Current Comments

Patient Compliance: A Multifaceted Problem with No Easy Solution

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Last year I noted that half of all depressed patients are treated with antidepressant drugs, among which the tricyclics are the most common.[1-3] Yet despite the widely documented effectiveness of these drugs, a significant number of patients show little or no improvement, simply because they fail to take their medicine.[4] The degree to which a patient follows a physician's advice is known as "patient compliance." Noncompliance is now a major problem that is by no means limited to the treatment of depression.

Estimates of the proportion of patients who fail to comply fully with prescribed treatments usually range from 30 to 60 percent, with some figures as high as 90 percent.[5] Indeed, one author flatly states that noncompliance is fast becoming "the most significant reason for failed therapy."[6] Furthermore, research has clearly demonstrated that physicians themselves are not aware of the extent of the problem.[7] More often than not, physicians overestimate the compliance levels of their patients. This essay will outline the magnitude of patient noncompliance, describe some of the causes, and detail the medical community's responses to the problem.

Noncompliance is a very old problem. But prior to this century, noncompliance may well have been the course of wisdom.[8] The physician's equipment and methods in bygone eras were far less effective in combating disease than they are now.[9] Even 60 years ago, the patient consulting the average physician had only a 50 percent chance of significantly benefiting from the encounter.[10]

The effectiveness of medical treatment has changed, but so too has the nature of disease itself. Until recently, physicians were most often confronted by acute diseases with obvious symptoms. In Western industrialized nations, however, such illnesses are being overshadowed by chronic, asymptomatic diseases. Consequently, "management" is replacing "cure" as a medical goal. Increasingly, the patient must actively participate with the health care provider in both restoring and maintaining health.[9]

It is well known that a patient's active understanding of and participation in a course of treatment is not always easy to secure. This is true even among conscientious patients who are willing to cooperate. As Edward G. Feldman, American Pharmaceutical Association, Washington, DC, points out, noncompliance is far more than simply misunderstanding instructions or forgetting to take pills.[11] In fact, the intractability of the problem is in large part due to the variety of forms noncompliance may take.

For instance, some patients may, for reasons beyond their control, fail to have their prescriptions filled. Others may stop taking their medication when they begin to feel better, regardless of instructions to finish all the medication. Some patients, forgetting one or more doses of their medication, may try to make up for their oversight by taking

two or three times their usual dose all at once. Still other patients alter the therapeutic properties of their medication without even knowing it. For instance, some drugs are destroyed by stomach acid. So these are coated with a substance which will carry them through the stomach unharmed and into the small intestine, where they are digested. Unfortunately, some people who have trouble swallowing pills crush the tablets into powder and dissolve them in some fluid—rendering the medication totally vulnerable to stomach acid.[11]

Perhaps the most bizarre form of noncompliance is that which Albert Soloway, College of Pharmacy, Ohio State University, Columbus, Ohio, has dubbed "supercompliance."[12] Supercompliers by definition are conscientious patients who see a number of practitioners and religiously obey all their instructions. Unfortunately, they simply do not think to volunteer this information to the various physicians involved, each of whom will be busily proceeding on the basis of a different diagnosis and treatment. Thus, a supercomplier may end up taking as many as 15 to 20 different drugs at the same time, risking dangerous interactions and overdose.[12]

Noncompliance can obviously disrupt or invalidate the potential benefits of a given treatment. But it can have other, less obvious consequences as well.[7] Noncompliance often results in unnecessary additional testing, as the practitioner attempts to explain the failure of a therapy that should have worked. It may confuse the results of clinical trials for new drugs. Perhaps most seriously, noncompliance may cause the development of resistant strains of certain disease organisms by allowing the most resistant organisms to survive and reproduce.[7]

Reflecting the enormous research interest that compliance behavior has generated, the compliance literature is highly interdisciplinary, and has been doubling in volume every five years.[13] In Table 1 there is a selected bibliography of papers from the research front entitled "Study of medical compliance in prescribed drug therapy." This is just one of the research fronts identified through *ISI/BIOMED* ™, our new online search system.[14] Table 2 shows the core papers for this research front.

