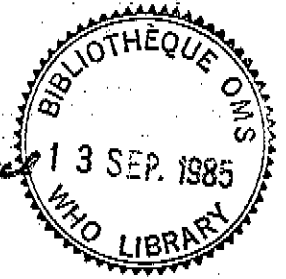




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*Drugs. Magasin de la haute
 addition + dosage
 patient compliance*



PHARMACEUTICAL DISTRIBUTION, PRESCRIPTION AND USE

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PHARMACEUTICAL DISTRIBUTION, PRESCRIPTION AND USE

1. Not less than 75% of the world's consumption of drugs takes place in the developed countries, the remaining 25% in the developing countries, where three-quarters of mankind live. In the developed countries, too, each inhabitant spends more than US\$ 50 on drugs every year, whereas in the developing countries the average is US\$ 6 (1). This profound imbalance between North and South is one of the expressions of the world's maldevelopment: while millions of human beings suffer from lack of medicaments, other millions, mostly in another hemisphere, use too many.

2. This paper considers some of these problems and some of the solutions.

Drug distribution

3. The object of distribution systems is to make the drugs required to meet the health needs of the population always available everywhere in the country at all levels of the health services. Developed countries have little by little created such systems in accordance with their needs; the drugs authorized by the regulatory authorities are distributed through commercial intermediaries and pharmacies.

4. In some developed countries the geographical distribution of pharmacies is regulated by law on the basis of such criteria as the density of the population served, the distance between pharmacies, or transport facilities (2). To enable patients living in sparsely populated areas to have access to drugs, the authorities provide extra remuneration for pharmacists who have a very low turnover; this occurs, for example, in Denmark, Italy, Norway, and the United Kingdom (3).

5. The situation is totally different in developing countries. On the basis of a number of actual incidents in countries, the following chain of events might occur. Reports of shortages of essential drugs (obtained in bulk through a non-profitmaking agency) lead to the discovery that the freight van in which half the year's supply is shipped is still in the customs warehouse because of a dispute with the Ministry of Finance over clearance and demurrage charges. Once cleared, a crate of drums of bulk tetracycline powder falls off a central stores truck during a rainstorm. Some drums are recovered, soaked through, and others are later found in bazaars, the contents being sold as antidiarrhoeal powder in glassine envelopes to individuals. Meanwhile someone measures the interior temperature of the vans transporting the drugs to remote health centres, a three-day journey in a tropical area, and finds it to be 82°C. No one asks which drugs are spoilt or rendered toxic. Pilferage at the docks and along the way decimates the stocks, drugs being a valuable commodity. The remaining drugs are then allocated to health centres by dividing what is available by the number of centres. A survey soon shows that centres in populous areas have run out of their annual allotment of drugs within three months, while the drugs accumulate in the centres in remote underpopulated areas. Patients then stop coming to the centres where there are no drugs and the whole rural health network is dislocated (4).

6. Yet another picture is of the main teaching hospital in a drought-stricken country receiving as many drugs as the entire rural health network, although it serves only 5% of the population. Government-supplied oral rehydration salts have not been delivered to village dispensaries for several months, as the Ministry of Health lorries have little fuel and fewer spare parts. However, a well-known soft drink, a commercial brand of sulfamethoxazole-trimethoprim, a useful antimicrobial, and some ineffective antidiarrhoeal drugs are found even in population clusters of 10 000, delivered by private truckers (5).

7. These sketches of real situations show that distribution systems in developing countries rarely meet the needs of the population for drugs and especially for essential drugs. Why is this so, whether the distribution systems are entirely controlled by the government, as in Mali (6) or Guinea (7) or a public and a private sector co-exist, as in Cameroon (8) or Kenya?

8. A number of reasons explain the notorious ineffectiveness of the public sector. One is the low budgetary allocation to the Ministry of Health for the purchase of drugs; in a number of developing countries the allocation for health is a mere 1-2% of the GNP and even if a considerable proportion was spent on drugs it would be insufficient. Although, too, many countries have accepted the concept of essential drugs and established lists of such drugs, a part of their health resources still goes to the purchase of pharmaceutical products that do not meet the priority needs of the population.

9. Another reason for the ineffectiveness of the public sector is that a number of developing countries must, in the absence of a drug manufacturing industry of their own, import all the drugs they use. The currency they need for that purpose is scarce, and drugs must compete for it with other commodities that sometimes have a more strategic value for the governments.

10. Most health systems are still oriented towards curative services, and the few drugs available in the developing countries go to supply the hospitals rather than other branches of the health services (10). This inequitable distribution is accentuated when each health echelon distributes drugs to the echelon below; health centres and, especially, dispensaries, the last to be served, get little or nothing.

11. The ineffectiveness of supply and distribution systems is an additional factor contributing to the scarcity of essential drugs. The reasons for its ineffectiveness are complex and in part purely technical, arising from the lack of resources, the shortage of personnel, and a certain bureaucratic mentality that places administrative precepts before initiative and a sense of responsibility. As a result:

- it takes years for orders to be delivered, mostly because of the complexity of the administrative labyrinth;
- information systems do not work, so that, for example, the quantities of drugs needed cannot be calculated;
- storage conditions are bad and drugs are not protected from sun, rain, or theft;
- transport is not properly organized, and in the absence of means of transport alternative solutions are not considered.

