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*Last Updated: 07/03/2024*

S11 214 SUNSCREENING AGENTS  
 ss sunblock or zinc(w)oxide or P-aminobenzoic acid/de  
 S12 0 SUNBLOCK  
 S13 8576 ZINC  
 S14 7374 OXIDE  
 S15 505 ZINC(W)OXIDE  
 S16 427 P-AMINOBENZOIC ACID/DE  
 S17 930 SUNBLOCK OR ZINC(W)OXIDE OR P-AMINOBENZOIC ACID/DE

c 11 or 17

214 11  
 930 17

S18 1114 11 OR 17  
 ss allers? or hypersensitivity

S19 13351 ALLERG?  
 S20 14897 HYPERSENSITIVITY  
 S21 23270 ALLERG? OR HYPERSENSITIVITY

c 18 and 21

1114 18  
 23270 21

S22 36 18 AND 21

limit 22/eng

S23 31 22/ENG

t 23/3

23/3/1

06130203 87104203

Allergic contact dermatitis to sunscreens.

Camarasa JG; Serra-Baldrich E

Department of Dermatology, Hospital Nuestra Senora del Mar, Barcelona, Spain.

Contact Dermatitis (DENMARK) Oct 1986, 15 (4) p253-4, ISSN 0105-1873

Journal Code: DP7

t

23/3/2

06078736 87052736

Allergic contact dermatitis from isopropyl dibenzoylmethane.

English JS; White IR

St. John's Hospital for Diseases of the Skin, London, UK.

Contact Dermatitis (DENMARK) Aug 1986, 15 (2) p94, ISSN 0105-1873

Journal Code: DP7

t

23/3/3

06078715 87052715

Cheilitis: occult allergy to cinnamic aldehyde.

Maibach HI

University of California School of Medicine, San Francisco 94143.

Contact Dermatitis (DENMARK) Aug 1986, 15 (2) p106-7, ISSN 0105-1873

Journal Code: DP7

t

23/3/4

06012210 86313210

Photoallergic and allergic contact dermatitis from dibenzoylmethanes.

Schauder S; Ippen H

Photodermatol Jun 1986, 3 (3) p140-7, ISSN 0108-9684 Journal Code:

PBA

t

~~23/3/5~~

~~05978755 86279755~~

~~Persistent light reaction: induction in the guinea pig.~~

Katsumura Y; Tanaka J; Ichikawa H; Kato S; Kobayashi T; Horio T  
J Invest Dermatol Sep 1986, 87 (3) p330-3, ISSN 0022-202X  
Journal Code: IHZ  
t

23/3/6  
05950574 86251574  
Potassium para-aminobenzoate and liver function test findings.  
Zarafonietis CJ; Dabich L; DeVol EB; Rossi C; Skovronski JJ  
J Am Acad Dermatol Jul 1986, 15 (1) p144-9, ISSN 0190-9622  
Journal Code: HVG  
t

23/3/7  
05945513 86246513  
Poison ivy dermatitis.  
Baer RL  
Cutis Jun 1986, 37 (6) p434-6, ISSN 0011-4162 Journal Code: ~~AXB~~  
t

23/3/8  
05861360 86162360  
Drug-induced photoallergy.  
Elmets CA  
Dermatol Clin Apr 1986, 4 (2) p231-41, ISSN 0733-8635  
Journal Code: DER  
Contract/Grant No.: AM 32593  
t

23/3/9  
05835380 86136380  
Protease inhibitor prevents bronchoconstriction in man.  
Slapke J; Hummel S; Wischniewsky GG; Winkler J  
Eur J Respir Dis Jan 1986, 68 (1) p29-34, ISSN 0106-4339  
Journal Code: EPS  
t

23/3/10  
05777797 86078797  
Respiratory disease in adult cattle.  
Breeze R  
Vet Clin North Am Food [Food Anim Pract] Jul 1985, 1 (2) p311-46,  
ISSN 0749-0720 Journal Code: CFP  
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ss s23  
s24 31 s23  
t 23/3/11

23/3/11  
05729134 86030134  
Sun-induced disorders.  
Bickers DR  
Emerg Med Clin North Am Nov 1985, 3 (4) p659-76, ISSN 0733-8627  
Journal Code: EGD  
t

23/3/12  
05573986 85189986  
Concomitant photocontact allergy to a benzophenone derivative and a  
sunscreen preservative, 6-acetoxy-2,4,-dimethyl-m-dioxane.  
Kalimo K; Fagerlund VL; Jansen CT  
Photodermatol Dec 1984, 1 (6) p315-7, ISSN 0108-9684 Journal Code:

PBA

t

23/3/13

05549728 85165728

Contact and photocontact allergy to sunscreens.

Thune P

Photodermatol Feb 1984, 1 (1) p5-9, ISSN 0108-9684 Journal Code:

PBA

t

23/3/14

05533048 85149048

Photocontact allergy to octyldimethyl PABA.

Weller P; Freeman S

Australas J Dermatol Aug 1984, 25 (2) p73-6, ISSN 0004-8380

Journal Code: 9IP

t

23/3/15

05509893 85125893

Antioxidants in cosmetics.

White IR; Lovell CR; Cronin E

Contact Dermatitis Nov 1984, 11 (5) p265-7, ISSN 0105-1873

Journal Code: DP7

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23/3/16

05440443 85056443

The effect of a sunscreen containing para-aminobenzoic acid on the systemic immunologic alterations induced in mice by exposure to UVB radiation.

Morison WL

J Invest Dermatol Dec 1984, 83 (6) p405-8, ISSN 0022-202X

Journal Code: IHZ

Contract/Grant No.: N01-CO-23909

t

23/3/17

05277876 84201876

Allergic reaction to phenyl dimethicone in a sunscreen [letter]

Edwards EK Jr; Edwards EK

Arch Dermatol May 1984, 120 (5) p575-6, ISSN 0003-987X

Journal Code: 6WU

t

23/3/18

05246659 84170659

Spontaneous formation of immunogenic conjugates by 3-hydroxy-para-aminobenzoic acid--a biotransformation product of procaine and para-aminobenzoic acid.

Cirstea M; Suhaciu G; Cirje M

Physiologie Jan-Mar 1984, 21 (1) p25-31, Journal Code: P7P

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23/3/19

05245083 84169083

Acute allergic reaction to eugenol.

Barkin ME; Boyd JP; Cohen S

Oral Surg Oral Med Oral Pathol Apr 1984, 57 (4) p441-2, ISSN 0030-4220 Journal Code: QJU

Contract/Grant No.: 2S07RR05301

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23/3/20

05084250 84008250

Tissue response to allergenic leachables from dental materials.

Kallus T; Hensten-Pettersen A; Mjor IA

J Biomed Mater Res Sep 1983, 17 (5) p741-55, ISSN 0021-9304

Journal Code: HJJ

t

23/3/21

04923837 83156837

Allergic reaction to triethanolamine stearate in a sunscreen.

Edwards EK Jr; Edwards EK

Cutis Feb 1983, 31 (2) p195-6, ISSN 0011-4162 Journal Code: DXB

t

23/3/22

04700937 82243937

Treatment of selected photosensitivity diseases.

Bickers DR

Med Clin North Am Jul 1982, 66 (4) p927-39, ISSN 0025-7125

Journal Code: LU6

Contract/Grant No.: ES-1900; OH-01149

t

23/3/23

04691924 82234924

Allergic reaction to tertiary butyl alcohol in a sunscreen.

Edwards EK Jr; Edwards EK

Cutis May 1982, 29 (5) p476-8, ISSN 0011-4162 Journal Code: DXB

t

23/3/24

04667796 82210796

The phototoxic effects of benoxaprofen and their management and prevention.

Greist MC; Ozols II; Ridolfo AS; Muus JC

Eur J Rheumatol Inflamm 1982, 5 (2) p138-47, ISSN 0140-1610

Journal Code: ENG

t

23/3/25

04506713 82049713

Allergic reactions to benzyl alcohol in a sunscreen.

Edwards EK Jr

Cutis Sep 1981, 28 (3) p332-3, ISSN 0011-4162 Journal Code: DXB

t

23/3/26

04341291 81169291

Relationship between epidermal Langerhans cell density ATPase activity and the induction of contact hypersensitivity.

Lynch DH; Gurish MF; Daynes RA

J Immunol May 1981, 126 (5) p1892-7, ISSN 0022-1767 Journal Code:

IFB

Contract/Grant No.: CA22126; CA25917

t

23/3/27

04304265 81132265

Photocontact allergy to benzocaine.

Kaidbey KH; Allen H

Arch Dermatol Feb 1981, 117 (2) p77-9, ISSN 0003-987X

Journal Code: 6WU

t

23/3/28

04304260 81132260

Allergic reaction to sunscreen products [letter]

Kaminester LH

Arch Dermatol Feb 1981, 117 (2) p66, ISSN 0003-987X

Journal Code:

6WU

t

23/3/29

04112803 80223803

Contact allergy from Mexenone masquerading as an exacerbation of light sensitivity.

Millard LG; Barrett PL

Contact Dermatitis Apr 1980, 6 (3) p222-3, ISSN 0105-1873

Journal Code: DP7

t

23/3/30

04112793 80223793

Photo allergies from benzophenones and beta carotene in sunscreens.

Burry JN

Contact Dermatitis Apr 1980, 6 (3) p211-2, ISSN 0105-1873

Journal Code: DP7

t

23/3/31

04098092 80209092

Sarcoidosis. Part 2. More on the differential diagnosis. The usual course. Treatments of choice. Prognosis.

James DG

Med Times Jun 1980, 108 (6) p12s-16s, 21s-23s, 28s-29s, ISSN 0025-7583 Journal Code: MGE

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23/3/32

>>>Item 32 is not within valid item range

b 154

21may87 09:15:24 User008575

\$0.18 0.005 Hrs File154

\$0.04 Dialnet

\$0.22 Estimated cost this file

\$0.37 Estimated total session cost 0.008 Hrs.

File 154:MEDLINE - 80-87/JUNE

| Set                   | Items | Description               |
|-----------------------|-------|---------------------------|
| ss Patient dropouts   |       |                           |
| S1                    | 597   | PATIENT DROPOUTS          |
| ss Patient compliance |       |                           |
| S2                    | 4473  | PATIENT COMPLIANCE        |
| c 1 or 2              |       |                           |
|                       | 597   | 1                         |
|                       | 4473  | 2                         |
| S3                    | 4951  | 1 OR 2                    |
| limit 3/maj           |       |                           |
| S4                    | 1845  | 3/MAJ (major descriptors) |
| limit 4/eng           |       |                           |
| S5                    | 1549  | 4/ENG (English)           |
| ss review/id          |       |                           |
| S6                    | 0     | REVIEW/ID                 |
| ss review             |       |                           |
| S7                    | 37950 | REVIEW                    |
| c 5 and 7             |       |                           |
|                       | 1549  | 5                         |
|                       | 37950 | 7                         |
| S8                    | 41    | 5 AND 7                   |
| ss dt=review          |       |                           |
| S9                    | 77863 | DT=REVIEW (document type) |
| c 5 and 9             |       |                           |
|                       | 1549  | 5                         |
|                       | 77863 | 9                         |
| S10                   | 36    | 5 AND 9                   |
| t 10/3                |       |                           |

10/3/1

06179464 87153464

Treatment compliance in end-stage renal disease patients on dialysis.