Due to the sheer magnitude of the literature, as well as methodological differences that make it difficult to compare research results, a definite consensus on the causes of noncompliance has been elusive. In 1976, however, David L. Sackett and R. Brian Haynes, McMaster University Medical Centre, Hamilton, Ontario, edited a landmark review of the field, *Compliance with Therapeutic Regimens*.[15] The book includes a monumental bibliography of the literature on compliance through 1974. An updated version, *Compliance in Health Care*,[16] was published in 1979. Together, the publications have garnered almost 200 citations through 1981, according to *Science Citation Index*® (*SCI*®) and *Social Sciences Citation Index*® (*SSCI*®).

Finding an objective way to measure the degree of a patient's compliance has proved no easy task.[17] Both patients' self-reports and physicians' opinions tend toward overestimation.[18] Counting the number of pills left in a bottle and comparing the result with the number of pills the patient started with has been suggested as a fairly accurate measure of compliance.[17] Yet there is no guarantee that what has left the bottle has necessarily been ingested by the patient.[19]

One of the surest methods of estimating compliance is to measure the concentration of a medication or its metabolites (the products of the drug's breakdown by the body) in a patient's blood or urine.[17,20] Yet even this method is not without its disadvantages. Low metabolite levels may indicate poor absorption of the drug in the patient's intestines, rather than noncompliance.[17] More-

Table 1: A bibliography of papers selected from the research front entitled "Study of medical compliance in prescribed drug therapy," #80-0582, contained in the *ISI/BIOMED*™ online data base.

Ashburn F S, Goldberg I & Kass M A. Compliance with ocular therapy. *Surv. Ophthalmol.* 24:237-48, 1980.

Barsky A J. Defining psychiatry in primary care: origins, opportunities, and obstacles. *Compr. Psychiat.* 21:221-32, 1980.

Beck D E, Fennell R S, Yost R L, Robinson J D, Geary D & Richards G A. Evaluation of an educational program on compliance with medication regimens in pediatric patients with renal transplants. *J. Pediat.* 96:1094-7, 1980.

De Wet B & Hollingshead J. Medicine compliance in paediatric outpatients. *S. Afr. Med. J.* 58:846-8, 1980.

Ettlinger P R A & Freeman G K. General practice compliance study: is it worth being a personal doctor? *Brit. Med. J.* 282:1192-4, 1981.

Evers S E & Rand C G. Morbidity in Canadian Indian and non-Indian children in the first year of life. *Can. Med. Ass. J.* 126(3):249-52, 1982.

Goyan J. Fourteen fallacies about patient package inserts. *West. J. Med.* 134:463-8, 1981.

Kellaway G S M. Facing up to compliance-failure with prescribed drug therapy. *Meth. Find. Exp. Clin. Pharmacol.* 2:205-12, 1980.

Klein G L & Zenk K E. A medical allergy profile (map) card. *Ann. Allergy* 46:328-30, 1981.

Litt I F & Cuskey W R. Compliance with medical regimens during adolescence. *Pediat. Clin. N. Amer.* 27:3-15, 1980.

Lüscher T, Dorst K G, Vetter H, Scheu H, Greminger P, Hasse W & Vetter W. Determinants of compliance in hypertensives. *Schweiz. Med. Wochenschr.* 112(13):458-65, 1982.

Nazarian L F. Research in pediatric practice. *Pediat. Clin. N. Amer.* 28:585-99, 1981.

O'Hanrahan M & O'Malley K. Compliance with drug treatment. *Brit. Med. J.* 283:298-300, 1981.

Passero M A, Remor B & Salomon J. Patient-reported compliance with cystic fibrosis therapy. *Clin. Pediat.* 20:264-8, 1981.

Rehder T L, McCoy L K, Blackwell B, Whitehead W & Robinson A. Improving medication compliance by counseling and special prescription container. *Amer. J. Hosp. Pharm.* 37:379-85, 1980.

Shope J T. Medication compliance. *Pediat. Clin. N. Amer.* 28:5-21, 1981.

Tanrisever B, Cedrato A E & Trujillo H. Cefadroxil monohydrate compared with cephradine in bacterial respiratory infections in children. *Curr. Ther. Res.* 29:452-62, 1981.

Weitzman M, Moomaw M S & Messenger K P. An after-hours pediatric walk-in clinic for an entire urban community: utilization and effectiveness of follow-up care. *Pediatrics* 65:964-70, 1980.