12. Ineffectiveness is found throughout the echelons of the health services, the drug situation not being followed up or the records properly kept. A large number of drugs are utilized by health personnel for their private purposes (nearly 30% in some cases) (11), and storage conditions are often defective. This state of affairs has disastrous consequences for peripheral health services, which have lost all credibility in many countries; the rural dispensaries, lacking drugs, are no longer frequented by the population but the government continues to pay the staff, which without the attraction of drugs has not even the possibility open to it of carrying out health education (12).

13. The private sector, on the other hand, is on the whole expanding; in Cameroon it distributed 75% of drugs in 1978 as against 60% in 1976 and its sales had quintupled in two years (13). This sector, which consists of pharmacies and pharmaceutical outlets, may purchase drugs from a government importing agency which has a monopoly of importation, as in Algeria, or order direct from foreign suppliers or local wholesalers, as in Cameroon. In the first case the range of drugs distributed by the pharmacies and pharmaceutical outlets is theoretically under the control of the government; but in practice in some of the countries concerned such control is little exercised to ensure that drugs meet health needs adequately.

14. The private sector, which is actuated by the profit motive, is much more efficacious than the public sector, but suffers from major disadvantages in the developing countries:

- because of the weakness of control measures, drugs of doubtful efficacy, sometimes dangerous and often inessential (tonics, multivitamin products, etc.) are strongly promoted and therefore in demand and use up scarce currency (14);
- drugs sold by pharmacies are in general expensive branded drugs and so not accessible to most of the population (15);
- most pharmacists do not wish to establish themselves in the rural areas where purchasing power is low, thus perpetuating the inequitable distribution of drugs.

15. Because of the inadequacies of the two sectors and their inability to meet the needs of the population, some governments have created a paragonovernmental sector, with the objective, as in Togo, of developing a health-oriented not exclusively commercial form of distribution that would provide the rural areas with proper supplies of drugs. These paragonovernmental bodies (Togopharma, the Office national de pharmacie du Bénin, etc.) were entrusted with the purchase and distribution, through pharmaceutical outlets, of a limited range of essential drugs to be sold cheaply to the public. Often the initial objective has not been attained, the bodies concerned having increased the range of their products and distributed a number of relatively inessential drugs (16). The main reason is that all these drugs sell easily and make money for the government.

On the proper use of drugs: prescription practices and compliance problems

16. "Modern drugs are such potent weapons that the responsibility for their safe production and use can no longer be left entirely to the manufacturer and prescriber" (17). "Physicians should note that very often patients do not speak the truth when they assert that they have taken their medicines" (18).

17. Whereas the problems of the distribution of drugs are entirely different in the developed and developing countries, the problems of taking drugs on prescription or in self-medication are relatively similar in both. They may be illustrated as follows:

- A woman in her forties goes to her doctor. "Doctor, I'm tired and don't want anything. At night when the children are in bed and the house is in order I can't read or prepare my course for tomorrow or even get to sleep". The doctor prescribes vitamins, a tranquillizer, and a mild hypnotic.

- A veiled woman stands in a crowded clinic, her uncle by her side. "What's your problem?" asks the doctor without looking up. The complaints are commonplace: generalized pain in the back and chest, palpitations, dizziness, and "a jerking soul". The doctor diagnoses beriberi and rheumatism and prescribes vitamin E, vitamin B injections, and analgesics (19).
- Mexican village men flock to a pharmacist's helper's house. He has a new supply of intravenous saline, "artificial life", which they greatly desire. Each man feels stronger after the infusion (20).
- A paediatrician examines a child with diarrhoea and prescribes an antibiotic combination, a constipative, and rehydration fluid. "But doctor", the mother wails, "he has had diarrhoea so many days." The doctor adds an antimotility drug and vitamins. This is the third physician consulted and the child now has a total of 12 drugs, some identical chemically but in boxes of different colours and labelled in a foreign script. Seven different antimicrobials may be found in the dozen preparations. The child is given intermittent doses of some of the drugs in the succeeding days because the mother tries, with help from neighbours, to give the most appropriate drug for this "hot" disease. As the stool changes in colour and consistency she applies different therapies (21).
- A child is ill with fever and a cough. The parents, too poor to consult a doctor, try a variety of home remedies and changes in diet and consult a spiritual healer to get amulets. Finally they administer tablets from a red box left over from an earlier illness that may have been similar (22).
- A university hospital internist in a developed country takes a detailed case history from a 45-year-old sales executive who complains of tiredness and mild pain in the chest and arms. The physical examination and laboratory tests indicate nothing special, but the patient is obviously tense and his systolic blood pressure approaches the upper range of the normal. The internist prescribes a cardiostimulant, an antihypertensive, a diuretic, and a tranquillizer, which the patient takes for a few days and then forgets in a cupboard (23).

18. These illustrations show that medical personnel and other prescribers are far from utilizing drugs rationally. The reasons for such a situation are many and complex.