Wolcott DL; Maida CA; Diamond R; Nissenson AR

Department of Psychiatry and Biobehavioral Sciences, University of California, Los Angeles.

Am J Nephrol (SWITZERLAND) 1986, 6 (5) p329-38, ISSN 0250-8095

Journal Code: 3MB

t

10/3/2

06162876 87136876

Adolescents' compliance with therapeutic regimens. Psychological and social aspects and intervention.

Friedman IM; Litt IF

Department of Ambulatory Services, Children's Hospital Medical Center, Oakland, California.

J Adolesc Health Care (UNITED STATES) Jan 1987, 8 (1) p52-67, ISSN 0197-0070 Journal Code: HAM

(This could be important since children's exposure is critical)

10/3/3

05969457 86270457

Medication noncompliance in schizophrenia: codification and update.



Youngs JL; Zonana HV; Shepler L  
Bull Am Acad Psychiatry Law 1986, 14 (2) p105-22, ISSN 0091-634X  
Journal Code: BAR X  
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10/3/4  
05964613 86265613  
The patient who refuses medical treatment: a dilemma for hospitals and  
physicians.  
Swartz M  
Am J Law Med 1985, 11 (2) p147-94, ISSN 0098-8588 Journal Code: 3IP  
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10/3/5  
05948792 86249792  
Antidepressant drug therapy in the elderly: enhancing safety and  
compliance.  
Halaris A  
Int J Psychiatry Med 87 1986, 16 (1) p1-19, ISSN 0091-2174 X  
Journal Code: 68J  
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10/3/6  
05780155 86081155  
Understanding and enhancing patient compliance with diabetic regimens. X  
Rosenstock IM  
Diabetes Care Nov-Dec 1985, 8 (6) p610-6, ISSN 0149-5992  
Journal Code: EAG  
t

10/3/7  
05767388 86068388  
Long-term compliance.  
Ice R  
Phys Ther Dec 1985, 65 (12) p1832-9, ISSN 0031-9023 Journal Code:  
P6W X  
t

10/3/8  
05641382 85257382  
The direct effects of compliance on health outcome.  
Epstein LH  
Health Psychol 1984, 3 (4) p385-93, ISSN 0278-6133 Journal Code:  
EJL  
t

10/3/9  
05632088 85248088  
Patient compliance.  
Ruffalo RL; Garabedian-Ruffalo SM; Paulson LG  
Am Fam Physician Jun 1985, 31 (6) p93-100, ISSN 0002-838X  
Journal Code: 3BT  
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10/3/10  
05593625 85209625  
Current status of institutionalized mental health patients' right to  
refuse psychotropic drugs.  
Kemna DJ  
J Leg Med (Chicago) Mar 1985, 6 (1) p107-38, ISSN 0194-7648 X  
Journal Code: IWX  
t



10/3/11

05587450 85203450

Oral contraception--starting, stopping or changing.

Drug Ther Bull May 20 1985, 23 (10) p37-9, ISSN 0012-6543

Journal Code: EBV

t

10/3/12

05504460 85120460

Antiarrhythmic therapy: the issue of patient compliance.

Somelofski C; Peters RW

Ann NY Acad Sci 1984, 432 p286-95, ISSN 0077-8923 Journal Code: SNM

t

10/3/13

05433001 85049001

Compliance and motivation in cardiac exercise programs.

Oldridge NB; Stoedefalke KG

Clin Sports Med Apr 1984, 3 (2) p443-54, ISSN 0278-5919

Journal Code: CSM

t

10/3/14

05385926 85001926

Overview of patient compliance with medication dosing: a literature review.

Greenberg RN

Clin Ther 1984, 6 (5) p592-9, ISSN 0149-2918 Journal Code: CPE

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10/3/15

05239171 84163171

Drug therapy of the aged: the problem of compliance and the roles of physicians and pharmacists.

Gryfe CI; Gryfe BM

J Am Geriatr Soc Apr 1984, 32 (4) p301-7, ISSN 0002-8614

Journal Code: H6V

t

10/3/16

05237561 84161561

Compliance with therapeutic regimens.

Jay S; Litt IF; Durant RH

J Adolesc Health Care Apr 1984, 5 (2) p124-36, ISSN 0197-0070

Journal Code: HAM

t

10/3/17

05199213 84123213

Popular medical concepts in Jamaica and their impact on drug use.

Mitchell MF

West J Med Dec 1983, 139 (6) p841-7, ISSN 0093-0415 Journal Code:

XN5

t

10/3/18

05178752 84102752

Understanding and improving patient compliance.

Eraker SA; Kirscht JP; Becker MH

Ann Intern Med Feb 1984, 100 (2) p258-68, ISSN 0003-4819

Journal Code: 5A6

t

10/3/19

05163568 84087568

Role of patient compliance in the management of asthma.

Voyles JB; Menendez R

J Asthma 1983, 20 (5) p411-8, ISSN 0277-0903 Journal Code: HF7

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10/3/20

05149297 84073297

Social support and compliance: a selective review and critique of treatment integrity and outcome measurement.

Levy RL

Soc Sci Med 1983, 17 (18) p1329-38, ISSN 0277-9536 Journal Code:

UT9

t

10/3/21

05148115 84072115

A compliance model for diabetic instruction.

Jenny J

Rehabil Lit Sep-Oct 1983, 44 (9-10) p258-63, 299, ISSN 0034-3579

Journal Code: R35

t

10/3/22

05138692 84062692

The application of theory in childhood asthma self-help programs.

Bruhn JG

J Allergy Clin Immunol Nov 1983, 72 (5 Pt 2) p561-77, ISSN 0091-6749 X

Journal Code: H53

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10/3/23

04952253 83185253

Compliance by persons with schizophrenia: a research issue for the nurse.

Davidhizar RE

Issues Ment Health Nurs Jul-Sep 1982, 4 (3) p233-55, ISSN 0161-2840

Journal Code: GY7

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04898170 83131170

The problem of non-compliance with drug therapy.

Evans L; Spelman M

Drugs Jan 1983, 25 (1) p63-76, ISSN 0012-6667 Journal Code: EC2

t

10/3/25

04897224 83130224

Compliance with pediatric therapy. A selective review and recommendations.

Jones JG

Clin Pediatr (Phila) Apr 1983, 22 (4) p262-5, ISSN 0009-9228

Journal Code: DHE

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04818583 83051583

Methods of self monitoring of diabetic control.

Peacock I; Tattersall R

Clin Endocrinol Metab Jul 1982, 11 (2) p485-501, ISSN 0300-595X

Journal Code: DCR

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10/3/27  
04463676 82006676  
Patient compliance with dapsone administration in leprosy.  
Huikeshoven H  
Int J Lepr Other Mycobact Dis Jun 1981, 49 (2) p228-58, ISSN  
0148-916X Journal Code: INU  
t

10/3/28  
04452670 81280670  
Investigation of compliance in the severely injured: a literature review.  
Rheiner NW; Aslakson MA; Morin P; Patach D  
Rehabil Nurs Jul-Aug 1981, 6 (4) p12-5, ISSN 0278-4807  
Journal Code: R25  
t

10/3/29  
04323452 81151452  
Patient compliance.  
Robbins JA  
Primary Care Dec 1980, 7 (4) p703-11, ISSN 0095-4543 Journal Code:  
P99

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04313152 81141152  
Medical noncompliance.  
Zisook S; Gammon E  
Int J Psychiatry Med 81 1980, 10 (4) p291-301, ISSN 0091-2174  
Journal Code: GSJ  
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10/3/31  
04233002 81061002  
An assessment and nursing application of the concept of locus of control.  
Arakelian M  
ANS Oct 1980, 3 (1) p25-42, ISSN 0161-9268 Journal Code: 6E9  
t

10/3/32  
04078351 80189351  
Compliance with medical regimens during adolescence.  
Litt IF; Cuskey WR  
Pediatr Clin North Am Feb 1980, 27 (1) p3-15, ISSN 0031-3955  
Journal Code: OUM  
t

10/3/33  
04037273 80148273  
Compliance with ocular therapy.  
Ashburn FS Jr; Goldbergs I; Kass MA  
Surv Ophthalmol Jan-Feb 1980, 24 (4) p237-48, ISSN 0039-6257  
Journal Code: VCT  
t

10/3/34  
04005964 80116964  
Compliance-oriented prescribing: simplifying drug regimens.  
Fischer RG  
J Fam Pract Mar 1980, 10 (3) p427-35, ISSN 0094-3509 Journal Code:  
I4L  
ss suncreening agents



# Clinical Therapeutics

THE INTERNATIONAL JOURNAL OF  
DRUG THERAPY

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## Overview of Patient Compliance with Medication Dosing: A Literature Review

*Richard N. Greenberg*

*Department of Internal Medicine, St. Louis University School of Medicine, St. Louis, Missouri*

## ABSTRACT

The literature was reviewed in an effort to relate frequency of dosing and other influences with patient compliance in medication taking. Once-a-day and twice-a-day regimens were associated with significantly better compliance (73% and 70%, respectively) than were three-times-daily (52%) and four-times-daily (42%) regimens. Compliance is not related to income, social class, occupation, or educational background, and it cannot be accurately predicted by physicians. Unintentional errors in taking medication are made by 50% to 90% of patients.

## INTRODUCTION

**Lack of patient adherence to prescribed drug regimens has become an important medical issue. Failure to follow medical advice can lead to such problems as treatment failure, medication overdose, otherwise avoidable hospitalization, emergence of resistant bacteria, and unnecessary medical expense. Several recent literature reviews<sup>1-6</sup> have described the seriousness of patients' failure to comply with drug regimens. They document an incidence of noncompliance**

ranging from 15% to 93%, depending upon the population studied and the medical regimen.

This paper reviews the literature from the perspective of a physician interested in improving patient compliance in a cost-effective and time-efficient manner. An attempt is made to formulate a statement about dosing of medication and improvement of patient compliance. Several other issues also seem relevant, such as duration of therapy, physician-patient interactions, and prescribing techniques to improve compliance. The overall goal of this review is to concisely summarize the literature on patient compliance with dosing schedules and drug regimens to make objective statements. The results suggest that once-a-day (QD) or twice-a-day (BID) medical regimens correlate with the best compliance rates.

## MATERIALS AND METHODS

More than 100 articles and book chapters were reviewed for data on patient compliance to dosing of medication. From library computer searches and examination of cited references, I identified 57 articles that examined patient compliance

R. N. GREENBERG

to dosing of m  
of the 57 studi  
ance with one  
three studies  
patients receiv  
evaluated patie  
acid regimens,  
medication reg  
(three), hyper  
(one), juvenil  
(one), immunos  
atric or neurolo  
placebo (one),  
of illnesses (1  
of the 57 studi  
in the pediatric  
(56%) involved  
and one includ

[illegible]

Statistics cite  
two-tailed Stud  
samples. Data  
plus or minus s

## RESULTS

In spite of great  
patients, medica

to dosing of medications.<sup>7-63</sup> Thirty-six of the 57 studies limited data to compliance with one particular agent. Twenty-three studies evaluated compliance in patients receiving antibiotics, five studies evaluated patient compliance with anti-acid regimens, while the rest dealt with medication regimens for heart failure (three), hypertension (three), asthma (one), juvenile rheumatoid arthritis (one), immunosuppression (four), psychiatric or neurological disorders (three), placebo (one), or several different types of illnesses (13). Twenty-four (42%) of the 57 studies evaluated compliance in the pediatric age group, 32 studies (56%) involved only adult populations, and one included both age groups.