Wiholm B E. Irregular drug intake and serum chlorpropamide concentrations. *Eur. J. Clin. Pharmacol.* 18:159-63, 1980.

Windorfer A, Maier-Lenz H, Bauer P & Alterthum K. Cefadroxil in infections of the upper respiratory tract in pediatrics. *Infection* 8(Suppl. 5):S610-3, 1980.

Table 2: Core papers forming the basis for the research front entitled "Study of medical compliance in prescribed drug therapy," #80-0582, contained in the *ISI/BIOMED*™ online data base.

Bergman A B & Werner R J. Failure of children to receive penicillin by mouth. *N. Engl. J. Med.* 268:1334-8, 1963.

Charney E, Bynum R, Eldredge D, Frank D, MacWhinney J B, McNabb N, Scheiner A, Sumpter E A & Iker H. How well do patients take oral penicillin? A collaborative study in private practice. *Pediatrics* 40:188-95, 1967.

Francis V, Korsch B M & Morris M J. Gaps in doctor-patient communication. *N. Engl. J. Med.* 280:535-40, 1969.

over, some patients degrade and excrete a drug more rapidly than others.[20] And the absorption rates of some drugs, such as lithium (used in the treatment of bipolar affective disorder, or manic-depression), are so rapid that a patient taking only a few doses prior to seeing his or her doctor may demonstrate the proper therapeutic concentration.[21]

Finally, some patients may deliberately attempt to affect the results of such tests—especially when they are self-administered. In one case, a number of children at a special summer camp for

diabetics falsified the results of self-administered urine tests used to monitor their blood-sugar levels. They believed that if their results were normal, they would no longer have the disease.[22] The false results led the camp staff to erroneously adjust the children's insulin levels. Undetected, such noncompliance could have led to poor control of blood-sugar levels, inadequate growth, and even diabetic coma.

Extensive efforts have been made to identify specific demographic and personality traits that might predispose one to noncompliance.[7,15,16] But no significant, consistent association between compliance and such characteristics as intelligence, marital status, income, or education has ever been established.[15,16] And although a patient's beliefs and attitudes—especially those relating to health and disease—have been found to have a significant impact on compliance,[23] they have shown considerable variation across socioeconomic lines.[24] Nevertheless, a number of seemingly "safe" conclusions concerning noncompliance have emerged.[15,16]

Noncompliance is likely to be a problem in any disease for which medication is prescribed[5]—particularly if the medication is to be taken over a long period.[23] The number of drugs prescribed, and the frequency of their administration, are also linked with noncompliance: the more drugs prescribed, or the more daily doses required, the lower the degree of compliance.[5,15,16,23,24] Compliance may also be poor if the medication is expensive or causes side effects,[23] or if the regimen requires alterations in life-style—such as in smoking, drinking, or eating habits.[5] Noncompliance has also been linked with extremes of age: young children resist bad-tasting medicine, while the elderly are prone to forgetfulness and self-neglect.[25] The elderly also encounter physical barriers to good compliance. Child-proof caps sometimes are also elderly proof,[26,27] and lettering on prescription labels is often so small as to be illegible to aged eyes.[27]

Another factor influencing compliance is the nature of the patient's illness. High levels of compliance have been associated with symptomatic diseases, as well as acute, or short-term, illnesses.[23] Conversely, compliance is lower for chronic, or long-term, illnesses; diseases with no obvious symptoms;[15,16,23,24] and treatments intended to prevent the onset of disease.[23] One disease combining many of these elements is hypertension, or high blood pressure.[28] Untreated, it can cause stroke, heart attack, congestive heart failure, and death.[29] Yet hypertension, the "silent killer," is often asymptomatic and painless.[30] It is estimated that as many as 40 percent of those Americans afflicted with high blood pressure aren't even aware of it. And although treatments for hypertension are effective,[31] untreated patients often feel well, and feel less well when put on the complex medication regimen required to achieve control of their blood pressure.[32] Consequently, perhaps another 40 percent of American hypertensives on medication do not exhibit good blood pressure control—simply because they fail to take their medicine properly.[30]

