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- Abbreviations: Ala, alanine; Asn, asparagine; Asp, aspartic acid; Arg, arginine; Cys, half-cystine; Gly, glycine; Gln, glutamine; His, histidine; Ile, isoleucine; Lys, lysine; Leu, leucine; Met, methionine; Phe, phenylalanine; Pro, proline; Ser, serine; Thr, threonine; Tyr, tyrosine; Trp, tryptophan; Val, valine. We thank P. A. Neumann, who first suggested this relationship to us, and G. R. Marshall for their many helpful and stimulating discussions. Supported by research grants from NIH (AM-13362) and a Health Science Advancement Award (5-SO4-FR-06115) to Washington University. W.A.F. is supported vancement Award (5-SO4-FR-06115) to Washington University, W.A.F. is supported by an NSF training grant and R.A.B. is the recipient of a Research Career Development Award from NIH (AM-23968).

The Overmedicated Society: Forces in the Marketplace for Medical Care

Prescribing levels are determined by converging interests of manufacturers, doctors, and others.

Charlotte Muller

Overmedication is one source of reduced human welfare. This reduction is expressed directly in economic terms insofar as avoidable expenditure on drugs occurs. Avoidable expenditure is a class of outlay that includes ineffective drugs and drugs or dosages that do harm to health. Loss of welfare through death, disability, and fetal damage traceable to inappropriate drug use is translatable into economic terms to the extent that productive years are taken away, although accurate measurement of intangible costs is lacking.

The use of a variety of drugs and the use of drugs in frequent doses open the door to confusion and mishaps in the dispensing and distribution of drugs, in adherence by patients to a dosage

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schedule, and even in the prescribing process. The probability of side effects when many drugs are used is not simply additive, but multiple, because of interactions. Besides wasting money on a course of medication, the patient may waste time that could have been invested in a superior method of improving his health. He is also getting less value from the doctor's input because the memory and judgment of the doctor are to some extent devoted to sorting out the properties of the profession's cluttered armamentarium.

The evidence that overprescribing occurs is varied. It includes the sale of specific drugs and classes of drugs in volumes far out of proportion to the known incidence of diseases in which such drugs are of known value, as well as practitioners' own statements of what drugs they select for given diagnoses and purposes. Fixed combinations belong in the group of drugs whose

rational basis has been sharply questioned. The evidence for overmedication also includes the proportion of total prescribing made up of drugs for which the practitioner has only a probable, possible, or placebo expectation of success. The indirect evidence of the content of pharmaceutical advertising is also pertinent. (If the doctor is using the drug for the reasons and symptoms suggested by the advertising, overmedication must exist.) Finally, the uneven quality of the experimental and statistical demonstrations of efficacy used to support marketing approval and to justify prescribing decisions is also indicative of a use of drugs beyond rational limits.

Some of these issues are brought out in connection with psychoactive drugs (part of the class of pharmaceuticals acting on the central nervous system), which accounted for 28.3 percent of total manufacturers' domestic sales of drugs in 1969. An example of the type of promotional efforts conducive to questionable prescribing is found in an advertisement carried in the New England Journal of Medicine for an amphetamine-like substance widely promoted "for children with an entity that is virtually without definite limits." Four physicians from Duke University Medical Center wrote to the journal to express their disturbance over this promotion, stating their belief that the manufacturer "seems to blur intentionally the distinctions between hyperkinesis and minimal brain dysfunction" (1).

The problem of validity of clinical research underlying drug use is illustrated with respect to another class of psychoactive drugs, the antidepressants.

Analysis of the research done to

establish the effectiveness of antidepressant drugs—83 single drugs and 28 combinations—showed, in many of the 490 studies reviewed, great deficiencies in terms of: (i) control groups; (ii) "blind" techniques; (iii) reporting of degree of depression, sex, age, and length of trial; (iv) control for use of adjunctive treatment; (v) regulation of dosage; and (vi) methods used to measure improvement. In general, the less rigorous the technique, the more the improvement (2).