19. All countries are affected by the steady increase in drug consumption. In the United Kingdom the number of prescriptions in the National Health Service rose by 22% between 1974 and 1977, much faster than the increase in the population. In the United States the number of prescriptions per head rose from 2.4 annually in 1950 to 7.2 in 1977 (25). In France drug consumption is rising on average by 13% per annum (26). Should the conclusion be drawn that people are therefore in better health? There is much evidence to cast doubt on such a conclusion; the reasons for increased drug consumption are rather to be sought in prescription practices and the attraction that drugs exert.

20. Much has been written on prescription practices. The main problems are excessive prescribing - a drug is prescribed when it is not necessary or when there is no medical indication for its use; inadequate prescribing - no drugs or not enough drugs are prescribed; and incorrect prescribing - the drug is not in keeping with the diagnosis or is ineffective (27).

Excessive prescribing

21. A study carried out in seven European countries showed that there are marked differences in the utilization of antidiabetic drugs, specially oral preparations. There are no data available to suggest that the incidence of diabetes differs as markedly as does drug utilization between the countries (28). Another comparative study has shown that patients hospitalized in the United States receive twice as many drugs as patients hospitalized in Scotland (29). There is a similar great variation in Nordic countries in prescribing antihypertensives, a variation that cannot be explained either by differences in morbidity or in the training of or information received by those prescribing (30). Whereas the number of drugs per prescription is around two in Switzerland (31), in the hospitals of South Brazil it is 8.6 (32), three as a minimum in Tunisia (33) and in Kenya (34), and five in most health centres in Cameroon (35). In France in 1983 one prescription in four was for antibiotics, in 57% of cases for respiratory infections of viral origin that do not respond to antibiotics (36).

22. The volume of sales of certain drugs far exceeds the incidence of the disease they are supposed to treat. Skegg has shown in a population of 40 000 that 33% of women between the ages of 45 and 59 years were receiving tranquillizers, as against 9.7% for men of all ages (37). As an advertisement of the pharmaceutical industry suggested, this is a method of producing "a less demanding and complaining patient" (38). All these studies concur in the conclusion that for a considerable proportion of the population in the developed countries taking drugs has become a habit that is often encouraged by the medical profession and the pharmaceutical industry. The public demand for drugs accords very little with real needs, and the resulting polypharmacy is not without economic consequences - waste of public and private money; social consequences - medicalization of society; and health consequences. In the comparative study mentioned above 26% of the American patients who were taking more drugs had side effects, as against 15% of Scottish patients. According to Steel et al. (39), side effects occur on the average in 18-30% of hospitalized patients; 80% of these effects could be avoided and are due to the prescriber's lack of therapeutic knowledge (40). Iatrogenic diseases caused by drugs, most of which have been prescribed by doctors, are responsible for 20% of admissions to American hospital services (41).

Prescribing in inadequate quantities

23. In developed countries it is difficult to give exact examples of prescribing in inadequate quantities, but it seems to exist for certain classes of drug (42). In developing countries drugs are not always available or are available in such small quantities that the prescriber gives too little to each patient, thus often favouring the development of drug resistance. Many common but serious conditions no longer respond except to second-line drugs, which are generally more expensive (43).

Incorrect prescribing

24. Incorrect prescribing is also a major cause of the development of drug resistance. It is probably the commonest form of irrational prescribing and has at least two aspects: either the drug prescribed is ineffective or doubtfully effective for the condition concerned or, although it is pharmacologically active, it is administered in unsuitable circumstances.

25. In the United States, according to Kunin et al. (44), more than 60% of hospitalized patients are wrongly given antibiotics. Antibiotic abuse has

generated a considerable amount of literature, but antibiotics are not the only class of drugs that are incorrectly prescribed. Also in the United States the prescribed treatment is not in accordance with the diagnosis in 20-40% of cases (45,46). In France an analysis of some 500 prescriptions showed that 36% contained anomalies; in 31 the same active principle was present in several drugs, 23 contained antagonistic substances (for example stimulants and sedatives), and 41 (8.3%) were of potential danger to the patient (47). The same problem exists in Spain, since in 1980 the second drug on the market in the class of antimicrobials was a combination of penicillin G, streptomycin, dihydrostreptomycin, albuminoids, etc. and was alleged to provide "non-specific immunotherapy". The fifth drug in the same class was a combination of tetracycline, sulfadiazine, dexamethasone, triflupromazine, pentetrazol, sodium benzoate, and balsam of tolu (48). In India a recent study carried out at Hyderabad showed that 16% of doctors had prescribed at the same time several vitamin preparations that contained the same ingredients and that more than 30% of prescriptions contained an antibiotic (49). Many other examples could be cited that would merely strengthen the conclusion that, in the developed as in the developing countries, prescribing is far from meeting the scientific criteria established by the therapeutic sciences.

26. A second problem brought out in the illustrations is that of the use of drugs by patients, whether prescription drugs or drugs taken in self-medication. A correct diagnosis and appropriate treatment are of little value if the patient does not follow the treatment prescribed. Non-compliance is nowadays considered to be a major problem in the health services of both developed and developing countries; it has been the subject of more than a thousand publications, mostly Anglo-Saxon, and a recent review of the literature suggests that the compliance rate is approximately 50% and decreases with time (50). Another analysis shows that between 30% and 75% of patients do not take all the drugs prescribed, do not take them in the prescribed dosage, or use them wrongly; and 40% of the mistakes may be harmful (51). The low compliance rate with effective remedies results in the failure of curative or preventive treatment and may have negative effects on the patient and society, such as the development of resistant strains, or economic costs.

