989;7:537-49.
- Morganroth J, Brown AM, Critz S, et al. Variability of the QT<sub>c</sub> interval: impact on defining drug effect and low-frequency cardiac event. *Am J Cardiol* 1993;72:26B-31B.
- Smith SJ. Cardiovascular toxicity of antihistamines. *Otolaryngol Head Neck Surg* 1994;111:348-54.
- Simons FER. H<sub>1</sub>-receptor antagonists: comparative tolerability and safety. *Drug Safety* 1994;10:350-80.
- Monahan BP, Ferguson CL, Killeavy ES, Lloyd BK, Troy J, Cantilena LR Jr. Torsades de pointes occurring in association with terfenadine use [brief report]. *JAMA* 1990;264:2788-90.
- Honig PK, Woosley RL, Zamani K, Conner DP, Cantilena LR Jr. Changes in the pharmacokinetics and electrocardiographic pharmacodynamics of terfenadine with concomitant administration of erythromycin. *Clin Pharmacol Ther* 1992;52:231-8.
- Zechnich AD, Hedges JR, Eiselt-Proteau D, Haxby D. Possible interactions with terfenadine or astemizole. *West J Med* 1994;160:321-5.
- Brunton LL. Agents for control of gastric acidity and treatment of peptic ulcers. In: Gilman AG, Rail TW, Nies AS, Taylor P, editors. *Goodman and Gilman's the pharmacological basis of therapeutics*. 8th ed. Elmsford (NY): Pergamon Press, 1990:901.
- Powell JR, Vozzesh S, Hopewell P, Costello J, Sheiner LB, Riegelman S. Theophylline disposition in acutely ill hospitalized patients: the effect of smoking, heart failure, severe airway obstruction, and pneumonia. *Am Rev Respir Dis* 1978;118:229-38.
- Greenberg RN. Overview of patient compliance with medication dosing: a literature review. *Clin Ther* 1984;6:592-9.
- Brushwood DB, Simonsmeier LM. Drug information for patients: duties of the manufacturer, pharmacist, physician, and hospital. *J Legal Med* 1986;7:279-340.
- Bluestein HG, Redelman D, Zvaifler NJ. Procainamide-lymphocyte reactions: a possible explanation for drug-induced autoimmunity. *Arthritis Rheum* 1981;24:1019-23.
- Cush JJ, Goldings EA. Drug-induced lupus: clinical spectrum and pathogenesis. Southwestern Internal Medicine Conference. *Am J Med Sci* 1985;290:36-45.
- Cornacchia E, Golbus J, Maybaum J, Strahler J, Hanash S, Richardson B. Hydralazine and procainamide inhibit T cell DNA methylation and induce autoreactivity. *J Immunol* 1988;140:2197-200.
- Richardson B, Cornacchia E, Golbus J, Maybaum J, Strahler J, Hanash S. Nacetylprocainamide is a less potent inducer of T cell autoreactivity than procainamide. *Arthritis Rheum* 1988;31:996-9.
- Furrow BR, Johnson SH, Jost TH, Schwartz RL. Informed consent: the physician's obligation. In: Furrow BR, Johnson SH, Jost TH, Schwartz RL, editors. *Liability and quality issues in health care*. St. Paul (MN): West Publishing, 1991:322-70.
- Flannery FT, Armitage DA, Hirsh HL, Wachsman H. Consent to treatment. In: Hirsch HL. *Legal medicine: legal dynamics of medical encounters*. American College of Legal Medicine textbook. St. Louis (MO): CV Mosby, 1988:196-207.