However, the use of antidepressants and other psychoactive drugs has had dramatic practical effects in terms of length of stay and size of resident population in mental hospitals, as well as in cost per hospitalized case. Jerome Levine (3, pp. 5295-5296) presented to a congressional committee figures showing that the choice of psychoactive drugs is rational when related to the various classes of mental disorder in which these drugs are used-for example, doctors rightly prescribe major tranquilizers for schizophrenia. He also argued that the use of psychoactive drugs in general practice is, in the main, justified by medical reasons—the necessity, for example, of relieving anxiety in coronary artery insufficiency.

In contrast, it was pointed out by Henry Brill (3, p. 5316) that the use of minor tranquilizers did not have a dramatic success with ambulatory patients, as the major ones did with hospital inmates, but filled a public demand for relief of emotional stress at a time when the country was in a mood of optimism about drugs. This mood came to an end with thalidomide and with the present epidemic of nonmedical drug abuse. Another witness, Fritz Freyhan (3, p. 5329), noted that ophthalmologists were critical of the use of antidepressants by general practitioners, internists, and psychiatrists because of the risk of glaucoma. In explaining unsatisfactory prescribing behavior, he implicated failure to teach evaluation of medical history or physical examination as steps to be taken before prescribing psychoactive drugs, and he cited data showing among physicians who are psychoanalytically oriented a lack of knowledge about the adverse effects and pharmacological typology of these drugs.

It is difficult to measure the amount of overmedication because many factors are considered in the process of rejecting or accepting a given use of drugs, including the severity of the condition, the capacity of the patient to function in daily tasks and roles if unmedicated, the risk of side effects, the probability of success, and the practical availability of alternative therapies. I have found disagreement among expert evaluators about prescribing choices (4). There is, however, reason to believe that overuse is a problem with respect to the prescribing of psychotropic drugs, antibiotics, antiarthritics, and other classes of drugs.

Self-medication is also implicated. Self-medication amounts to something under \$2.6 billion (1969 figures), compared with \$4.0 billion for prescribed drugs (5, p. 7). An evaluation of 400 broadly representative, over-the-counter (OTC) drugs showed 15 percent to be effective, 27 percent probably so, and 47 percent possibly effective for the claimed indications (6, p. 9). These drugs comprised all of the OTC drugs put on the market between 1938 and 1962; it is believed by Food and Drug Administration (FDA) officials that these 400 preparations contain all but a small minority of the 200 significant active ingredients found in proprietary remedies. A method of evaluating all of the 100,000 or more drugs in the OTC market is said to be in the process of development within the FDA.

If the factors that contribute to a less than ideal use of the power of pharmaceutical technology for human benefit can be identified, progress can be made toward correcting the undesired results—without losing the command over illness, suffering, and attendant economic costs that drugs can confer.

The Role of Various Parties in the Market

Rather than condemning or deploring the self-serving behavior of some persons and the deficient knowledge and judgment of others, one may take as a point of departure the fact that the existing situation is, paradoxically, understandable, in the sense that it can be explained by objective factors. That is, overuse of drugs maintains itself because certain characteristics of the medical care market cause several different parties to contribute to raising the level of medication to a certain height. Each actor-drug company, doctor, patient, pharmacist—is impelled to do so because he is making a trade-off between drugs and some alternative that is less advantageous to him. Each actor is able to do so because the responsibility for medical care is fragmented and

because the increment to drug use contributed by each individual decision is so small that cumulative effects are ignored.

The principal active parties are drug companies and physicians. The drug company is impelled to raise the level of drug use in order to maximize the gains on individual products in its line before obsolescence is created by the release of new substitutes. The number of new products, although smaller in recent years than before the Kefauver-Harris Act of 1962, was up to 105 in 1970 from the average of about 78 in the preceding 4 years (5, p. 25).