One of the more intangible, yet perhaps most important, aspects of patient compliance is the relationship between the health practitioner and the patient. In Western nations, the traditional close, long-term relationship with the family doctor is yielding to short-term encounters with highly trained specialists, who often attach little importance to personal rapport with the patient.[33] Focusing predominantly on technical knowledge, physicians often express themselves in terminology that the average patient may find mystifying. In fact, according to Barbara M. Korsch and Vida Francis Negrete, Children's Hospital, University of Southern California, Los Angeles, good "bedside manner" is often viewed as a concession to

salesmanship beneath the dignity of a medical scientist.[33]

Yet time after time, research results have shown that the degree of compliance is greatest in those patients whose physicians take the time to explain themselves, and exhibit sincere regard for the patient's concerns.[23,33-36] As a letter to the *Journal of the American Medical Association* puts it, doctors should work to establish and maintain a climate of openness and concern for the patient.[37] By listening to a patient's fears—both spoken and unspoken—and responding in a supportive fashion, the physician may be offering the most potent tool in his or her medicine chest.

It is but a small step from describing the conditions that might predispose a patient toward noncompliance to developing strategies aimed at ensuring compliance. This raises the question, however, of whether or not health practitioners have either the right or the responsibility to go beyond their usual chores of diagnosing and prescribing. Sackett and Haynes suggest three conditions which should be satisfied before any attempt at improving compliance is made: the diagnosis must be correct, the therapy must be known to do substantially more good than harm, and the patient must be an informed and willing partner.[15,16] However, with the completion of several well-designed control trials of strategies for improving compliance, a new condition can be added to these three: the method employed to increase compliance must be of established value.[38,39]

A favorite target for intervention by compliance-oriented practitioners is the medication regimen, due to the ease with which it may be manipulated. "Tailoring," or linking the medication's administration to the patient's daily activities, makes it more difficult for the patient to forget his or her medicine at the same time that it increases the regimen's convenience.[39,40] For example, if a drug must be taken several times a day, and the patient eats at the same time each day, the practitioner may prescribe the medication to be taken with meals. To further aid the patient's memory, the medication might be left in the refrigerator! It should be noted, however, that the prescribing physician must take into account the possibility that the absorption rate of the drug will be altered if taken with food.[20]

Other successful strategies for increasing compliance include: introducing successively more difficult treatment procedures only after the patient has demonstrated proficiency in each prior component;[41] initiating a written contract between patient and practitioner, outlining the responsibilities of each and the goals of the treatment program;[42,43] using environmental cues to facilitate the patient's memory, such as brightly colored self-adhesive stickers bearing appropriate instructions and placed prominently in the patient's home;[40] and prescribing fixed ratio combination (FRC) drugs, which combine within one dosage two or more different medications.[44]

Each of these methods has inherent problems, however. The nature of an illness may not allow a doctor the luxury of waiting for the patient to demonstrate mastery of the therapeutic program.[41] Written contracts are time-consuming to compose and are no guarantee against noncompliance.[42,43] And many health practitioners are opposed to the routine prescription of FRCs because they do not permit the physician to adjust the dosage of one constituent without affecting the dosage of the other constituents.[44] Moreover, FRCs expose patients unnecessarily to possible carcinogenic or teratogenic (birth-defect causing) effects. And many patients given FRCs will receive drugs they do not require. FRCs also pose the danger of potential drug interactions. Finally, the common practice of prescribing two or more combination drugs, frequently on different dosage schedules, offsets any

presumed advantage gained from prescribing a combination of several drugs in one dosage form in the first place.[45]

Compliance-improving strategies that alter the patient's medication regimen depend for their success on the accuracy of the assumption that simplifying the medication schedule will make it easier for the patient to comply. However, Haynes warns of a number of myths and misunderstandings concerning the manipulation of a patient's medication regimen.[46] He maintains that no *conclusive* evidence establishes the effectiveness of reducing the dosage frequency or the number of drugs administered, and that no direct evidence supports the claim that combination drugs promote compliance. In fact, Haynes argues that the most potent method for improving compliance is direct supervision by the practitioner.

Also disputed is patient education and the role it plays in improving compliance. Due to differences in learning ability, language usage, and the intellectual background of patients, the effectiveness of patient educational methods varies widely, according to how and to whom they are applied. The results of some studies have shown that formally organizing pertinent information into a planned presentation can improve a patient's understanding of his or her treatment program and promote compliance.[47,48] Yet other studies have indicated that even a simple phone call checking on a patient's progress can have a positive effect on compliance.[49,50] Indeed, even the extra attention involved in counseling a patient is a significant factor in improving compliance.[51] Victims of chronic disease clearly benefit from participating in the process of administering their own treatment,[15] and patient education is viewed by many as a way of forging a genuine partnership between patient and practitioner.