The measurement or definition of compliance varied from study to study. Fifteen studies used the presence of the drug in urine or serum at time of clinic visit as a measurement of compliance. Eleven studies used pill counting, nine studies used an interview, one study used therapeutic outcome as measurement of compliance, while the remaining studies combined several of these methods. The definition of compliance also varied from study to study but generally relied on presence of medication in urine, therapeutic blood levels of medicine, or 66% to 100% compliance by pill count or interview. Some authors had narrower limits for compliance as measured by pill counting (91% to 100% of pills absent).

Statistics cited in this paper use the two-tailed Student's *t* test for unpaired samples. Data are expressed as means plus or minus standard error.

## RESULTS

In spite of great divergence in ages of patients, medications, illnesses, durations

of dosing, measurements of compliance, and definitions for compliance, I shall make an attempt to objectively examine the composite picture of the relationship between dosing and compliance. I shall also review data as they relate to multiple drugs, supply of medication, patient instruction, and sociodemographic characteristics.

## Dosing and Compliance

Table I summarizes 26 studies relating compliance (as defined per individual study) and dosage schedule of the particular agent.<sup>7-32</sup> Fourteen pertain to children and 12 to adults. Thirteen studies evaluate patients receiving chronic therapy (medicine given for at least several months). The total number of patients evaluated per study ranges from 15 to 705, with a median of 96 patients. Overall, better compliance is seen with QD (73%) and BID (70%) regimens than with either three-times-daily (TID) or four-times-daily (QID) regimens ( $P < 0.05$ ).

Six studies were not included in the table and subsequent calculations.<sup>33-38</sup> Each of these studies involves single daily doses of penicillin or sulfadiazine for prophylaxis against streptococcal infection in a population of rheumatic children without immunosuppressive conditions. Three papers<sup>33-35</sup> describe the same study and are counted only once. The mean compliance rate of  $39\% \pm 8\%$  is remarkably low in this group (Table II). The authors have conjectured that compliance tended to be poor because many of the patients were adolescents who were otherwise healthy.

Fourteen papers<sup>39-52</sup> give compliance data but do not specify precise dosage regimens. These papers describe studies



Table I. Compliance rate by dosage schedule.

| Dosage Schedule             | Percent Compliance |                   |
|-----------------------------|--------------------|-------------------|
|                             | Range              | Mean ( $\pm$ SEM) |
| QD <sup>7-13</sup>          | 42-93              | 73 $\pm$ 6        |
| BID <sup>7,8,13-18</sup>    | 50-94              | 70 $\pm$ 5        |
| TID <sup>8,13,19-24</sup>   | 18-89              | 52 $\pm$ 7        |
| QID <sup>7,8,13,25-32</sup> | 11-66              | 42 $\pm$ 5        |

$P < 0.05$  when comparing compliance of QD and BID groups with that of either TID or QID groups.

Table II. Compliance in a population of rheumatic children.

| Reference | Percent Compliance | Criterion for Compliance |
|-----------|--------------------|--------------------------|
| 33-35     | 32                 | Urine test               |
| 36        | 19                 | Interview                |
| 37        | 55                 | Pill count               |
| 38        | 49                 | Pill count               |

Mean compliance = 39%  $\pm$  8%.

in children (four) or in adults (ten) with a range of patients from 21 to 2,622 (median, 134). The overall compliance rates range from 18% (a study using TID and QID dosing in adults) to 83% (a study of renal transplant patients) with a mean compliance rate of 56%  $\pm$  5% (median compliance, 57%).

Six studies<sup>11,21,29,44,51,53</sup> evaluate physician ability to predict patient compliance. The predictions in these studies were correct in only about two thirds of patients (a mean of 66%  $\pm$  4%). Six studies<sup>10,54-58</sup> suggest that compliance rates decrease with increasing dosing frequency or increasing the number of drugs a patient must take each day. Five studies quantify patient errors as follows: 60% of 178 elderly patients made errors

in dosing (26% were serious errors)<sup>59</sup>; 36 of 40 patients in another study made some kind of medication error<sup>57</sup>; only about 66% of 47 patients in one study knew their medicines or their dosing schedules<sup>60</sup>; in another study of 47 outpatients, 56% of instructions given to the patients were forgotten shortly after they left the doctor<sup>61</sup>; only 50% of doctor-patient instructions were remembered by 54 patients upon leaving a medical clinic.<sup>62</sup> Several other studies<sup>15,20,21</sup> suggest that patient compliance decreases over time. Attendance at clinic or physicians' offices does not correlate precisely with compliance,<sup>28</sup> neither were patient interviews always reliable.<sup>20,29</sup> One study<sup>63</sup> reported that physicians in a middle Georgia community lost contact

within three months with 10% of patients who were hypertensive.

Neither patient occupation, or correlate directly with compliance rates.<sup>36,62</sup> Interventions which include monitoring, chiding, and tailoring of prescriptions have been found to improve compliance.

## DISCUSSION

This overview establishes one point: patient compliance with a dosing regime cannot be predicted by income, social class, educational background, or attendance record. Reporting adherence always correlates with compliance, though not infrequently (50% errors), patient compliance over time, and lost to follow-up with medical papers reviewed.

With the issue of directly related patient compliance, physicians need techniques, procedures to improve patient compliance. Strongly suggests that dosage schedule will significantly affect compliance rates. The analgesic compliance for BID, 52% for



|                       |
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|                       |
|                       |
| Mean<br>(±SEM)        |
| 73 ± 6                |
| 70 ± 5                |
| 52 ± 7                |
| 42 ± 5                |
| er TID or QID groups. |

|                             |
|-----------------------------|
| Criterion for<br>Compliance |
| Urine test                  |
| Interview                   |
| Pill count                  |
| Pill count                  |

vere serious errors)<sup>59</sup>; in another study made dication error<sup>57</sup>; only patients in one study cines or their dosing other study of 47 out- nstructions given to the otten shortly after they only 50% of doctor- ns were remembered pon leaving a medical l other studies<sup>15,20,21</sup> it compliance decreases dance at clinic or phy- loes not correlate pre- liance,<sup>28</sup> neither were vs always reliable.<sup>20,29</sup> rted that physicians in a community lost contact

within three months with 56% of their patients who were receiving therapy for hypertension.

Neither patients' income, social class, occupation, or education were found to correlate directly with compliance rates.<sup>36,62</sup> Intense patient counseling, which includes instruction sheets, special monitoring, charting of medication, and tailoring of patient's dosing schedule have been found in some studies to improve compliance rates.<sup>19,25,26,30,49,50</sup>

DISCUSSION

This overview on patient compliance establishes once again the evidence that patients frequently fail to comply with dosing regimens. Patient compliance cannot be predicted with accuracy, and compliance is not related to patients' income, social class, occupation, or educational background. Neither patients' attendance records at clinic nor interviews reporting adherence to medical regimens always correlate with compliance. Although not intentional, patient errors are frequent (50% to 90% of patients make errors), patient compliance decreases over time, and patients are frequently lost to follow-up. Overall compliance with medical schedules reported in papers reviewed for this study was 56%.

With the issue of cost-effective therapy directly related to patient compliance, physicians need to establish methods, techniques, procedures, or guidelines to improve patient compliance. This review strongly suggests that attempts to reduce dosage schedules to no more than BID will significantly improve compliance rates. The analysis of data showed 73% compliance for QD dosing, 70% for BID, 52% for TID, and 42% for QID.

A significant difference ( $P < 0.05$ ) was found when QD and BID compliance rates were compared with either TID or QID rates. It appears that selection of pharmacological agents that can be prescribed once or twice a day will improve patient compliance. This finding may justify the use of more expensive medications that will allow for QD or BID dosing if such regimens improve compliance and prevent or reduce the incidence of hospitalization.<sup>5,64,65</sup>

Certain other factors relating to patient compliance are evident from the review. It seems that there is generally poor compliance in patients required to take antimicrobial prophylaxis for rheumatic fever, especially in otherwise healthy adolescents. Such patients appear to require careful monitoring to improve compliance. On the other hand, physicians can improve patient compliance by (1) shortening duration of therapy; (2) reducing number of medications prescribed for their patients; (3) offering intense counseling, which includes instruction sheets, charting, and frequent monitoring for therapeutic effect; and (4) offering medication in specialized dose dispensers or calendar packs (eg, birth-control dose packs).<sup>64-68</sup>

Further research examining patient compliance should evaluate techniques to improve compliance in randomized comparison trials. Ideally, measurement of compliance rates should be standardized. In the past, researchers have used the interview, pill counting, and presence of drug in urine as the criteria for assessment of compliance. These techniques all suffer from problems that make them imprecise and not easily comparable. As more effective medications become available, it seems

reasonable to utilize therapeutic effects as the means of measuring compliance. Pharmaceutical companies should be encouraged to develop effective and safe drugs that can be administered less frequently.

### ACKNOWLEDGMENTS

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# Journal OF Adolescent Health Care

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## REVIEW ARTICLE

## Compliance with Therapeutic Regimens

SUSAN JAY, M.D., IRIS F. LITT, M.D., AND ROBERT H. DURANT, M.A.

[The physician] should keep aware of the fact that patients often lie when they state that they have taken certain medicines

Hippocrates

Compliance as a topic of medical concern has come of age. Recent studies suggest that one-quarter to one-half of patients seen in a medical setting fail to comply in some way with their prescribed regimen (1). In a comprehensive review of the literature, Haynes et al. reported that the degree of noncompliance across all medical procedures (e.g., medication, exercise, regular checkups) ranges from 30 to 70% among adults (2). The implication of this finding is staggering in terms of the course and outcome of the patient's illness, as well as in the effect on doctor-patient relationships.

As evidenced by the introductory quote, noncompliance has undoubtedly always been a problem in the medical field. The importance of compliance has become more salient in recent years, as evidenced by the increased number of publications and conferences devoted to this issue (3). This increased focus on compliance has paralleled current trends in medicine toward lifestyle diseases resulting from abuse and neglect of our bodies. No longer are diphtheria, smallpox, and bacterial pneumonia major health problems in our society. Diseases associated with lifestyle, such as heart disease, cancer, and strokes, now account for 70% of all deaths (4). Accidents (e.g., motor vehicle), suicide, and homicide are the leading causes of death in the adolescent age group (5). These health problems may be ameliorated to a large degree through modification of the general public's behavior. However, the transition from an emphasis on infectious-type illnesses to diseases that are generally influenced by an individual's lifestyle warrants certain changes and assumptions that have not been readily accepted by either the public or the medical profession. In order to fully comprehend the resistance that the medical profession may experience when dealing with compliance as a behavioral problem, it is instructive to consider the educational experience of physicians. Educated and trained to look for underlying disease causes, the medical professional is often at a loss to understand the reluctance of patients to adhere to even simple recommendations.

The disease model, which is premier in medical training, implies that for every disease there is a specific causative agent for the patient's illness (4). For diseases such as syphilis, gonorrhea, or tuberculosis it has been possible to discover a single antecedent agent and effect a cure. While such a model is of great value within the domain of infectious disease, the transition to a behavioral approach is not without pitfalls.