27. Self-medication is a phenomenon that exists in every society and is tending to increase in the industrialized countries, as is shown by the increase in the number of books devoted to the subject. A WHO study in Canada showed that 50% of the population observed had taken medicaments in the 48 hours before the investigation, half of which had not been prescribed by doctors (52). Self-medication, while desirable in certain cases, may at times have negative effects on the consumer, inasmuch as the mode of action of the medicaments is rarely well understood, the length of treatment is difficult to judge (53), and very often the manufacturer's labelling does not provide sufficient data for appropriate treatment. The rationality of self-medication may also be queried in the light of the finding of the United States National Academy of Sciences that only 42% of 400 OTC preparations studied were effective or probably effective (54).

28. How have drugs within no more than three decades managed to become so widespread and in such great demand and yet be so badly used? How can the differences in patterns of prescriptions in similar countries be explained? Why do so many prescriptions not correspond to any satisfactory therapeutic norm? Why, in spite of the attraction of drugs, do patients follow their course of treatment so badly? Why, in spite of the many efforts to improve the use of drugs, is the situation so far from being satisfactory?

* * *

29. In fact, when a doctor prescribes a drug for a patient, many factors other than the biochemical properties of the drug come into play, a process Mazzullo has called "the non pharmacological basis of therapeutics" (55). The doctor is primarily influenced by the education in therapeutics he has received, an education that explains in part the existence of therapeutic schools or habits that create certain regional or national differences. The education he receives should give him the necessary basis for his profession. According to some studies, however, "the lack of knowledge and sophistication in the proper therapeutic use of drugs is perhaps the greatest deficiency of the average American physician today" (56), and there is no reason to think that the situation is any better in the rest of the world. Very often the doctor is simply not in a position to choose the best drug for his patient. In many countries continuing education is lacking (57) and this reduces the positive effect training in prescribing could have. Many studies suggest that training has indeed a positive effect on the quality of prescribing (58).

30. The promotional efforts of the pharmaceutical industry play a considerable part. Multinational firms produce a large number of drugs, many of which add little to the therapeutic armamentarium. An analysis of volume 25 of the scientifically objective Medical letter (Medical Letter Inc., New Rochelle, United States of America) shows that ten new products were reviewed that were biochemically similar to existing products. Two were considered an improvement; six provided no additional benefit and were more expensive; and two were thought less effective. In the United States 94 generic antibacterials are available; Medical letter recommends 31 as first-line, and then only 13 that need no elaborate diagnostic tests for proper use (59). All these drugs are promoted by aggressive and well-contrived methods. Promotion, as is shown by an analysis of 14 quantitative studies between 1940 and 1964, seems to be the factor that has most influence on medical prescribing (60); and Hemminki reached the same conclusions, stressing the role of sales representatives (61). A study carried out in 1978 in Switzerland showed a very significant correlation between the turnover of a drug or therapeutic group and the number of pages of publicity given to it in medical journals; thus the number of pages of publicity for the "nervous system" group represented 15.5% of the total analysed and the turnover for the group was 18.2%, the corresponding figures for one of the drugs of the group being 40.9% and 43% (62).

31. The availability of the preparations placed on the market by the pharmaceutical industry also influences prescribing. This could be illustrated by the following hypothetical conversation between doctor and patient: "Well, Mr Smith, I have listened to your story and examined you, and it seems to me that you are a case of diazepam. You had better have some anxiety." (63). Most of the doctors questioned do not realize to what extent this commercial promotion influences their prescribing. In a study of propoxyphene, considered by scientific opinion to be less effective and more dangerous than aspirin, the doctors who considered it very effective did not think that they were influenced by unscientific sources of information (64).

32. The pharmaceutical industry is not solely responsible for irrational prescribing practices. The demands of society and patients also push the doctor into prescribing for, we must not deceive ourselves, the responsibility for overconsumption of medical care and drugs falls not only on those who sell the drugs but also on those who buy them. Prescribing has a powerful symbolic effect, confirming the roles played by the doctor and the patient and maintaining their relationship. For many doctors "it is prescribing which makes a clinical situation legitimately medical" (65). In prescribing the doctor assures himself that he is treating the patient, gives him visible proof that he has done well in coming to consult him, and increases his dependence so that he will come again. For the

patient, prescribing symbolizes the doctor's interest in him and confirms his own role as a patient (66). The result is a tacit complicity between the prescriber and the patient, a complicity that may also include the pharmaceutical industry since it places the desired drugs at their disposal. Although the demands of the patients undoubtedly exercise a powerful influence in concert with that of the pharmaceutical industry, they are possibly less powerful than doctors would like to have it believed. A study by Stimson shows that in 80% of cases the doctor thinks that the patient has come to consult him so as to get a drug, whereas only 50% of the patients interviewed really wanted one (67).