Shouldering some of the responsibility for educating patients are pharmacists, who increasingly are disseminating information to patients, conferring with doctors and nurses, and making recommendations to improve the convenience of prescribed treatments.[52] Some pharmacists are now providing written product information on the medications they dispense in the form of preprinted sheets, written in easy-to-understand language, that describe a drug's risks, benefits, and instructions for use.[53] Although providing such information is currently voluntary, the practice received a boost from a pilot program instituted by the US Food and Drug Administration (FDA). The program mandated that patient package inserts (PPIs) accompany the dispensing of many drugs. The program began in 1980, but has since been discontinued by the Reagan Administration.[54]

Jere Goyan, School of Pharmacy, University of California, San Francisco, was the FDA commissioner when the PPI pilot program began. He described the program in a recent article published in *Western Journal of Medicine*.[54] According to Goyan, the purpose of PPIs was merely to restate and emphasize the information that the physician should have given the patient when the prescription was written. Concerns that PPIs would have a detrimental psychological effect on patients were taken quite seriously by the FDA, but no hard evidence supporting such objections was found. Goyan and others believe that PPIs and similar forms of patient information increase the patient's awareness of a drug's possible interactions and side effects, and encourage the patient to report those side effects.[53-55]

Critics claim, however, that written product information on drugs can disrupt the doctor/patient relationship, increase inappropriate self-medication, produce suggestion-induced side effects, and may even alarm patients to the point where they will refuse to take their medication.[53,56] Many physicians also voice much the same objections to patient counseling by pharmacists, citing a

loss of control over the information given to their patients, as well as the possibility of confusing or frightening them.[57]

However, Soloway asserts that pharmacy students acquire significantly greater knowledge of pharmacology than do medical students, and that the pharmacist should not be constrained from providing patients with appropriate information.[12] "Rather than disrupting the doctor/patient relationship," says Soloway, "the pharmacist can and should be a positive force in enhancing the patient's confidence in his or her medical care.... If we are to use all available health professionals and maximize their contribution to society, then the patient is not the physician's, nurse's, or pharmacist's patient, but is instead the patient of a particular health care team. Each member of that team must be supportive of the others."[12] Soloway acknowledges, however, that we are a very long way from that ideal. And although some favorable evidence concerning the effectiveness of written product information and pharmacist counseling has been compiled,[58-60] other investigators deny that conclusive evidence has been established.[61]

Much of the compliance literature assumes that the problem of noncompliance originates with patients, and that the solution lies with practitioners. But there is an undercurrent of opinion in the medical community that this is not necessarily so. As patients have become more sophisticated and knowledgeable, they have also become more hesitant about accepting medical judgments unquestioningly.[8] Noncompliance may represent no more than disagreement with the physician over the diagnosis or prescribed treatment.[62] Hence, the root of many noncompliance "problems" may be the assumption by practitioners that they are "in charge" of their patients. Under certain circumstances, noncompliance may actually safeguard the patient's health, since studies have shown that noncompliance is more likely to occur when the diagnosis or recommended treatment is inaccurate, or when the prescribed dosage of medication is inadequate.[23] Presumably, some patients stop taking their medication when they realize it is doing little good.

Kay Jamison, Affective Disorders Clinic, University of California, Los Angeles, feels that under certain conditions, noncompliance is understandable. She points out, for example, that although lithium carbonate has been proved effective in the management of bipolar affective disorder, many patients actually enjoy the elevated, manic phase of their mood swings and stop taking their lithium.[63] Many also rebel against the idea that their moods are being controlled by medication.[64] But Jamison notes that clinicians are now more aware of compliance problems than they were several years ago. "Patients are being treated in a collaborative way much more often now than in the past," Jamison says. "Certainly patients are getting far better information than they used to, and are far more involved in medical decision-making."[65]

Michael Weintraub, University of Rochester, New York, goes so far as to label the patient's conscious rejection of all or part of a prescribed course of treatment "intelligent noncompliance," so long as the treatment was rejected without detriment to the patient.[66] Elderly patients, he says, may have especially good reason to tinker with a treatment program. They have become attuned to their body's rhythms and reactions over the years, and may have an instinctive sense for the most effective dosage levels of their medication. Moreover, such patients have seen treatment fads come and go, or may have lived through eras in which ineffective and even dangerous treatments were commonly prescribed.