We who care for adolescents are constantly faced with the stereotypes of adolescents as abusers of nonprescribed drugs on the one hand and nonusers of prescribed drugs on the other hand (3). These commonly held beliefs often result in a different standard of care for this age group since this problem has only recently undergone serious study and many questions remain unanswered. Are all adolescents noncompliant? Is noncompliance related to the characteristics of illness or features of the medical regimen? Does the adolescent's level of physical or psychosocial development influence the degree of compliance noted? These and other questions must be answered if our adolescent patients are to be well served. This article will focus on the issue of adolescent compliance with medical regimens. Past re-

lated to a large degree through modification of the general public's behavior. However, the transition from an emphasis on infectious-type illnesses to diseases that are generally influenced by an individual's lifestyle warrants certain changes and assumptions that have not been readily accepted by either the public or the medical profession. In order to fully comprehend the resistance that the medical profession may experience when dealing with compliance as a behavioral problem, it is instructive to consider the educational experience of physicians. Educated and trained to look for underlying disease causes, the medical professional is often at a loss to understand the reluctance of patients to adhere to even simple recommendations.

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search in this area will be reviewed and recommendations suggested that may enable physicians to enhance the compliance of their adolescent patients.

### *Compliance—a Definition*

Compliance has been defined as the extent to which a person's behavior (in terms of taking medications, following diets, or executing lifestyle changes) coincides with medical or health advice. The terms "adherence" and "conformity" may be used interchangeably with "compliance." Just as it is important to note factors associated with compliant behavior, it is important to be aware of patterns of noncompliance (3). In studies involving adult patients, several types of noncompliance have been detailed. The first is complete failure to take the prescribed medication. This group can include patients who continue to see their physician but take virtually no medication as well as a greater number of patients who drop out of treatment or are lost to follow-up. Other groups include patients who take their medications, but not as instructed, and patients who miss several doses of medication. Increasing or reducing the dose or number of doses of medication, taking medication for the wrong purpose, or taking medicines that are out of date or have been discontinued by the physician are patterns of noncompliant behavior.

### *Incidence of Noncompliance*

Most studies of noncompliance have focused either on adults or both children and adults with relatively few studies including only children or adolescents. The studies involving children tend to show different results than those involving adults since they not only measure the compliance of the patient, but also of the parent. Of nine reported studies of noncompliance relating only to children, the average rate of compliance was 54% (6-14). However, these studies involved both clinic settings and physicians' offices and included determination of long-term and short-term compliance, as well as measuring compliance with both medication and routine health counseling. Consequently, this figure of 54% encompasses too much diversity to be of value except to indicate that compliance in children is generally low. The belief that adolescents are more noncompliant than younger children is not supported by a study using salicylate levels in juvenile rheumatoid arthritis patients as a measure of compliance (15). In contrast, Korsch's study of compliance among renal

transplant patients found more noncompliance among adolescents than children (16). Similarly, adolescents who have been prescribed steroid medication for the treatment of malignancy were more noncompliant than younger children (17). Finally, in a study evaluating theophylline compliance in adolescent patients with chronic asthma, only 10% of the patients were found to have serum levels in a therapeutic range (18).

It has been reported that there is more noncompliance associated with long-term prescriptions than with those of shorter duration (3). In a pediatric study of compliance with short-term medication therapy prescribed in clinics staffed by house officers, only 18% of patients were taking penicillin on the ninth day of treatment for streptococcal pharyngitis, impetigo, and otitis media (7). In a second study, only 7% of clinic patients completed 10 days of therapy for otitis media (8). In a study of compliance with long-term medication therapy in a rheumatology clinic, 55% of both younger children and adolescents were found to have good compliance (15). According to Sackett (1), a U- or J-shaped curve is typical of long-term regimens of asymptomatic conditions, with roughly one-third of the patients taking no medication, one-third almost all, and one-third distributed between these extremes.

### *Methods of Measuring Compliance*

#### *Direct Measures*

Quantitative or qualitative analysis of body fluids to determine the presence or absence or actual levels of the prescribed medication, its metabolite, or an added marker substance provides the most objective compliance measure. Determinations of serum levels of anticonvulsants, salicylates, digoxin, and theophylline are frequently utilized in a clinical setting (19,20). However, direct measures are limited by bioavailability of the drug resulting from interactions with other medication, interference by food, or individual differences in rates of metabolism (21,22). These problems might inadvertently lower the drug analyzed and result in an incorrect assessment of patient compliance. In addition to these methodological limitations, the use of blood as a compliance measure is further limited by the necessity of performing a venipuncture (23). The fact that this procedure is painful, time-consuming, and frequently aesthetically unacceptable to the adolescent patient has encouraged increased interest in developing methodologies for analyzing drug or metabolite lev-

els in body fluids that can be more readily obtained (24). The reliability of anticonvulsant, theophylline, and digoxin levels in saliva has been demonstrated in clinical trials (25-29). Friedman et al. have shown that salivary levels of anticonvulsant correlate better with appointment adherence and other measures of compliance in adolescent patients than traditional serum phenobarbital levels (30). Moreover, routine quantitative analysis of body fluids to monitor compliance with a medical regimen is frequently impractical because of the cost factor.

Certain qualitative tests are more practical, as well as adaptable, to office practice. A bioassay for determining a patient's compliance with penicillin therapy has been described (31). Certain substances such as mefenamic acid, flufenamic acid, and riboflavin fluoresce when present in urine exposed to fluorescent light (3). Riboflavin combined with oral contraceptives has been used as an effective measure of adolescent compliance with contraceptive regimens in our ongoing studies (32,33).

Although it has been suggested that the act of collecting specimens will itself increase compliance, this has not proven to be the case. Gordis et al. has found good concordance between levels of penicillin found in urine specimens collected during unannounced home visits and those obtained at the time of clinic visits (34).

### Indirect Measures

When used alone, methods utilizing any step other than analysis of body fluid can only provide clues about compliance. In combination, however, they may provide as much information as do more objective measures. The most commonly used methods include pill counts, self-report, physician assessment, and outcome assessment (35). Pill counts are commonly used to monitor compliance in research settings but are not very practical in most clinical settings (3). This method requires the patient to return the medication bottle at the time of the visit so that the remaining pills may be counted and discrepancies between the number remaining and those that should have been utilized documented. If the situation warrants pill counts taken at home, visits by the physician or a visiting nurse will provide a quantitative measure of compliance during the preceding period. A situation in which a home visit for a pill count might be indicated is when a patient with a seizure disorder denies missing or forgetting medication and continues to have problems despite prescription of large doses of appropriate antiepi-

leptic agents. On the other hand, counting pills that an adolescent brings to the office or clinic is probably no more accurate than simply asking the patient whether he or she is taking the medication, since noncompliers often fail to bring their pills or alter the amount of medication in the container to reflect better than actual compliance (36).

Asking the patient (self-report) if he or she is taking the medication as prescribed is yet another parameter to assess patient compliance. If this is done in a nonthreatening, nonjudgmental manner, about half of the noncompliant patients will admit to missing at least some of their doses (37). An important point to remember is that even patients who confess that they are not taking some of their medication will overestimate the extent of their compliance (by about 20% on the average) (35). Thus, the admission of any noncompliance should be taken as an indicator for implementing compliance-improving strategies. Furthermore, half of the noncompliers will deny that they are not following a prescribed regimen so that more elaborate methods of determining noncompliance must be employed. Despite these limitations, "asking the patient" has advantages: it is easy and there is a much better correlation between reported and actual compliance than between therapeutic response and compliance (37). In our oral contraceptive compliance study, we found that adolescent's self-reports correlated well with serum norethindrone and urinary riboflavin measures (33). Moreover, in a study by Sackett and Haynes, the only patients who responded favorably to intervention strategies designed to improve compliance were those who themselves had initially admitted noncompliance (38).

Monitoring a patient's response to treatment is not a very effective way to assess compliance because with most therapies the correlation between drug dosage and therapeutic response is far from perfect. However, monitoring patient responses does help to narrow the search for the noncomplier. If a patient fails to respond to usually adequate doses of a drug, noncompliance should be considered as a possible reason. It is much easier to evaluate a patient's therapeutic response if successive assessments are recorded in the form of a graph on the patient's chart rather than buried in the physician's handwritten notes on the patient. A graph can also be useful for explaining to the patient why further efforts are required to bring the condition under control (35). However, we must always remember that patients may fail to display clinical improvement for reasons other than that the prescribed medication

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has not been taken. In short, assessment of treatment effect as an index of compliance can be but one measure in assessing patient compliance with medication.

Monitoring appointment adherence is yet another tactic for measuring compliance because it is relatively easy to do and because dropping out of care entirely is one of the most common and most serious forms of noncompliance with chronic medical regimens. If attendance is to be monitored effectively, patients must be given specific appointments for their next visit before they leave the office or clinic, even if they are not sure of their schedule and must call back to change their appointment (35).

Clinical judgement or physician estimate of compliance is probably the most common method physicians use to assess compliance. It would be logical to assume that experienced physicians might become adept at estimating compliance among their own patients. A number of studies have examined this hypothesis, with discouraging results. In one study by Davis (39), medical students were found to be better than attending physicians in identifying patient noncompliance. A study of pediatricians in private practice found that these physicians' predictions of compliance were no better than chance alone and that compliance tended to be overestimated (6). Whether it is because physicians need to believe that the patient follows their advice and accepts their authority or simply because of a low index of suspicion, the physician's estimate of the patient's compliance cannot be relied upon as an accurate measure in most clinical situations.

### *Noncompliance as a Diagnostic Issue*

Compliance is usually defined in absolute terms and patients are described as either compliant or noncompliant. However, the physician who limits his investigation of this important clinical issue to the labeling of noncompliance as aberrant behavior does this group of patients a great disservice. A better goal is to move beyond the identification of noncompliance and to recognize it as a diagnostic problem. The physician's first and most critical task is to differentiate between noncompliance secondary to 1) sociocultural factors, 2) psychological dysfunction, 3) physiological dysfunction, 4) patients whose noncompliance is appropriate, and 5) those whose noncompliance is iatrogenically induced (1,40).

Factors such as lower social, cultural, and economic status may all be linked to noncompliance. If, for example, the patient cannot afford medica-

tion, he will not have a prescription filled. Psychological factors also can contribute to noncompliance. Psychotic states, phobic conditions, and obsessional preoccupations can present themselves as noncompliance in a patient. Also, apathy, inertia, helplessness, and hopelessness may also be manifested as noncompliance. Certain pathophysiological processes and, in particular, the organic mental syndromes may result in noncompliance behavior as a consequence of impaired memory and cognition (41). The ingestion of psychotropic drugs, antihypertensive agents, and chemotherapeutic medications may also produce confusional states that lead to noncompliance. Finally, a patient's capacity to comply with a medical regimen may also be compromised by physical phenomena such as severe pain, extreme anxiety, or impaired hearing or vision (41).

Previously, the term "noncompliance" has been used to refer to patients who have been told of the necessity of an established medical regimen and have full confidence in their physician but fail to follow medical recommendations. In contrast, those patients who consciously chose not to comply with their physician's prescription because they questioned his judgment or believed the therapy to be inappropriate would not, strictly speaking, be classified as noncompliant.

Finally, there are certain iatrogenic cases where a physician can initiate or accentuate noncompliance. If an adolescent does not comply with an antibiotic regimen because he does not understand why he should take a particular pill four times a day, how the pill works, and how it will make him better, the physician has essentially contributed to noncompliance.