33. Other factors that play a part are the influences of colleagues, government regulations, the characteristics of doctors, etc., but their role is minor and difficult to delineate exactly. On the other hand, the genuine placebo effect of drugs has to be taken into account. Medical literature has abundantly documented the placebo effect, both positive and negative, of drugs on hypertension. In its extreme, however, the practice of administering placebos may replace more fundamental support to people in coping with their problems. In some societies the ability of people to cope with misfortunes through family and community rituals has been replaced by treatment with drugs; thus grief is treated with tranquillizers (68,69).

34. Another factor favouring irrational drug consumption is the emphasis some people place on prevention and the strengthening of the body against outside forces. In traditional contexts prevention is achieved through diet, cleanliness, purges, and rituals. Many people assume that it can now be bought, manufactured tonics, vitamins, calcium, and saline intravenous infusions having a special status (70,71).

35. In developing countries, even more than in developed countries, communication between the patient and the health staff is a problem. Very often the health staff subscribe to norms that are different from those of the patients, and by their training belong to a subculture close to that of health staff in other countries than to that of the population in which they work. Communication is established with difficulty, and the easiest method of meeting the needs and expectations of patients in such circumstances is to prescribe drugs.

36. But it should not be forgotten that what people ultimately seek is a cure for illness. Even the poorest family will spend money and time and mortgage its assets to cure a sick child; and polypharmacy is a way of assuring it that it has done everything possible. Doctors and other prescribers are only too happy to encourage this feeling; thus their prestige and their income are linked to long prescriptions and the system becomes self-reinforcing. The family may not, in the heat of the moment, realize that it can no longer afford to buy enough food for the sick child or its siblings.

* * *

37. Like prescribing, compliance is a complex phenomenon. Much research has gone into attempts to define the most important factors influencing compliance; but the results vary and are difficult to systematize. The illness, the treatment, the form in which the drug is administered, and the number of doses or of preparations to be taken daily all have a positive or negative influence on compliance. But the most important factor seems to be the doctor; a study has shown that compliance improves when the doctor demonstrates that he is competent and takes the situation and the needs of his patient into account (72). Many investigators have similarly found higher compliance levels when the prescriber provides ample information and follows up the patient attentively (73).

38. These results, however, have not been confirmed by a recent study based on 185 compliance studies: "An interesting finding at sharp variance with conventional wisdom is that there appears to be no relationship between patients' knowledge of their disease or its therapy and their compliance with the associated treatment regimen. Although some studies have concluded that patient knowledge does lead to better compliance, a statistical comparison reveals that studies concluding no relationship are of greater methodological soundness. Accordingly it appears that the gap between clinical prescription and the patient's subsequent compliance behaviour is at best marginally narrowed by knowledge possessed or, indeed, imparted to the patient. That this is so is further supported by a lack of association between patients' intelligence or educational achievements and compliance" (74). This conclusion is strengthened by recent research on compliance. In opposition to the studies cited, which start from the hypothesis that the doctor prescribes and the patient must comply, these studies see the patient as an active agent in treatment. Non-compliance then becomes a voluntary act of the patient, who evaluates the behaviour of his doctor and the drugs prescribed in the light of his knowledge of and beliefs about the illness and the drugs (75), which are not always rational and influenced by education.

39. People all over the world have definite ideas about health, about how to strengthen health, how to prevent illness, how to cope with sickness. These ideas are part of the larger fabric of beliefs, assumptions, and practices concerning the body and people's relationships with each other and to natural and spiritual forces. The preparations used to provide care or cure are at several levels; they may be popular, provided by the individual himself or by relatives or neighbours, or "folk", provided by traditional healers using sacred or secular methods, or professional, provided by persons with formal training and qualifications. The more complex a society, the greater the range of choice an individual has for health care. This range of choice is termed "medical pluralism" and it exists in traditional rural communities as well as in westernized urban societies (76).

40. Modern pharmaceutical preparations are now part of the armamentarium of medical practitioners and healers at every level and are universally perceived to have - and often do have - powerful effects. They are consequently beginning to create a common medical system. They arose from a specific rational scientific model which assumes that virtually all illness is attributable to measurable biochemical mishap, either from without, as by infection, or from within, as from genetic susceptibility or immunological deficiency, and that a chemical preparation can be found to prevent, overcome, or improve the biochemical situation. Modern science lends weight to this view: cancer and the illnesses of age are increasingly being related to immunological and genetic failures; some mental illnesses to imbalances of small peptide molecules; and infections to imbalances between external assaulting organisms and multiple internal defence mechanisms. Drugs are being developed specifically to combat each biochemical failure or shore up normal biochemistry. Since the beginning of the twentieth century, when Ehrlich discovered a specific drug for the treatment of syphilis, medical scientists have aimed at discovering "a pill for every ill". This search for specificity is illustrated at present by the prospects being held out for gene replacement therapy. People throughout the world in all forms of society have great expectations for such "magic bullets". But while allopathic drugs are being absorbed into all systems of health care, they may not always be used in accordance with the scientific model.

41. With increased access to drugs, which is one of the stated goals of primary health care, the misuse of drugs may increase. A vital question that has not received an answer is whether the proliferation of drugs is on balance helpful or harmful, or even justified in terms of opportunity costs for poor families or poor countries. The question is almost irrelevant for the vast majority of people

living in the developing countries, particularly in the rural areas; for them access to the 20 or 30 drugs essential to their health needs can make the difference between life and death, or at least between a life plagued by disease and a life that is socially and economically productive.