Considering the amount of interest and controversy stirred up by patient compliance, it seems curious that no

journal devoted exclusively to the topic exists. But Haynes, who together with Sackett published the *Newsletter on Compliance with Therapeutic Regimens* from 1973 until 1976, thinks that a journal devoted exclusively to reporting the results of compliance research might be counterproductive.[67] He and Sackett turned down an opportunity to publish such a journal because they felt it would result in a dialogue between compliance-oriented researchers, with very little impact on the practicing physician. Most doctors simply don't have time to devote to specialized journals outside their own fields. At present, compliance research is published in a number of general and clinical journals, where it reaches a diverse audience whose interests may include, but are not limited to, patient compliance.

The medical community is far from a consensus on the matter of patient compliance. Some researchers focus on describing the causes of noncompliance, while others seek, instead, reliable methods for improving compliance. Still others question what right any practitioner has to attempt to ensure that patients comply with advice.

It may be, however, that the heart of the noncompliance problem lies in the relationship between each individual doctor and patient. One cannot underestimate the importance of a humanistic outlook in effective medical practice. Noncompliance may never disappear, since there will always be some patients who are simply forgetful or otherwise inadvertently noncompliant. But at least noncompliance resulting from needless misunderstandings between patients and practitioners could be made a thing of the past.

As an information specialist, it's natural for me to want patients to have maximum access to information. More often than not, information is enlightening, useful, and liberating. Many information dispensing habits still prevalent are products of an age when doctors were generally more educated than their patients. But today, literacy and higher education make a very big difference. It behooves doctors to regard patients as knowledgeable individuals. On the other hand, information technologists know from experience that doctors and patients can suffer from information overload. Such legitimate concerns must enter into the design of PPIs. Clearly, doctors must take the trouble to determine whether patients can absorb the information imparted. But from the number of requests I receive on how to find a particular specialist, it would appear that many doctors are still unwilling to share information with patients and their families. Indeed, the notion of a "second opinion" is something I would like to take up in the future. It may not be obvious, but often a confirming second opinion may be the best guarantee of patient compliance.

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REFERENCES

1. **Garfield E.** What do we know about depression? Part 1: etiology. *Current Contents* (19):5-12, 11 May 1981.
2. ----------. What do we know about depression? Part 2: diagnosis and treatment. *Current Contents* (20):5-12, 18 May 1981.
3. ----------. What do we know about depression? Part 3: children and adolescents. *Current Contents* (27):5-11, 6 July 1981.
4. **Hull R C & Marshall J A.** Single-dose imipramine pamoate in the treatment of depressive neurosis. *Psychosomatics* 16:84-7, 1975.
5. **Ozuna J.** Compliance with therapeutic regimens: issues, answers, and research questions. *J. Neurosurg. Nurs.* 13:1-6, 1981.