### *Theoretical Approaches to Compliance Research*

#### **Individualistic Models**

The most common approach to the study of nonconforming health behavior has been to identify individual factors that are associated with various forms of noncompliance (42). The assumption has been that noncompliant patients possess a unique set of characteristics that differentiate them from compliant patients. Based on this assumption, research has been directed at discovering individual factors that identify compliant versus noncompliant patients. Behavioral scientists have focused primarily on social, demographic, and personality variables that are associated with compliance. However, much of this research has produced inconsistent findings.

Haynes et al. (43) report in their annotated bibliography that substantially more studies have found positive than negative associations between compliant behavior and age, education, socioeconomic status, occupational status, and income (6,44-57). Significant associations have also been found between compliance and sex, race, marital status, ethnic background, and religion (44-57). The problem is that more studies have reported no statistical association between these factors and compliance than all the studies with significant positive and negative associations combined (43). The only exception appears to be that the very young and the very old tend to be more noncompliant and make more medication errors (44-58).

Inconsistent results have also been reported for intelligence, anxiety, defensiveness, internalization, authoritarianism, Rorschach scores, and MMPI scores (59-67). Attitudinal orientations such as locus of control (68-71), future orientation, and concept of self have also produced nonpredictive or contradictory associations with compliance (44,50,56,68-71). The only consistent findings have been that both adult and adolescent psychiatric patients (particularly those with schizophrenia, paranoia, or personality disorders) tend to demonstrate higher noncompliance with medications and appointment keeping (72). Litt et al. (73) are currently in the process of studying the impact of self image as well as the achievement of developmental tasks of adolescence as determinants of compliance.

Although no single factor can predict whether a patient will adhere to medical advice, there is some evidence that adult patients do not behave consistently across different situations and when following different types of medical advice (43). On the other hand, a recent study of adolescents suggests consistency of compliance behavior with various medical regimens (74). One of the problems with the individualistic model's approach to explaining conforming health behavior is its failure to take into consideration the possible interactions between behavioral, psychological, environmental, structural, and physical and/or medical variables. A second weakness of the individualistic model is that too much emphasis is placed on patient characteristics and too little on the health-care provider (43).

### Health-Belief Model

Multivariable models have been more successful in predicting conformity with medical advice (43). Among these, the model that has received the most

attention and study, and which has influenced much additional research, has been the Health-Belief Model (HBM). Based on a well-established body of socio-psychological theory developed by Lewin et al. (71), the HBM postulates that health behavior is a function of: 1) susceptibility to the particular illness perceived by patients; 2) the degree of severity or the consequences (physical and/or social) which might result from contracting the condition; 3) the perceived benefits or efficacy in preventing or reducing susceptibility if the health action is taken; and 4) the physical, psychological, financial, and other barriers or costs related to the particular health behavior (72,75,76).

A number of studies have found positive associations between patients' perceptions of their susceptibility or vulnerability to a particular disease and compliance with the prescribed medical advice. These include immunizations against various illnesses (77-80), well-child clinic visits (81), and long-term penicillin prophylaxis for rheumatic fever (82). Becker et al. (83) reported strong correlations between mothers' appointment adherence and compliance with penicillin regimens for otitis media and perceptions of their child's resusceptibility. The mothers' belief in the accuracy of the diagnosis and their perceptions that the child was "easily susceptible to disease" resulted in improved compliance. A high index of perceived susceptibility has also been found to be correlated with greater compliance with dietary regimens for obese children (71,84,85) and drug regimens to prevent or control asthma attacks in children (86). However, two studies have reported inverse relationships between susceptibility and compliance. Persons who were more likely to use the dentist preventively (87) and persons who were compliant with prophylaxis medication for rheumatic fever (49) tended to report low resusceptibility perceptions. These findings suggest that not only do perceptions of susceptibility increase compliance, but successful preventive health behavior can in turn lower a person's feelings of vulnerability to disease.

Research on the relationship between perceptions of severity of illness and patient conformity with medical advice have produced contradictory results. Becker (83) reported that the level of perceived severity of health problems (either self or one's child) regularly predicts compliance with prescribed medications. Similarly, perceptions of severity are also associated with preventive health behavior such as postpartum contraception (88) and bringing a child to a clinic for preventive care (81). However, no associations were found between perceptions of the



severity of illness and participation in several types of disease screening or immunization programs (89,90). Becker proposed that, for asymptomatic individuals, very low levels of perceived severity are not sufficiently motivating to increase compliance, and very high levels of perceived severity tend to inhibit or immobilize preventive health behavior (76). In summary, the data suggest that fear of a particular disease can lead to acceptance of medical advice and increased compliance. Yet, once a threshold of fearfulness is reached, it is unlikely that any increase in perceived severity will enhance conformity with medical advice (76).

The next component of the HBM is the patient's evaluation of the perceived benefits of conforming with medical advice versus the costs of compliant behavior. A number of studies have reported significant positive relationships between beliefs in the accuracy of the physician's diagnosis, the value of the physician's medical advice, the accuracy of a diagnostic test, or the efficacy of the prescribed medication and/or other therapies and compliance (72,75,76,81,83,86,89,90). For example, Heinzelmann (82) found that belief in the ability of penicillin to prevent recurrence of rheumatic fever was predictive of compliance with the drug regimen. Only Gordis (49) was unable to find a relationship between belief in the efficacy of prophylaxis to prevent future illness and long-term compliance.

The perceived costs of compliance are many. Uncertainty about a medication's safety or side effects have been found to be associated with noncompliance. Concerns about pain, discomfort, or monetary cost resulting from a prescribed health regimen are also negatively associated with compliance (83,87,91,92). Haynes (43) points out that patients who must acquire new habits, such as taking medications, will exhibit greater compliance than patients who must alter old habits, such as dietary or vocational habits, or must break personal habits, such as smoking or drinking. Such behavioral changes often represent substantial costs to the patient that usually outweigh the perceived benefits of the compliant behavior. Only when the perceived susceptibility and severity are at optimal levels will the perceived benefits of changing one's lifestyle outweigh the costs.

Other important costs to compliant health behavior are the perceived barriers encountered during interaction with the health-care delivery system. For example, compliance is greater when continuity of care is provided, in contrast to when the prescription is made in an emergency-room setting. Greater com-

pliance has also been reported by members of prepaid medical practices than in pay-for-service programs (93). The nature of the provider-patient interaction also appears to be an important determinant of compliance with medical advice (42), and will be discussed in more detail. Briefly, the clinical setting and practitioner can have important effects on compliance. Long waiting times at office or clinic visits are strong deterrents to continuing treatment (35). The patient's satisfaction with the physician, the type of physician, and the patient's perception of the physician's demeanor have been studied to better understand the factors that influence compliance. In pediatric studies, doctors who were described by the patient's mother as responsible, organized, and intelligent achieved greater compliance with their recommendations (6). Also influencing compliance is patient satisfaction with care. In a study of adolescent patients' compliance with appointment keeping, it was found that having a consistent physician and scoring high on a standardized adolescent patient satisfaction questionnaire were associated with good compliance (3).

The treatment regimen also has a powerful effect on compliance. The longer the duration of treatment and the more complicated the regimen, the more difficult it is to maintain compliance. Simultaneous prescription of more than one medication reduces the likelihood of compliance, as does the prescription of multiple rather than single doses. The decline of compliance rates over time has been demonstrated. Haynes (36-38) reported that only 63% of hypertensive patients continued to take their medication after two years. In the pediatric literature, compliance with medication, even for acute conditions, falls off dramatically soon after the patient has symptomatically improved.

An important component of the HBM that has never been experimentally tested for compliance is the "cue to action" (76). The HBM stipulates that a cue to action or stimulus must occur to trigger the appropriate behavior by making the individual consciously aware of his feelings about the health threat. Such cues can be either internal (physical symptoms) or external (mass media campaigns, interpersonal interactions, or advice from a health provider). Much additional research is needed on what "cues" trigger a patient to compliant behavior.

While there is empirical support for several of the components of the HBM, it does have some limitations. As Svarstad points out, the HBM tends to neglect the possibility that noncompliance can be unintentional (42). Patients who may be motivated



to take their medication may not take the medication correctly for reasons such as not remembering or understanding the physician's instructions. Second, the HBM does not clearly specify the determinants of patient motivation (42). The HBM hypothesizes that various social agents or cues-to-action, such as a health-care provider, can affect patient motivation, but the model does not specify how such social influences as cues-to-action occur or why they might fail (72). Becker proposes that each component of the model should undergo experimental testing. While Becker et al. (76) have experimentally tested the "severity" component with success, all other tests of the HBM have been subexperimental. Finally, like the individualistic models, the HBM places too much emphasis on the patient and not enough emphasis on the process by which health-care providers transmit their expectations and attempt to motivate their patients (42).

### The Provider-Patient Relationship

It has been proposed that the interaction or relationship between the health-care provider and the patient is one of the primary determinants of compliance (94). Although much has been written on the relationship between physician-patient interaction and patient compliance with medical advice, few empirical studies have been conducted.

In a series of studies on patient-physician interaction utilizing Bale's Interaction Process Analysis, Davis reported that patients were more compliant if the physician had provided suggestions and opinions and if the patients had asked for the physician's suggestions, expressed agreement with the physician, and expressed tension release (39,95,96). If the patients gave their own opinion and if the physician engaged in passive acceptance of the patient's active participation in the encounter, asked the patient questions without giving feedback, or expressed disagreement with the patient, then less compliance was demonstrated. Korsch et al. (97,98) conducted a similar study of pediatrician-patient communications and conforming behavior by the parent. Korsch found that physician friendliness or antagonism was significantly related to parent compliance. She also found that those patients that were more active in the encounter with the physician were more compliant with medical advice. Differing from Davis's studies were her findings that parental agreement with the pediatrician's opinions, the parents' level of questioning, and the permissiveness of the pediatrician were not associated with patient compli-

ance (97,98). In support of Davis was the finding of higher noncompliance when physicians asked for information without giving any feedback to the patient. The contradictory findings in these studies may be due to the differences in the samples studied. However, Svarstad (42) suggested that the Bales system for analyzing interactions is inadequate for studying the complexity of provider-patient interactions.

Hulka (94) studied various aspects of patient-physician interaction and medication compliance among adult patients with congestive heart disease and diabetes mellitus. She found that, among heart disease patients, the better the quality of communication of instructions and information provided by the physician, the lower the drug error rates. In turn, the patient's level of knowledge about a drug's action was inversely associated with errors of commission and medication errors. In addition, confirming previous reports, more complex medication regimens were associated with increased patient error.

In a detailed study of physician-patient communication, Svarstad identified four major problems with the physician's instructions to the patient (42). First, physicians frequently did not discuss their expectations with the patient in an explicit manner. Second, physicians often failed to give patients written instructions regarding medication use. Third, in 20% of the cases, the pharmacists failed to include all of the physicians' prescription requests on the medicine labels. Last, in 29% of the cases, the physicians gave no information to the patient concerning the purpose and/or names of the drugs to be taken. As expected, the amount of physician instruction was associated with the accuracy of the patients' perceptions of what the physician expected, which in turn was related to compliance with the medical advice.