A more effective distribution of drugs

42. Given the economic situation of most developing countries, it is not very likely that the financial resources at the disposal of health ministries will increase much in the coming years. It is therefore essential that they be used to good effect. A first step, one that many governments have already taken, is to adopt a national list of essential drugs; not only can developing countries not afford the luxury of ineffective drugs (77), but among effective drugs they must also choose in the light of the priority needs of the population (78). Governments that have not created a system of purchase by tender could, as a second step benefit by making use of the experience of other countries or could request WHO to help them organize their purchases more economically.

43. In the public sector the management of drug distribution agencies could technically be fairly easily improved by increased staff training, the creation of information networks to determine what drugs are essential (on the basis of a simplified collection of morbidity data), the introduction of more efficient stock control procedures, etc. The use of a restricted list of drugs is already an important step forward, for with such a list the number of drugs to order, stock, and distribute is reduced, management is greatly simplified, and costs fall as a result.

44. Such measures, which are relatively easy to introduce, will improve the performance of the system, but they will not really be effective unless they are accompanied by measures to motivate the personnel and make them responsible. Research is required to study ways of motivating the various categories of personnel in government service.

45. The problem of distributing drugs from the centre to the periphery is more difficult to solve, for indeed vehicles and fuel are often lacking in the public sector. Governments may have to find alternative solutions for distributing drugs to the health services; in some cases private transport can be used, since it often goes to the most remote areas. Research should be carried out on other systems of distributing drugs to the rural areas, systems that could achieve a more equitable distribution between urban hospitals and rural centres such as that developed by WHO and already in operation in Kenya, in which appropriate quantities of essential drugs are sent directly to dispensaries and rural health centres in sealed containers (79).

46. The free distribution of drugs in health services has been denounced by many authors as one of the principal causes of wastage and drug shortages. It would be desirable to study the possibility of replacing such a costly free public distribution by one selling essential drugs at low prices. Studies in this area should take into account the successes and failures of existing systems (cooperative pharmacies, revolving funds in the health services, etc.) and propose feasible solutions.

47. A number of solutions for the improvement of the performance of existing systems will be without effect unless the roles of the different sectors in the supply and distribution of drugs at the national level are redefined with precision. Additional research is required on the impact of the expanding private sector on the services of the public sector, which comprise not only the supply of drugs.

48. Because of the difficulties of supplying the rural areas in many countries and the effectiveness of the private sector, a solution might be considered integrating that sector in a system of distribution of drugs in the villages; pharmacies might be authorized to procure and sell certain essential drugs at a low price. But for such a measure to be successful it would be necessary to take steps to encourage pharmacists to install themselves in the rural areas, as for example by subsidizing the price of essential drugs.

The rational use of drugs

49. How can the behaviour of prescribers and patients in relation to drugs be transformed? How can the use of drugs be rationalized? Most of the attempts in this area have tended to control drug prescribing by regulation or by persuasion (80). In general regulatory measures are taken more against those who make profits - the pharmaceutical industry, distributors, and pharmacists - and are accompanied by structural changes, whereas in the case of prescribers and patients the control system rests essentially on voluntary changes. Regulatory measures include drug control, prescriber control and patient control.

Drug control

50. The control authorities that ought to be established in all countries have to ensure inter alia that all old and new drugs on the market fulfil a certain number of basic conditions in relation to safety and efficacy.

Prescriber control

51. In certain states of the United States the maximum amounts of drugs that can be dispensed on prescriptions paid for by Medicaid are fixed in advance (81). In France, Social Security exercises qualitative control over prescribing, the best example of such control being the "medical profile", which represents each doctor's prescribing costs and makes it possible to discover who departs from the agreed norms and to take the necessary steps (82). The steps range from drawing the doctor's attention to the situation to excluding him from the Social Security agreement.

52. Another and probably more effective form of control is to limit prescribing to the drugs included in a formulary or list. In a recent study of the effect of several methods of control over prescribing antibiotics and tranquillizers in an American hospital, the most effective method of reducing prescribing was to withdraw them from the formulary, the next being the requirement that the prescription should be countersigned by the head of the service. In the first case the administrative difficulties in obtaining the drugs discouraged the prescribers; in the second the prescribers gave more thought to prescribing because they had to account for their action to a superior (83).

53. These restrictions, although very effective, are little appreciated by doctors, who see in them an infringement of their freedom to prescribe; but they are being more and more imposed in developed and developing countries. One method of persuading the medical profession to accept formularies is to create local and national therapeutic committees animated by prescribers. Formularies, however, are not a guarantee that the medical profession will use drugs rationally, but they limit the use of dangerous, ineffective, or very specific drugs.

Patient control

54. The main forms of control over drug consumption exercised by government are (1) the obligation to provide a prescription for certain drugs - an obligation that exists everywhere to a greater or lesser extent and is more or less respected; and (2) price fixation. In France, Social Security reimburses only 40% of the cost of drugs treating minor upsets (84). A Commission de la Transparence has been entrusted with the task of studying and proposing prices and reimbursement rates to the Ministry of Social Affairs.