Limited by the incidence of disease, the company extends the use of its product by training doctors to prescribe in response to symptoms and by a generous definition of the diseases for which its product has an answer. That it also promotes its own brand name does not imply overmedication as such, but any emphasis on the magical is conducive to prescribing.

The case of rheumatoid arthritis has been described by William O'Brien. Over a short period, the drug of choice was successively claimed to be corticosteroids, phenylbutazone, chloroquine, indomethacin, and dimethyl sulfoxide. The immunosuppressive drugs then took their turn (7).

The result of the marketing efforts of the leading drug companies is total sales of over \$4 billion for prescription drugs in 1969, compared with \$2.2 billion in 1960 and \$1.0 billion in 1950, as well as a per capita expenditure of \$19.31 in 1969, compared with \$6.74 in 1950. In the period from 1957 to 1970, in which prices as measured by industry sources went up roughly from 80 to 110 (1967 = 100), an increase of 33.3 percent in real per capita expenditure occurred (5, pp. 7, 8, and 33).

Time and the Doctor

The doctor's contribution to overmedication is to be seen in the context of his recurrent need to balance the time available for practice against the time demanded for medical care. A simplified example can be developed from American Medical Association figures on medical practice. There are about 190,000 doctors in office-based practice. They see in the office 91.6 patients a week; they practice 47.9 weeks a year, 51.3 hours per week. The number of patients seen per week is considerably higher for general prac-

titioners (129.5) and pediatricians (125.3), and slightly higher than average for obstetricians-gynecologists (96.8). If the general practitioner spends as much time with each hospital patient as he does with each office patient, he will have 37.1 hours, out of a total of 47.8 hours of direct care, in which to see his 130 office patients. He therefore has about 17 minutes to spend on each patient (8). And even if he spends no time at all with his hospital patients, he has no more than 22 minutes per office patient. His income depends on his fee, which is set on a per visit basis, even though fees for initial visits, with physical exam, history, and possibly tests, are considerably higher than those for follow-up visits. Prescribing is, theoretically at least, a means of terminating the interview in a fashion that satisfies both doctor and patient. The doctor does not have to charge the patient for additional office time spent in diagnostic study or therapeutic management. The patient's resistance to costs may be lessened by the fact that the filling of the prescription is a separate action and the bill is payable to another vendor. For every dollar the patient spends on physicians' services, he spends about 32 cents on prescribed medicines (5, p. 8). The act of prescribing in this situation conforms to the requirements of successful termination strategies in psychological theory, as outlined by Stuart Albert: the prescription is a signal for the approaching end of the encounter, it both summarizes and carries forward the relationship, it is an expression of concern, and it deals with interests of both parties in a manner perceived as equitable (9).

By keeping the length of appointments within bounds, the doctor does not have to extend his workday to satisfy requests for appointments and to maintain his income; nor does he have to cut down his income by seeing fewer patients. He could turn his patients over to aides for instruction, physical therapy, or other ministrations, but he would have to be compensated for the costs he incurs by doing so.

The significance of the time factor in elevating prescription levels, hypothesized here, can be investigated statistically as various changes in the health care system provide an opportunity. For example, if cheap culture services to determine etiological microorganisms in respiratory infection are provided, what happens to prescribing? If ancillary personnel in direct contact with the patient are made available, is

prescribing reduced? If the patient has no out-of-pocket expense for the drug because of insurance, to what extent does this make a prescription a more satisfactory way of ending an interview? Stolley's finding that those doctors who prescribed less often made prescribing decisions which were rated as medically better suggests the operation of nonmedical factors in the doctor's decision to prescribe (10). The relative importance of certain of these factors can be determined by appropriate methods of study directed toward specific therapeutic classes such as antibiotics and analgesics.