Svarstad (42) also analyzed various processes often used by physicians to modify patient behavior: friendliness, justification, authority, and emphasis. She found that when a friendly approach to the patient was combined with a high level of instruction concerning medications, higher compliance was achieved. Exerting medical authority by itself was not effective in increasing compliance. However, when instruction was combined with authority, 71% of the patients conformed with the treatment plan. In addition, when physicians placed emphasis on their expectations, 65% of the patients subsequently conformed with advice. Svarstad also found that when physicians engaged in extensive monitoring or fol-

low-up of the patient's compliance, 52% of the patients conformed with advice. In contrast, under less intense monitoring conditions, only 26% of the patients conformed. These data suggest that when physicians engaged in more extensive follow-up, their patients were more apt to express their complaints and to admit that they had not been conforming with previous advice. When the patient admitted non-compliance and/or complained that the medication did not help or caused side effects, the physician tended to make a greater effort to motivate the patient. Under these conditions, physicians were more apt to express friendliness, provide justification for the medication, exert authority, emphasize what was expected, or engage in more intense efforts to enhance compliance.

In conclusion, the findings from these studies suggest that despite the characteristics of the patient, the behavior of the health-care provider can largely determine whether the adult patient will be compliant or not with the medical advice. Further study will determine if adolescents behave in a similar manner.

### *Adolescent Compliance with Oral Contraceptives*

A particularly frustrating problem for those caring for adolescents is the issue of noncompliance with oral contraceptives, which has been shown to be an important antecedent of adolescent pregnancy (99,100). While a variety of medical, social, psychological, and economic factors have been found to be associated with contraceptive use and adolescent pregnancy (100-107), little is known about why many adolescents fail to comply with their contraceptive regimen (105). We are now aware that knowledge of contraceptive availability is not enough to prevent adolescent pregnancy and other modalities must be employed to reach our adolescent population.

In an effort to identify adolescents at risk of non-compliance with oral contraceptives, Litt et al. (108), in a retrospective study, evaluated the influence of a variety of sociomedical factors on contraceptive compliance. They found that adolescent females who 1) made their own clinic appointment, 2) came to the clinic specifically to receive some form of birth control or see a physician about a specific medical problem, 3) were willing to receive birth control at the initial visit, 4) had sexual intercourse two or more times a week, and 5) had only one sexual partner in the last three months were significantly more compliant with their birth control regimens over a three-

month study period. When the first four of these factors were combined in a model "with method of payment" it was possible to correctly predict compliance in 72% of the cases.

In a similarly designed retrospective study, Scher et al. (107) found seven factors to be significantly associated with oral contraceptive compliance in adolescents. They reported that if the adolescent's parent made the clinic appointment and accompanied the patient to the clinic, significantly higher compliance was obtained. Adolescents were also more compliant if they considered the physician helpful and were satisfied with the clinic. If the adolescent expressed satisfaction with the pill and if no side effects from the pill were experienced, the adolescent tended to be more compliant. Finally, if the adolescent expressed a desire to go to college, higher compliance was demonstrated. These findings are congruent with the interaction models proposed by Hulka (94) and Svarstad (42). However, unlike Litt et al. (108), Scher et al. (107) did not attempt to build a predictive model from those variables found significantly associated with compliance.

In a prospective study, DuRant et al. (32) tested the influence of psychosocial factors on adolescent compliance with oral contraceptives over a four-month period. They identified six factors that were associated with noncompliance: multiple sexual partners during the previous three months; appointment made by the adolescent; low evaluation of personal health or well-being; feelings of hopelessness; worry about becoming pregnant; and having had a previous abortion.

In a follow-up study, Jay et al. tested the effect of using peer counselors compared to nurse counselors on adolescent compliance with oral contraceptives (109). Fifty-seven females aged 14-19 from a lower socioeconomic background were randomly assigned to either a peer- or nurse-counselor group. At the initial visit and at 1-, 2-, and 4-month follow-up visits, subjects received Ortho-Novum 1/35 combined with a tablet marker and were counseled by a nurse or peer. Noncompliance was measured using a Guttman scale consisting of: 1) avoidance of pregnancy; 2) appointment adherence; 3) pill count; and 4) urinary fluorescence for riboflavin. At the first and second follow-ups, the adolescents counseled by a peer had a significantly lower noncompliance level than the nurse-counseled group. Several other factors were found to significantly influence how these adolescents responded to either a peer or nurse counselor. Adolescents having greater sexual frequency, with one sexual partner, who worried that



they might become pregnant had significantly lower noncompliance when counseled by a peer than by a nurse. At the fourth month, follow-up adolescents who expressed feelings of hopelessness about the future had a significantly higher noncompliance when counseled by a nurse than when counseled by a peer (109).

Confirming previous reports (42), our findings suggest that the nature of the interaction between the health-care provider and the patient, combined with the adolescent's sexual behavior and social psychological status, may influence how compliant she will be with her oral contraceptive regimen. More ongoing research that will allow physicians to identify adolescents at risk of noncompliance so that appropriate intervention strategies may be employed is needed in this area.

### *Improving Adolescent Compliance with Therapeutic Regimens*

Health-care providers who wish to increase the likelihood that adolescent patients will follow prescribed treatment regimens have a variety of strategies from which to choose. However, the physician should first consider certain ethical issues implicit in such a decision. First, the practitioner must ensure that the diagnosis is correct and that the efficacy of the prescribed treatment has been established. Second, the patient must be an informed and willing partner in any attempt to increase compliance. Finally, the techniques utilized to improve compliance should have strong research support. In general, this would mean that they have been tested in controlled clinical trials and produced statistically significant and clinically important increases in compliance and concomitant improvements in therapeutic outcome.

Compliance with therapeutic regimens of less than two weeks' duration falls off rapidly, presumably as the patient's symptoms improve or fail to improve despite treatment (43). Near maximal levels of compliance with short-term therapy can be achieved by a number of techniques (1), the simplest of which is to clearly explain to the patient that the medication should be continued until the full treatment course has been taken. Written instructions should also accompany the verbal information regarding the treatment plan. An alternative to this approach may be intramuscular injections, where applicable. However, such strategies may not be necessary in view of the success of straightforward instructions (35). Another approach that has not been thoroughly evaluated experimentally, although it is employed

widely clinically, is to administer a drug in one large dose, e.g., for a urinary tract infection (110).

Maintaining good patient compliance with chronic medical regimens is a more difficult task. There is no single approach that will ensure good compliance. In order to be successful in ensuring compliance, a number of strategies must be utilized. Long waiting times for appointments and complex lists of medications are strong deterrents to compliance and should be avoided, if possible. Often, scheduling appointments at times that are convenient for both practitioner and patient can avoid the first problem.

Organizing a clinic or office to promote compliance is essential. In one study, when an ambulatory pediatric facility was upgraded from an episodic-care clinic to a primary-care unit providing more convenient hours and continuous, comprehensive care, compliance in appointment keeping increased from 65% to 81% (111).

The type and duration of therapy, as well as its cost and the presence of side effects, have been investigated as determinants of compliance. Contrary to popular belief, these studies have shown that neither side effects, medication cost, nor the form of medication (liquid versus pill) is responsible for poor compliance. The complexity of the drug regimen and duration have proved important (112). Simultaneous prescription of more than one medication reduces the likelihood of compliance, as does the prescription of multiple rather than single doses. However, although treatments should be as simple as possible, compliance is not always satisfactory even with once or twice daily regimens, and additional maneuvers are often necessary.

*Cueing compliance.* The patient should be reminded about the importance of compliance at each and every visit. In addition, many patients do not naturally take their medications at the same time each day and, thus, frequently forget or miss a dose. Physicians can help these patients by examining their daily routines and identifying daily activities that can serve as "cues" for taking medication (3). For example, if an adolescent brushes her teeth each morning on arising, it can be suggested that she take her pill following this task. The ritual of brushing the teeth can act as a cue to compliance. Other similar tactics include asking a reliable family member to remind the patient to take medication or having the patient regularly monitor and record some measure of his or her therapeutic response and bring results to office visits. Again, cueing alone will seldom be sufficient to ensure a high degree of com-



pliance. Furthermore, it remains questionable as to whether increased parental supervision of adolescent patients will achieve the desired result of increased compliance. If the youngster is engaged in a struggle for independence and autonomy, an intervention strategy that interferes with this phase of adolescence may actually be counterproductive. Supervision by a nurse or even a best friend may be an alternative if the adolescent appears receptive. We tested the effect of using peer counselors in an oral contraceptive study and determined that they are effective adjuncts to the health-care team (109).

*Improving the physician-patient relationship.* The most productive methods for improving compliance are frequently overlooked by the health-care provider. For example, simply paying more attention to the patient will improve compliance, particularly if the additional time spent with the patient is focused on compliance. First, and probably most important, patients should be contacted if they miss appointments and should be encouraged to reschedule them. Second, it has been found that physicians can encourage better compliance by redistributing the time they spend with the patient so that the discussion of compliance is given more importance (35). In addition, increasing the frequency of appointments when a health condition is not being adequately controlled enhances compliance. Similarly, increasing the number of people who pay attention to the patient can improve compliance (112). Having other health care professionals such as nurses, pharmacists, and health educators, as well as the patient's family and friends, reinforce the need for compliance can be helpful. Obviously, if these efforts are well-coordinated the process will be more efficient. In general, it appears that it is the frequency of these encounters rather than their duration that is important (35). A one-hour period of time spent with a patient yearly is less effective than monthly contacts of five minutes each provided that the time at each visit is spent productively. As discussed earlier, physicians who clearly emphasize what is expected of the patient in a friendly manner and provide explanation and justification for the prescription will have enhanced compliance.

*Rewarding and reinforcing compliance.* A basic principle of behavioral modification is that behaviors that are rewarded tend to be repeated, while behaviors that are not rewarded tend to stop. This principle seems to underlie many successful compliance strategies. In some instances, the operative reward has

been a tangible object such as tokens or return of an initial monetary deposit (113,114). However, in other cases the reward has simply been encouragement from the physician. Recognition and praise for good or improving compliance are reinforcers that should be applied where indicated in clinical settings. Along these lines, a combination of strategies that has proven fruitful is to have the patient keep records of his or her compliance and treatment response and present them at each visit for assessment and reward, if appropriate (35). However, it is important to remember that the efficacy of a reward system is complex and that the type of reward is critical, especially for adolescents. For example, the "reward" of good health or increased longevity is too abstract for most adolescents (3).

It is worth remembering that strategies from at least two of the above categories are needed if compliance is to be improved. It is unclear whether this is due to the fact that responses to compliance tactics are subject to individual variation or to the fact that no single approach is compelling enough to have a clinically important effect. Second and equally important, there is no single remedy for noncompliance and successful strategies for improving compliance must be continued for as long as compliance is required. [Table 1]

In conclusion, compliance behavior among adolescents is complex and incompletely understood. Although the study of compliance is important for understanding the adolescent's developmental progress, its true importance lies in improving the likelihood that medication will be appropriately utilized. Systematic monitoring of compliance, rather

**Table 1. Strategies for Enhancing Patient Compliance**

1. Attempt to establish a good relationship with the adolescent.
2. Consider the possibility of noncompliance.
3. Reduce barriers to compliance (e.g., long waiting times, inconvenient hours).
4. Instructions should be emphatic, structured, and written so that they may be posted in a convenient place at home.
5. Patients should be provided with an explanation and justification for the prescription.
6. Simplify the drug regimen as much as possible and cue compliance to specific times of the day and/or to a daily activity.
7. Increase the amount of attention paid to the patient and, by careful follow-up, insure that therapeutic regimens are carried out.
8. Reward and reinforce good or improving compliance, especially in the form of praise and encouragement.

than monitoring only when noncompliance is suspected, is essential, and utilization of compliance strategies should be initiated early. Although compliance with short-term treatments is more easily resolved, ensuring compliance with long-term regimens is a more difficult task to achieve. Combining strategies aimed at reducing barriers to compliance, cueing compliance, paying increased attention to the adolescent patient, and rewarding or reinforcing medication adherence are all necessary to enhance compliant behavior.