Methods of persuasion

55. Although legislation is an important weapon in combating drug misuse, it needs to be accompanied by more persuasive methods to make the medical profession and consumers aware that drugs are not ordinary commodities and must be used in accordance with certain scientific criteria. One of the causes most often identified of the misuses noted in prescriptions is the prescribers' lack of knowledge of therapeutics and pharmacology. Better training in those subjects during their studies and then during their active career is therefore essential. Clinical pharmacology needs to be taught more extensively. The basic training must aim at developing in the student a critical attitude that will enable him to judge rationally the flood of information to which he is subjected. For postgraduate training, methods have been developed (85) that help prescribers to criticize themselves and to discuss their prescriptions with their colleagues. Such methods could be used more widely and adapted to the different countries.

56. It is also necessary in each country for reference works and periodic information bulletins prepared by official agencies to be provided for prescribers. Objective drug information services should be encouraged and, if the country cannot itself furnish them, WHO should do so. In Great Britain, for example, several journals (Drug and therapeutics bulletin, Prescribers' journal) that are completely independent of the pharmaceutical industry and the British national formulary are distributed free to doctors (86).

57. In some countries advisers are available on request to help doctors (87). They are doctors (Netherlands), clinical pharmacologists, or pharmacists (United States). Such a measure is difficult to take in most developing countries, but advisers of that kind could have a part to play in the organization of seminars or programmes of continuing education.

58. Another measure, home visits to doctors by clinician pharmacists, has been shown to be very effective in the United States. Prescribers who had received such visits accompanied by "anti-advertisements" cut down their prescriptions of target drugs by 14% (88). This new form of medical visitor may provide a way of improving prescribing and reducing costs in a number of countries.

59. Other measures can be envisaged and are widely discussed in the literature. One that might be mentioned is the value of drug utilization studies at local or national level (89,90).

60. As far as patients are concerned, education is the essential method of breaking the vicious circle of medicalization. This has to begin at school and has to stress that treatment without drugs is sometimes preferable to treatment with drugs and that a visit to a doctor need not always end with a prescription. In the United States public and private organizations, including the American Medical Association, have set up a National Council on Patient Information and Education (NCPPIE), which has embarked on a widespread public education campaign recommending

that patients ask doctors about the drugs they prescribe and trying to develop people's critical judgement in this hitherto relatively "reserved" area (91). Several initiatives in Sweden are aimed at improving the information of the public. The Association of the Swedish Pharmaceutical Industry publishes regularly a manual for patients containing a description of all the drugs on sale in Sweden (92); the information, provided in a language easily understood by the public in general, is approved by the Swedish National Board of Health and Welfare. At the national level a group of experts nominated by the Government also prepares general manuals on self-medication, and each county council group does the same, the manuals being distributed free in the pharmacies.

61. Non-compliance, which represents another aspect of the misuse of drugs by patients, may also be remedied by education enabling consumers to better understand the role of drugs. Compliance would be improved too by such simple measures as simplification of prescriptions, improved presentation of drugs, written and spoken information given by the prescriber and the dispenser, and directions in simple language prepared in collaboration with consumers.

62. All these measures to influence the behaviour of prescribers and consumers, whether by the control of promotion, education, information, or other, have an impact on drug use, but their effect has very often been exaggerated and none has been irrefutably shown to be both necessary and cost-effective. In fact "the concept of the rational man or woman, be that doctor or patient, has limited, albeit, important applicability" (93); more searching studies are needed on the cultural, anthropological, and social factors influencing the prescribing and use of drugs. Studies, for example, on the behaviour of individuals in relation to drugs, on popular knowledge of the properties and use of medicines, or on the beliefs of doctors would enable better strategies to be developed to influence behaviour. Research comparing the situation in different countries should also enable drug use to be better understood, forecast, and improved.

REFERENCES

1. Patel, M.S. Drug costs in developing countries and policies to reduce them. World Development, 2: 195-204 (1983).
2. Commission of the European Communities. Pharmaceutical consumption studies. Brussels, ECE.1978 (Social Policies Series), p. 41.
3. Ibid, p. 54-55.
4. Fabricant, S. & Hirschhorn, N. Composite picture of actual events encountered in several countries (1985).
5. Ibid.
6. Rougemont, A., Fournier, P. & Balique, H. Mali et Haute Volta, une étude des systèmes d'approvisionnement et de distribution des médicaments. Basel, Institut Sandoz, (Série tiers monde, No. 4), (1983).
7. Brudon, J.P. Rapport de mission OMS, 1985.
8. Van der Geest, S. La pathologie de services médicaux, la distribution de médicaments au Sud Cameroun. Amsterdam, Anthropological Sociological Centre, 1981.
9. Peretz, M. Providing drugs to the third world: an industry view. Multinational business, 2.
10. Van der Geest, S. Op. cit., reference 8, p. 70.
11. Van der Geest, S. Op. cit., reference 8, p. 147.
12. Melrose, D. Double deprivation: public and private drug distribution from the perspective of the Third World poor. World development, 2: 181-186 (1983).
13. Van der Geest, S. Op. cit., reference 8, p. 139.
14. Melrose, D. Bitter pills. Medicines and the third world poor. London, Oxfam, 1982.
15. Brudon, J.P. Médicaments pour tous en l'an 2000? Lausanne, Editions d'En Bas, 1983.
16. Brudon, J.P. Rapport de mission, Cotonou, Bénin. Geneva, Institut universitaire d'Etudes de Développement, 1983.
17. Dunlop, D.M. Drug control and the British Health Service. Annals of internal medicine, 71: 237-244 (1969).
18. Hippocrates. Complete works. New York, Wood, 1930.
19. Myntti, C. (1979). Personal observations (adapted).
20. Bower, W. (1983). Personal observations.
21. Hirschhorn, N. (1983-1985). Composite of observations.
22. Oldham, L. (1985). Personal observations.