6. **Robbins J A.** Patient compliance. *Primary Care* 7:703-11, 1980.
7. **Malman L A & Becker M H.** The clinician's role in patient compliance. *Trends Pharmacol. Sci.* 1:457-9, 1980.
8. **Guze S B.** Patients who do not follow our advice. *Hosp. Pract.* 16(10):15-6, 1981.
9. **Bissonette R & Seller R.** Medical noncompliance: a cultural perspective. *Man Med.* 5:41-53, 1980.
10. **Cassell E J.** Death & the physician. *Commentary* 47(6):73-9, 1969.
11. **Feldman E G.** Telephone communication. 6 August 1982.
12. **Soloway A H.** Personal communication. 4 August 1982.
13. **Blackwell B.** Treatment adherence. *Brit. J. Psychiat.* 129:513-31, 1976.
14. **Institute for Scientific Information.** *Index to research fronts in ISI/BIOMED 1981.* Philadelphia: ISI Press, 1981. 205 p.
15. **Sackett D L & Haynes R B,** eds. *Compliance with therapeutic regimens.* Baltimore, MD: Johns Hopkins University Press, 1976. 293 p.
16. **Haynes R B, Taylor D W & Sackett D L,** eds. *Compliance in health care.* Baltimore, MD: Johns Hopkins University Press, 1979. 516 p.
17. **Seltzer A, Roncari I & Garfinkel P.** Effect of patient education on medication compliance. *Can. J. Psychiatry* 25:638-45, 1980.
18. **Roth H P & Caron H S.** Accuracy of doctors' estimates and patients' statements on adherence to a drug regimen. *Clin. Pharmacol. Ther.* 23:361-70, 1978.
19. **Roth H P, Caron H S & Hsi B P.** Measuring intake of a prescribed medication. *Clin. Pharmacol. Ther.* 11:228-37, 1970.
20. **Micozzi M S.** Psychotropic and anticonvulsant drug monitoring. *Lab. Manage.* 20(2):45-7; 49; 51; 53-4, 1982.
21. **Gengo F, Frazer A, Ramsey T A & Mendels J.** The lithium ratio as a guide to patient compliance. *Compr. Psychiat.* 21:276-80, 1980.
22. **Belmonte M M, Gunn T & Gonthier M.** The problem of "cheating" in the diabetic child and adolescent. *Diabetes Care* 4:116-20, 1981.
23. **Shope J T.** Medication compliance. *Pediat. Clin. N. Amer.* 28:5-21, 1981.
24. **Syred M E J.** The abdication of the role of health education by hospital nurses. *J. Adv. Nurs.* 6:27-33, 1981.
25. **Solomon H S.** How to improve patient compliance. (Lasagna L, ed.) *Controversies in therapeutics.* Philadelphia: Saunders, 1980. p. 567-72.
26. **Steane M A.** Letter to editor. (Drug compliance and the elderly patient.) *Brit. Med. J.* 1:622-3, 1979.
27. **Jenkins G H C.** Letter to editor. (Drug compliance and the elderly patient.) *Brit. Med. J.* 1:124, 1979.
28. **Glanz K, Kirscht J P & Rosenstock I M.** Linking research and practice in patient education for hypertension. *Med. Care* 19:141-52, 1981.
29. **Inui T S, Yourtee E L & Williamson J W.** Improved outcomes in hypertension after physician tutorials. *Ann. Intern. Med.* 84:646-51, 1976.
30. **Podell R N & Gary L R.** Hypertension and compliance: implications for the primary physician. *N. Engl. J. Med.* 294:1120-1, 1976.
31. **Vidt D G.** The struggle for drug compliance in hypertension. *Cardiovasc. Clin.* 9:243-52, 1978.
32. **Jack D B, Dean S & Kendall M J.** Letter to editor. (Evaluation of a simple method to check compliance with antihypertensive drug therapy.) *Brit. J. Clin. Pharmacol.* 10:183-5, 1980.
33. **Korsch B M & Negrete V F.** Doctor-patient communication. *Sci. Amer.* 227(2):66-75, 1972.
34. **Falvo D, Woehlke P & Deichmann J.** Relationship of physician behavior to patient compliance. *Patient Couns. Health Educ.* 2:185-8, 1980.
35. **Francis V, Korsch B M & Morris M J.** Gaps in doctor-patient communication. *N. Engl. J. Med.* 280:535-40, 1969.
36. **Roter D L.** Patient participation in the patient-provider interaction: the effects of patient question asking on the quality of interaction, satisfaction and compliance. *Health Educ. Monogr.* 5:281-315, 1977.
37. **Franco P C.** Letter to editor. (Physician-patient communication.) *J. Amer. Med. Assn.* 245:2028, 1981.
38. **Haynes R B.** Telephone communication. 3 August 1982.
39. **Levine R J.** Ethical considerations in the development and application of compliance strategies for the treatment of hypertension. *Patient compliance to prescribed antihypertensive medication regimens.* Bethesda, MD: US Department of Health & Human Services, Public Health Service, October 1980. NIH #81-2102. p. 229-48.
40. **Schmidt J P.** A behavioral approach to patient compliance. *Postgrad. Med.* 65(5):219-24, 1979.
41. **Becker M H & Malman L A.** Strategies for enhancing patient compliance. *J. Commun. Health* 6:113-35, 1980.
42. **Steckel S B, Funnell M M & Dragovan A.** Contingency contracting for patient adherence. *Prev. Med.* 9:430, 1980.