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Editor:



## MEDICAL NONCOMPLIANCE

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### ABSTRACT

Increasingly recognized as a major medical health problem, non-compliant patient behavior remains one of the least understood and most frustrating phenomena facing today's physicians. Although no single characteristic of behavior adequately defines the potential non-complier, a variety of factors raises the index of physician suspicion. This paper examines four general categories affecting non-compliant behavior: patient factors, illness factors, therapeutic regimen factors, and physician-patient interaction factors. Based on these elements, a set of management implications is defined and discussed as possible deterrents to non-compliant behavior.

Increasingly recognized and studied as a major medical health problem, non-compliant patient behavior remains one of the least understood, most frustrating phenomena facing today's physicians. In a medical school workshop on noncompliant behavior a second year student commented, "Whose problem is it anyway? Why should we worry about it? All we need to do is tell the patient what they need and then if they don't follow our advice it's their problem." The student group, though, swung to the consensus that noncompliant behavior is indeed a problem for physicians and that attempts to recognize, understand, and, most importantly, minimize its occurrence, are mandated.

Compliant behavior, generally regarded as the extent to which a patient's behavior coincides with clinical prescription, encompasses a variety of behaviors including taking medication, following diets, changing activities or making other

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life style adjustments, following up on referrals, keeping appointments, etc. Although reports on the frequency of noncompliant behavior vary considerably among studies depending on variables such as definition and behavioral measurement, the consistently striking magnitude of noncompliant behavior ranges from 15 to 93 per cent of patients who will not precisely follow prescribed treatment regimens [1]. This paper reviews major determinants of noncompliant patient behavior and offers practical management suggestions.

### SCOPE OF PROBLEM

Sackett and Haynes state from a review of 185 original reports of non-compliant behavior that noncompliance is a protean feature of any therapeutic regimen requiring patient self care [2]. Examining noncompliant behavior in two areas of patient care, appointment keeping, often the entry point to medical care, and following treatment recommendations in both chronic and acute illnesses, suggests the scope of the problem.

Failure of patients to make or keep scheduled appointments is a well documented problem in patient self care. Outpatient psychiatry clinics and community mental health centers, for example, report high attrition rates both after the initial treatment session and during ongoing treatment. In a survey of 137 new patients applying for treatment in a community mental health center, Tantam and Klerman report 32 per cent of patients did not attend at all, and of those attending, 31 per cent dropped out prematurely [3]. Zisook, et al., uncover a 35 per cent dropout rate between the first and second appointments in a university hospital outpatient clinic [4], somewhat less than the 50 per cent attrition rate reported by Rosenthal and Frank for the same time interval [5]. Baekeland and Lundwill find an overall psychotherapy dropout rate of 20 to 57 per cent [6]. Not confined to psychotherapy patients, failure to keep appointments is documented in both prevention and treatment of medical problems. A study of almost 1,000 patients discovered to be hypertensive following a blood pressure screening reveals only 50 per cent of the patients kept the resulting first appointment [7]. Of appointments in 150 peptic ulcer outpatients followed for two years, only 71 per cent of all appointments were kept [8]. Finally, in a study undertaken at a prepaid multispecialty group practice, Hurtado, et al., report over 16 per cent of all scheduled appointments resulted in appointment failure [9].

As a common and chronic illness affecting all age groups, diabetes mellitus lends itself well to noncompliance studies. Gabriele and Parable's study of children in a diabetes summer camp reveals that 61 per cent self-reported not carefully following their diet [10]. Other studies find children admit reporting false positive urine checks in order to get extra attention and even more report false negative tests to avoid anger, get extra sweets, or be granted permission to engage in extra activities. Parents, too, often predict their children as not

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accurately reporting urines, following their diet, or taking insulin properly, and frequently ascribe this behavior to expressions of anger [11]. Among adolescent diabetics, rebellion against parents and the wish to conform to peer group mores occur as common causes of overeating and other self-destructive behavior. Diabetic adults as well engage in noncompliant behavior. Watkins, et al., in home observations of adults, find 77 per cent did not sterilize needles properly while 50 per cent made errors in insulin dosage. Only one-third of the patients tested their urine correctly, and half of the patients used results of urine tests in a way destructive to their diabetic control. In that same study, about three-fourths of the patients had meals and spacing of meals unsatisfactory for diabetes [12].

High noncompliance rates in following treatment recommendations for chronic illnesses other than diabetes mellitus are also documented. In a study of children prescribed oral penicillin for ten days to treat otitis media, half the patients' urine had no traces of penicillin by the fifth day and 60 per cent of patients missed follow-up appointments [13]. Studies of three additional chronic illness patient populations offer similar low compliance rates. In hypertension, for example, probably the leading preventable cause of disease and death, one-eighth of all patients care adequately for themselves. A greater than 50 per cent attrition rate of newly identified hypertension patients occurs within one year of treatment onset and by the end of five years the dropout rate rises to 75 per cent [14]. Looking at adherence behavior associated with use of anti-anxiety medications in a research protocol, Lippman, et al. note a 40 per cent dropout rate by the fourth week of treatment. Of those remaining in treatment, about 30 per cent took less than the prescribed amount of medication, while another 10 per cent took more than the prescribed amount [15]. Another study synthesizes eight months of followup data on outpatients treated with prednisolone for arthritis. For more than one-half of the observation period, one quarter of the patients were in error by over 25 per cent of the recommended dosage [16].

Even as acute an illness as myocardial infarction has low compliance rates. Most deaths from this illness occur outside the hospital, often due to patient denial of the meaning of chest pains, even among patients warned to call the doctor or report to the hospital at the first sign of such pains. In coronary care units, a surprisingly great number of patients fail to comply. Johnson's study of post-myocardial infarction patients one month after hospitalization finds a compliance rate of 92 per cent in taking medications, but only 25 per cent in avoiding stress and strain. Both rates decreased over time [17].

This highly selective, brief overview of compliant behavior in two areas of patient care indicates the staggering amount of noncompliance that physicians must deal with. This behavior occurs in diverse behavioral patterns and in a variety of medical conditions where patient adherence to a regimen may be life-saving. Yet compliant behavior is frequently overlooked, underestimated,

and poorly understood by many physicians dealing with this essential health concern.

### PHYSICIAN SENSITIVITY

Physician sensitivity is a major variable in patient noncompliance. Most studies reveal physicians as either unable to predict or recognize noncompliant patients with any greater than chance probability [1, 18]. Even when noncompliance is recognized, the traditional physician assessments are inadequate. Sixty-seven per cent of senior physicians in Davis' study attributed noncompliance to the patient's "uncooperative personality" with only 26 per cent postulating physician factors as possibly contributing to the behavior [1]. When asked what they do to minimize noncompliance, most physicians would reply taking the following steps, in order:

1. thorough explanation of the regimen;
2. persuasion by rational argument;
3. threat tactics; and
4. withdrawal from the case.

None of these takes into account primary prevention, respect for the patient's point of view or beliefs, negotiations between different views, or appreciation of sociocultural factors. The first two steps imply that knowledge in and of itself insures compliance, never yet shown to be true [19]. The third step implies that arousing a patient's fear enhances compliance, but fear often evokes flight or fight behavior [20]. Finally, the fourth step, withdrawal from the case, helps no one [21].

### FACTORS ASSOCIATED WITH NONCOMPLIANCE

A number of studies attempt to identify the determinants of noncompliant behavior. The results, frequently inconclusive and contradictory, do not yet adequately explain the problem of compliance behavior. However, variables identified as contributing to noncompliant behavior have emerged: patient factors, illness factors, treatment factors, and patient-physician interaction factors.

#### Patient Factors

Demographic characteristics are probably the most often looked at of patient factors. Such characteristics, including age, sex, education, socioeconomic status, occupational status, income, marital status, race and religion have generally borne no consistent relationship to compliant behavior. While personality types have failed to be uniformly linked to either compliant or noncompliant behavior, certain personality traits, given specific illness and doctor combinations, may affect compliance rates. Kahana and Bibring outline seven personality types, often encountered in medical practices, that interact



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with response to illness and treatment [22]. For example, a very orderly or controlled person may see illness as a loss of control. If not provided some sense of control by the physician, such as precise and systematic explanation of the regimen, such a patient may become too anxious to accept the expected sick role and exert self control through noncompliant behavior.

The patient's psychological status has also been examined as a contributing factor in noncompliance. To comply, a patient must be sufficiently uncomfortable with or concerned about the illness. If too comfortable, the patient may lack sufficient motivation to adhere to a treatment regimen. On the other hand, if too uncomfortable, the patient may develop depression with its attendant hopelessness and failure to take positive action, or, feeling overwhelmed, may deny the fact or significance of the illness. Denial, a common reaction to any illness, and often an adaptive coping mechanism, may create a problem when it interferes with the person's seeking medical help or following through with treatment recommendations.

The social and family circumstances of the patient may also contribute to noncompliant behavior. For example, the position in the family hierarchy may be a crucial determinant of a patient's willingness or ability to follow medical recommendations. Porter's study of general practice patients treated for chronic illnesses identifies living alone as the major variable in nonadherent behavior [23]. Similarly, realistic social and family contingencies as lack of money, lack of transportation or pressing family problems can take priority over treatment adherence and need to be evaluated before therapy is initiated [24].

Perhaps the most crucial patient factor relates to the person's attitudes towards illness, their "health-belief model." [25] This model implies that noncompliers perceive themselves as less susceptible to or less threatened by actual or potential illness. They consider illness less severe and serious than compliers with the same diagnosis, are generally less concerned with their health and believe less in the efficacy of modern medicine. In a health attitude questionnaire reported on by Davis such patients tended to endorse statements like "if you wait long enough you can get over anything," "you only take medicine when you are ill, not when you feel better," "the old fashioned remedies are better than the things you can get at the drug store." [26] For these patients, then, the benefits of treatments appear less obvious and are subsequently less apt to motivate compliant behavior.

Additionally, this group's motivation for health care in general is minimal. For example, mothers of noncompliant children in a pediatric practice frequently were discovered to lack a household thermometer [13]. In one study, fully 40 per cent of noncompliant patients admitted never intending to comply [27]. Another study of psychotherapy dropouts reports a significant relationship between not intending to comply with early treatment attrition [4]. According to the health-belief model, if the perceived cost or barriers of treatment, such as fear of pain, discomfort or monetary expense outweigh

perceived benefits, or if the perceived severity of illness is not great enough, noncompliance is likely to result.

### Illness Factors

Rather than the severity of the illness per se, it is the patient's perception of severity that may determine the likelihood of compliance [25]. Thus, neither specific diagnosis, severity, duration of illness, previous bouts, previous hospitalization or well being seem related to compliance behavior [26]. For this reason, non-symptomatic illnesses such as hypercholesterolemia or uncomplicated essential hypertension carry a greater risk of noncompliance for most people than symptomatic illnesses.