It has been possible to reduce the prescribing of tranquilizers by substituting personal care. In the Harvard Family Health Care program, described by Richard Feinbloom (6, p. 523), "student physicians have longitudinal responsibility (several years) for the care of families with appropriate supporting personnel and supervision. The student is the family doctor available 24 hours a day. . . . In this setting where emotional disorders are common, prescribing of tranquilizers is so unusual it is a cause for comment. When psychotropics are used they are one part of the total management, not the sole treatment."

The doctor will not prescribe if he considers a drug inappropriate and not in the patient's interest—not only for ethical reasons, but as a matter of selfpreservation. However, his judgment is subject not only to time constraints, but also to the stimuli of promotional efforts directed toward him through his medical journals, visits of detail men, and advertising literature received in the mail. Many medical scientists have voiced objections to the quantity, optimistic exaggeration, and symptom orientation of drug advertising, although Raymond Bauer and Mark Field have called attention to the information that advertising may provide (11).

Individuals' varying responses to drugs, the subjective and cultural factors involved in sensitivity to pain and sources of anxiety, and the self-limited nature of much disease create a rather large gray area in which the physician's judgment about drugs can be molded by promotion built into his professional information system, given the "time is money" constraint within which he practices.

The separation of the world of the practitioner from the world of the academic doctor, who applies a strict standard to medications before accept-

ing them, has been noted by Harry Dowling. He shows how the prescribing of chloramphenicol decreased each time the FDA brought home the dangers pointed out by the academic authorities, and increased again rather shortly thereafter (12). Continued prescribing of fixed combination drugs offers another example of how the repeated pronouncements of the academicians had little impact on their colleagues in office practice.

The Patient's Dependency on the Doctor's Judgment

The patient is another actor in the transactions in the medical marketplace. So much is said about the forces influencing his willingness to be medicated that the situation appears, if anything, overdetermined. Both conscious promotional efforts and a stream of medical news teach the patient to value the products of the newer drug technology. He or she may be temporarily dismayed and frightened by the disclosure of serious side effects, as in the case of thalidomide and the birth control pill, but many disclosures do not come to public attention, and, in any event, the impact usually lessens over a period of time. Whatever the psychological mechanisms inducting individuals into the contemporary, drug-accepting way of life, the principal factor is the patient's dependence on the doctor's judgment in evaluating his need for therapy.

The patient is faced with uncertainties in coping with his illness. His decision to follow one doctor's advice is like consolidating all his liabilities in a single loan—he substitutes for uncertainties about food, rest, medication, and so on the single decision to select and consult his doctor. He is then likely to accept the prescribed regimen as long as he remains within the implied contract with that doctor and as long as he is feeling ill. He usually begins to substitute his own judgment for the doctor's-for example, ignoring prescribed restraints on behavior and skipping medication—only after he is feeling less like a patient.

The employed patient's dependence on health for economic reasons is a salient factor in his acceptance of the doctor's prescribing judgment. His desire to avert loss of time at work is based at least in part on the fact that sick leave and insurance benefits replaced only 33.7 percent of the income loss from short-term sickness in 1969. Over the previous decade, between 28 and 30 percent of income loss was replaced in this way (13); these figures include the first 6 months of a long-term disability.

The growing participation of women in the labor force has made the issue of time lost from work increasingly independent of sex. The fact that women work chiefly from economic necessity and for earnings inferior to those of men means that the value placed on not losing a day through illness is even greater for women.

Chronicity appears to make patients aware of medication costs, particularly at an age where earning power is low. This may lead to seeking cheaper sources, such as group or mail purchase of drugs, to self-medication, or to cutting down on food. Medication orders may not be followed, thus leading to undermedication. But when income is higher and the penalty for disability is uncompensated time lost from work, the basis for acceptance of the doctor's recommendation is present because drugs represent a small cost, relative to the doctor's bill. Major medical coverage is also conducive to acceptance.