43. **Hagner J N & Kohn R.** The health contract as a patient compliance tool in hypertension control. *Prev. Med.* 8:169, 1979.
44. **Weintraub M.** Fixed ratio combinations—pro position. (Lasagna L, ed.) *Controversies in therapeutics.* Philadelphia: Saunders, 1980. p. 166-71.
45. **MacCannell K L & Giraud G.** Fixed ratio drug combinations—sense and nonsense. (Lasagna L, ed.) *Controversies in therapeutics.* Philadelphia: Saunders, 1980. p. 172-9.
46. **Haynes R B.** The effect of the therapeutic regimen on patient compliance and the possible influence of controlled-release dosage forms. (Urquhart J, ed.) *Controlled-release pharmaceuticals.* Washington, DC: American Pharmaceutical Association, 1981. p. 121-39.
47. **Hecht A B.** Improving medication compliance by teaching outpatients. *Nurs. Forum* 13:112-29, 1974.
48. **Norell S E.** Improving medication compliance: a randomised clinical trial. *Brit. Med. J.* 2:1031-3, 1979.
49. **Guarino M A, Giovannoli S M, Loder N & Fisher B.** Improving patient compliance with telephone health counseling. *Prev. Med.* 8:168, 1979.
50. **Giovannoli S M, Guarino M A, Loder N & Fisher B.** Telephone health counseling for improving patient compliance. *Prev. Med.* 9:431, 1980.
51. **Malmon A M, Josephson R C, Kosloske N E & Panagis C.** Patient compliance: the impact of comprehensive outreach and follow-up in a community hypertension program. *Prev. Med.* 8:188, 1979.
52. **Anderson R A.** The professional role of the pharmacist. *J. Clin. Hosp. Pharm.* 5:319-21, 1980.
53. **Morris L A & Halperin J A.** Effects of written drug information on patient knowledge and compliance: a literature review. *Amer. J. Public Health* 69:47-52, 1979.
54. **Goyan J.** Fourteen fallacies about patient package inserts. *West. J. Med.* 134:463-8, 1981.
55. **Fleckenstein L.** Patient package inserts will benefit consumers. (Lasagna L, ed.) *Controversies in therapeutics.* Philadelphia: Saunders, 1980. p. 88-94.
56. **Barclay W R.** How appropriate is the proposed patient package labeling? (Lasagna L, ed.) *Controversies in therapeutics.* Philadelphia: Saunders, 1980. p. 95-6.
57. **Ascione F J & Ravin R L.** Physicians' attitudes regarding patients' knowledge of prescribed medications. *J. Amer. Pharm. Assn.* 15:386-91, 1975.
58. **Crichton E F, Smith D L & Demanuele F.** Patient recall of medication information. *Drug Intel. Clin. Pharm.* 12:591-9, 1978.
59. **McKenney J M & Harrison W L.** Drug-related hospital admissions. *Amer. J. Hosp. Pharm.* 33:792-5, 1976.
60. **McKenney J M, Slining J M, Henderson H R, Devins D & Barr M.** The effect of clinical pharmacy services on patients with essential hypertension. *Circulation* 48:1104-11, 1973.
61. **Sackett D L, Haynes R B, Gibson E S, Hackett B C, Taylor D W, Roberts R S & Johnson A L.** Randomised clinical trial of strategies for improving medication compliance in primary hypertension. *Lancet* 1:1205-7, 1975.
62. **Slack W V.** Letter to editor. (The patient's right to decide.) *Lancet* 2:240, 1977.
63. **Jamison K R, Gerner R H, Hammen C & Padesky C.** Clouds and silver linings: positive experiences associated with primary affective disorders. *Amer. J. Psychiat.* 137:198-202, 1980.
64. **Jamison K R, Gerner R H & Goodwin F K.** Patient and physician attitudes toward lithium. *Arch. Gen. Psychiat.* 36:866-9, 1979.
65. **Jamison K R.** Telephone communication. 28 June 1982.
66. **Weintraub M.** Intelligent noncompliance with special emphasis on the elderly. *Contemp. Pharm. Pract.* 4:8-11, 1981.
67. **Haynes R B.** Telephone communication. 19 April 1982.