A growing literature differentiates between disease (an error in body machinery) and illness (a person problem) [28, 29]. In most chronic conditions a marked discrepancy between structural abnormality (disease), personal discomfort, and functional impairment exists. Similar degrees of organ pathology may generate quite different reports of distress owing to differences in ethnicity, social setting, and personality. In a comparison of patients with identical signs of middle ear disease Zola found Italian and Jewish patients complained of much more distress than did Irish patients [30]. Beecher reports men with traumatic fractures of the femur resulting from military casualty required far less morphine for pain relief than victims of auto accidents [31]. Eisenberg suggests a case of a healthy patient, coming in for an annual checkup, whose physician discovers a diastolic pressure of 110 and considers placing the person on hypertensive medication. The patient may refuse because he has a disease in the absence of illness; contrawise the patient, entering feeling well, may now consider himself as "not well," begin treatment, and experience the fatigue, depression or loss of libido which are often side effects of anti-hypertensive medication. He is now for the first time "ill" although his "disease" may be considerably improved [32]. It may be easy to see how noncompliance in such a case might ensue, or how a patient may fail to adhere to a therapeutic regimen because (s)he does not accept the reality of the disease in the absence of illness. Thus, it is not simply the "disease" that determines whether or not the patient will follow treatment recommendations, but rather a variety of "illness" factors considered in the "health-sickness" model explained above.

### Treatment Factors

Many factors related to therapeutic regimens affect compliance. The route of administration of medication, for example, may influence compliance. In the treatment of both rheumatic heart disease and chronic schizophrenia, intramuscular medications elicited greater compliance rates than oral administration [2, 33]. Similarly, the therapeutic regimen's degree of complexity relates to

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noncompliance, with an inverse relationship existing between the number of directions given and the degree to which patients follow those directions [24]. Thus, patients are more likely to take one medication daily than two or three medications each day, or even one medication two or three times per day. The duration of therapy is directly related to noncompliance [34], as is the amount of behavioral changes required by the therapeutic regimen [35]. Active cooperation is more readily achieved from patients who must adopt new habits (such as taking medications) than from patients who must alter old habits (diet or vocational) or break established habits such as smoking, drinking, or non-medicinal drug taking.

### Physician-Patient Interaction Factors

Probably the most significant single factor in whether or not the patient will adhere to the treatment regimen lies within the physician-patient relationship. Patient satisfaction with the interaction has been consistently shown to be related to compliance behavior. Francis, et al., in a study conducted in a pediatric clinic, finds mothers are unlikely to comply who are dissatisfied with their doctor's friendliness, ability to understand their concerns and to carry out an active exchange with them. Mothers were more likely to give children a prescribed medication not on the basis of time spent with the physician or on their perceptions of the physician's competence but rather based on the mother's feeling the doctor had praised her as a mother and had established friendly and easy communication with her [24]. A recent study by the California Medical Association reports that the majority of the patients were critical of their physician's behavior, especially the lack of warmth and failure to demonstrate real concern [36]. And Koos reports marked dissatisfaction with medical care in almost 20 per cent of patients. Nearly half the patients criticized physicians for management of office practices, particularly making patients wait weeks for an appointment and hours in their waiting rooms. The strongest criticism, however, was directed at the physician-patient relationship. Patients seemed satisfied with the quality of medical care received but not with its provision. Good human relations proved to be the single most important quality patients look for in a physician, more significant than the physician's competence or service [37].

Patient expectations, an often overlooked component of the doctor-patient relationship, is another crucial determinant of satisfactory medical compliance [24, 38]. When the patient's hopes, desires, and expectations significantly diverge from the physician's, a strained relationship, resulting in poor compliance, is likely. Expectations, generally products of implicit socio-cultural health beliefs and values, must be made explicit, discussed and negotiated before full treatment adherence can be expected. For example, a blue collar worker, expecting his visit to result in immediate pain relief, may well balk at further diagnostic studies unless his expectations are first noted and discussed. Whether



or not differences in expectations are totally resolved, a physician who believes in the therapeutic regimen (s)he is prescribing, and who clearly communicates this belief, is more likely to elicit compliant behavior than the more skeptical physician.

Similarly, the doctor's communication and patient's comprehension of medical recommendations also affect compliance. The amount of information a patient forgets is directly related to the amount given by a physician. The most detailed study on communication problems in the doctor-patient relationship links deviant and difficult physician-patient communication with treatment adherence. Compliance was associated with the three item set of:

1. the patient's expressing agreement with the physician;
2. the patient's attempt to seek the physician's opinions; and
3. tension release in the therapeutic encounter.

Noncompliance, on the other hand, was associated with the contrasting three item set of:

1. the patient's expressing opinions;
2. the physician's exhibiting disagreement, formality or rejection of the patient; and
3. requests by the physicians for information without giving the patient appropriate feedback [39].

When communication is so faulty that the patient never learns, understands or remembers the regimen, noncompliance is likely.

Finally, all studies that look at the degree of supervision within the doctor-patient relationship find a positive correlation with compliance [2]. Therefore, hospitalized patients are more compliant than outpatients. Patients are more compliant when there is a greater frequency of appointments or when home visits are added to the treatment regimen. Referral to a specific doctor yields greater compliance than referral to clinics or groups, which, in turn, is further enhanced when the therapeutic setting is readily accessible in time and place. Similarly, when the physician involves the family in treatment recommendations, particularly in terms of helping them understand the treatment and become involved in its supervision, compliance is more likely to occur.

### MANAGEMENT IMPLICATIONS

The above considerations generate a number of evident management implications. They can be categorized as:

1. recognition;
2. education;
3. negotiation;
4. accommodation; and
5. simplification.

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Underlying these categories is the vital role of an effective doctor-patient relationship, characterized by openness, free communication, mutual respect, acceptance, and empathy.

By *recognizing* all patients as potential noncompliers, the physician may help ward off noncompliant behavior. It is important for the physician to take the time to notice what the patient believes about an illness and the accompanying physician advice. Tactful exploration of the patient's values, habits, life styles, and interpersonal relationships including past experiences with physicians may provide sensitive indicators of potential noncompliance. Asking the patient whether (s)he plans to follow treatment recommendations and what difficulties might be encountered in doing so uncovers ambivalence and facilitates further dialogue.

*Education*, in addition to being a vehicle for imparting didactic information, is a process of meaningful exchange between two active participants. Delivering factual knowledge about the disease or treatment plan is not enough to "educate" the patient, as it is not the illness itself but rather one's perception of the illness that relates to adherence behavior. Much more important, then, is the physician's attempt to understand the patient's unique view of his/her illness so that distortions, misinformation, maladaptive attitudes, beliefs, and perceptions can be identified, clarified and corrected. The patient may need to learn medical facts to better understand the severity of the illness, his/her vulnerability, and the value and efficacy of treatment. To make the therapeutic regimen seem more rational, the patient with chronic illness may require detailed explanations of his/her unique and crucial role in the management of that illness. Physician repetition of directions, particularly with multiple or complex recommendations is an essential feature of the education process, as is intermittent positive reinforcement of adherent behavior. Treatment adherence is further enhanced when the physician invites questions. Generally, open-ended questions ("What questions come to mind?") are more effective than directive questions ("Do you have any questions?") or leading questions ("No questions, are there?"). After fully answering all queries and being confident that the patient understands the replies the physician can ask the patient to repeat when (s)he understands. Finally, family members and significant others may need to be educated to help support the patient and maximize the likelihood of compliance.

If the patient's beliefs, goals, expectations, or wishes differ from the physician's, patient-doctor *negotiation* may help facilitate developing shared goals. The very process of negotiation itself is often helpful [38], as covert goals and wishes become overt and can then be explicitly dealt with. Ignoring such wishes, on the other hand, can lead to disparate goals and culminate in poor compliance. Many patients feel too embarrassed or presumptuous to express their desires and, unless specifically queried, would leave such wishes unspoken. If the physician, on the other hand, makes a point of asking the patient why (s)he were coming, what (s)he hoped to achieve from the visit, and how the

physician might help, the physician could then meaningfully intervene. A patient with hypertension, for example, may come to the physician's office complaining of dizziness and nocturia. Making the correct diagnosis, the physician may then prescribe an anti-hypertensive medication. The patient, perhaps afraid of medication, and covertly desiring only non-somatic treatment such as biofeedback, may not feel free to express these desires and nod compliantly, only to shop for another doctor or ignore the recommendations entirely. In this example, once the patient's wishes were made explicit, the physician could then discuss the appropriateness of the desires, educate the patient and negotiate a mutually acceptable treatment plan which would have a reasonably good chance of being actualized. Thus, considering the patient's wishes and desires is a legitimate, often overlooked aspect of the physician-patient encounter with negotiation of these desires being a vital aspect of management.

But, education and simple negotiation may not be enough when personality traits interfere with compliance. Here, the wisest strategy may need to include *accommodation* [21], whereby management directly incorporates a patient's unique attitudes and customary coping mechanisms. Many patients, for example, need to deny the significance of troublesome events such as an illness. In these patients, it may be prudent to delay treatment while maintaining the physician-patient relationship until the patient indicates at least partial illness acceptance. A very energetic, competitive, activity-oriented person suffering, for example, a myocardial infarct, may find it difficult to follow a regimen of strict bed rest during convalescence. Rather than leaving the patient on his/her own, or risking total disavowal of the treatment plan, the physician might prescribe a program of limited activity while emphasizing the patient's active role in planning and implementing the treatment which will maximize healing. In this, as in most cases, accommodation is best accomplished with negotiation and education. Once partial compliance is attained, negotiation continues for other aspects of the treatment plan. Other forms of accommodation are necessary for a very dependent or anxious patient who may need extra reassurance, time, and anxiety reduction before being expected to follow medical advice; a histrionic patient who needs more attention paid to physical appearance and external reinforcements of self esteem; or a more withdrawn, aloof patient who often needs to be left alone. A long suffering masochistic patient, on the other hand, requires acknowledgement of his/her pain, suffering and sacrifices [22]. For example, a masochistic diabetic patient who refused insulin treatment presented as the only course for recovery later accepted insulin when the physician explained how difficult and burdensome taking the medication would be but how necessary it was for the patient to continue providing for her family. Accommodation, then, requires a knowledge and willingness to work within the customary personality attitudes and coping strategies of the person requiring treatment.



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Finally, *simplification* of therapeutic regimens and other *practical measures* may be useful. The complexity of therapeutic regimens should be minimized as should the number of different directions. If medication is used, for example, the minimum number of different pills taken the minimum number of times each day is advisable. If the half-life of a particular drug is long, it can often be given daily in larger doses rather than two or three times each day in smaller doses. Ancillary aids, such as handouts or pre-packaged medication may also simplify the regimen and enhance compliance. Blackwell finds improved compliance and reduced blood pressures with a week's supply of anti-hypertensive medications packaged in plastic containers and labelled by time of day and day of week [40]. When behavioral changes are required, such as stopping smoking or dieting, it is useful for the physician to provide very precise, readily achievable goals and to expect only one change at a time. Support groups of other patients with similar illnesses, such as Alcoholics Anonymous and weight watchers groups, can help patients adhere to difficult treatment regimens. And, when environmental and social factors prevent optimal compliance, social service agencies may help in planning transportation, financial aid, or dealing with the time problems of follow-up appointments.

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