Hospitals' Role

The place of hospitals in the drug market is substantial: 20.1 percent of manufacturers' sales (5, p. 23) are made to hospitals; wholesalers also sell to hospitals. Hospitals play some role in controlling choice of drugs and drug utilization through their formulary committees, which have varying degrees of jurisdiction, sophistication, and influence. But hospitals are still largely organized around the principle of attracting and holding attending doctors, and they leave the doctors in control of the prescribing process as far as private patients are concerned, thereby avoiding confrontations and naked discipline. Since drugs are said to account for only 4 to 6 percent of total patient costs (excluding drug products used in diagnostic procedures and anesthesiology) (5, p. 2), it is unlikely that the cost of drugs imposes a significant check on their use, especially since a third party pays. By selling drugs above costs, pharmacy departments often yield earnings that are used to offset deficits from other activities, even in voluntary hospitals. This fact could reduce hospitals' interest in restricting prescribing.

Where there are not enough beds, as is the case at busy metropolitan hospitals, even though third parties stand ready to pay for additional days of care, the hospitals are committed to rapid turnover through efficient processing of patients—and this processing is facilitated by extensive use of drugs. Extra days of care are themselves conducive to the patient's receiving more medication, but the type of medication is likely to be different from that used for diagnostic and surgical processing. The ultimate check on hospitals is harm to patients: harm that would result in inefficient use of beds and staff time, thus interfering with general purposes; or that would lead to loss of reputation in the community and loss of revenue and staff; or that would incite malpractice suits. The hospital as an institution has the potential for improving the practices of prescribing if competition for its beds by doctors is dominant over the hospital's competition with other hospitals for qualified doctors in the various specialties.

Pharmacist as Drug Counselor?

The pharmacist plays a lesser role in the process of determining the level of drug utilization. So far as prescribed drugs are concerned, he merely facilitates their distribution. It has been proposed that he screen the patient's total prescribed medication for drugs working at cross-purposes or for excessive sedation and the like, but this is not typical in community practice. In the case of nonprescribed drugs, representing 25 percent of the business at the manufacturer's level, the pharmacist is more important: he may be used as a health counselor and recommender of drugs.

Counseling by a pharmacist as a substitute for a visit to a doctor would appear to be encouraged by lack of a regular doctor or health plan, low income, limited education, and illness below a threshold of severity justifying the time and cost of going to a doctor. However, the patient often makes his own choice of drugs based on his current information from public media and his family and social circle. Counseling by the pharmacist is associated with the use of drugs different from those prescribed by doctors, and possibly they are also different from selfprescribed medications, despite company promotion to pharmacists as well as to the public. Whether the total rate

of drug utilization is altered is another matter. The time taken in counseling can be compensated by sale of a drug, which lends an economic motive to this means of terminating a contact (6, pp. 344–351).

Ways to Modify the Use of Drugs

To modify the actual consumption of drugs toward some optimal level and mix requires imposing some constraints on the behavior of drug companies and other participants in the medical care market and attempting to exert a long-term influence on the relative desirability of the various options open to doctors, hospitals, patients, pharmacists, and suppliers of drugs.

Some observers would like to see drug advertising eliminated from medical journals (3, p. 5412); a less drastic approach calls for stronger control of therapeutic claims and warnings of side effects; restricted distribution of free samples has been advocated (14). Substituting for this source of information would be a compendium system, which would include distribution to physicians of "a comprehensive, objective reference work on all drug products marketed in the United States," supplemented by continuing education on specific types of drugs and deployment of a neutral detailing force to inform physicians about new and old drugs (15). The improvement of the medical student's education in clinical pharmacology would provide the basis for more sophisticated choices of drugs. The Medical Letter has established the marketability of a nonprofit, unbiased source of information; the application of this model on a larger scale has been recommended (14, p. 24).

In proposals for drug prepayment under national health insurance, a direct economic constraint on undesirable prescribing is created when coverage is restricted to safe, efficacious, and reasonably priced drugs, as listed in an official formulary (16). Such a formulary would have to be updated periodically. Even a scientifically excellent formulary would not exclude the possibility of inappropriate use of listed drugs. A review of drug utilization is another device that can be used, either to supplement a formulary or as an independent means of achieving rational prescribing; qualified professionals would evaluate the prescribing done by individual physicians on the basis of scientific standards (15, p. 328). Various forms of possibly inappropriate prescribing would thus be detected: excessive quantities, dubious efficacy, incompatible multiple drugs, and risk of adverse reactions. A firm assessment might require the difficult process of individual case analysis; therefore, utilization review might be limited to selected problem drugs. Following disclosures, attempts would be made to influence physician behavior by remedial education, disallowance of claims, prior approval for certain drugs, and other administrative controls.

These and related strategies attempt to enlist the professional pride and economic interest of physicians on the side of rational prescribing. Other possible approaches affect as well the other participants in the medical care market. Some examples of less familiar courses of action follow.

If prepayment were extended to services of ancillary health workers in the doctor's office or group center (nutrition, counseling, physical therapy, and so on), the emphasis on prescribing a drug as the finale of the doctorpatient contact would be reduced. Necessary manpower would have to developed. Increasing patients' knowledge about drugs is a familiar specific suggestion, but increasing their voice in the design and management of health programs might have spillover effects on their readiness to seek or accept medication, particularly where therapeutic indications are least clearly defined, as is the case with analgesic and sedative drugs. Even more broadly, drug-taking may be affected by improvement in the lifetime distribution of paid leisure as a preventive against time lost from work through illness, a change that calls for major social planning.

The pharmacist's role can be influenced by the development of a compensation base that is independent of the volume of medications sold and that encourages detection of excess prescribing and conflicting medication plans. In the hospital system, explicit controls over prescribing and dispensing to individual patients could be included in accreditation and reimbursement standards. Finally, should note that requiring drug companies to establish superior efficacy as well as safety and competitive efficacy, in the premarketing approval process would reduce the flow of new medications into the medical care system-if such a law could be enforced.

The vigor with which each such course should be pursued depends on the investment relative to the probable benefits. These may be hard to quantify, but the demonstrated responsiveness of actual prescribing practices to economic and social influences, rather than to medical necessity, suggests that welfare may be served by a trial of other consumption patterns.

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NEWS AND COMMENT

Nuclear Reactor Safety: At the AEC the Way of the Dissenter Is Hard

A number of disquieting indications have turned up in the past 2 years to suggest that a vital safety feature of nuclear power reactors may be far less capable of preventing a catastrophic accident than has long been assumed. As this disturbing information trickled into the Atomic Energy Commission from the nuclear industry, and from the AEC's own national laboratories, it carried with it the gravest of implications for public safety. For the feature in question—the emergency core cooling system (ECCS)—is a lastresort device meant to guard against what is thought to be the "maximum credible accident" that a reactor can possibly sustain, a major loss of cooling water through a broken pipe or valve.

Now, after pondering this unseemly problem for 2 years, the AEC is engaged in a showdown public hearing on it with environmentalists, utilities, and reactor manufacturers. From the testimony so far, it has begun to look as if the AEC's own administrative safeguards are in as questionable shape as the reactors it licenses. For a large amount of evidence has accumulated suggesting that AEC policy-makers have been studiously ignoring, rejecting, and even discouraging dissenting views from within the agency in the matter of emergency core cooling.

The argument over ECCS is neither academic nor trivial. Should a reactor's searingly hot core run dry, the ECCS is supposed to reflood it with water within seconds after the leak occurs. Should the ECCS fail—or even hesitate for long-the core could melt and ensuing steam explosions could scatter its radioactive contents over a wide area. The indications are that existing designs of backup cooling systems might not adequately reflood a reactor after a major leak.

For more than a year, the AEC kept its growing apprehensions largely to itself, sharing them with the four companies that manufacture reactors but telling the public essentially nothing. Late in 1970, to its credit, the AEC appointed a "task force" of four senior members of the regulatory staff to take a look at the problem and suggest some answers.

In an offhand sort of way, the task