23. Brudon, J.P. (1985). Personal observations.
24. Stickler, G.B. Polypharmacy and poisons in pediatrics - the epidemic of overprescribing and ways to control it. Advances in Pediatrics, 27: 1-29 (1980).
25. Lee, P.R. America is an overmedicated society. In: Lasagna, L., ed., Controversies in therapeutics. Philadelphia, Saunders, (1980).
26. Tisseyre-Berry, M. & Soucaret, J.R. Economie du médicament. Paris, Masson, 1985.
27. Council of Europe, European Committee on Public Health. Misuse of drugs. Strasbourg, 1975.
28. WHO. Studies in drug utilization. Methods and applications. Copenhagen, World Health Organization, 1979. European Series, No. 8.
29. Stickler, G.B. Op. cit., reference 24.
30. Baksaas, I. Patterns in drug utilization. National and international aspects: anti-hypertensive drugs. Acta medica scandinavica (suppl.), 683: 59-66 (1984).
31. Berthoud, S. Réflexions au sujet de la prescription médicale. Journal suisse de pharmacie, 121: 411-422 (1983).
32. Victoria, C.G. et al. Drug usage in Southern Brazilian hospitals. Tropical doctor, 12: 231-235 (1982).
33. Bouraoui, K. et al. Prescription médicale, santé publique et relations médecin-malade. Tunis med., 59 (4): 323-328 (1981).
34. Maitai, C.K. & Watkins, W.M. A survey of outpatient prescriptions dispensed in Kenyatta National Hospital. East African medical journal, 57: 641-645 (1980).
35. Brudon, J.P. (1983). Personal observations.
36. Rapport officiel de la Caisse nationale de l'assurance maladies des travailleurs salariés. Quoted in Le Monde, 12-13 May 1985, p. 20.
37. Skegg, D.C.G., Doll, R. & Perry, J. Use of medicines in general practice. British medical journal, 1: 1561-1563 (1977).
38. Lee, P.R. Op. cit., reference 25.
39. Steel, K. et al. Iatrogenic illness on a general medical service at a university hospital. New England journal of medicine, 304: 638-639 (1981).
40. Melmon, K.L., Sheiner, L.B. & Rosenberg, B. Medical benefits and risks associated with prescription drugs: facts and fantasy. Drug development and marketing, 5-13 (1975).
41. Frisk, P.A., Cooper, J.W. jr & Campbell, N.A. Community hospital pharmacist detection of drug related problems upon patient admission to small hospitals. Amer. J. hosp. pharmacy, 34: 738-742 (1977).

42. Morgan, J.P. The politics of medication. In: Lasagna, L., ed., Controversies in therapeutics. Philadelphia, Saunders, 1980, p. 15-21.
43. Michel, J.M. Why do people like medicines? A perspective from Africa. Lancet, 1: 210 (1985).
44. Kunin, C.M., Tupasi, T. & Craig, W.A. Use of antibiotics: a brief exposition of the problem and some tentative solutions. Ann. intern. med., 79: 555-560 (1973).
45. Palombo, F.B. et al. Detecting prescribing problems through drug usage review: a case study. American journal of hospital pharmacy, 34: 152 (1977).
46. Maki, D.G. & Schuna, A.A. A study of antimicrobial misuse in a university hospital. American j. med. sci., 275: 271-282 (1978).
47. Dangoumau, J. et al. Ordonnances illogiques, ordonnances dangereuses. Revue médicale de l'Assurance Maladie, 2: 40-43 (1981).
48. Laporte, J.R. Drug consumption in Spain. Lancet, 1: 103-104 (1981).
49. Survey conducted by the National Institute of Nutrition and Directorate of Drug Control Administration and A. P. Chemists and Druggists Association. Hyderabad, 1983.
50. Haynes, R.B., Taylor, D.W. & Sackett, D.L. Compliance in health care. Baltimore, Johns Hopkins University Press, 1979.
51. Huyghe, B. La consommation et le mauvais usage des médicaments en Belgique 1970-1980. Document présenté au colloque de l'Association des Epidémiologistes de Langue française (ADELF). Geneva, 1981.
52. Kohn, R. & White, K.L. Health care: an international study. London, Oxford University Press, 1976.
53. Turakka, H., Vainio, K. & Enleund, H. Unused drugs in home - indication of non compliance or poor prescription habits. In: Bonal, J. & Poston, J., ed., Progress in clinical pharmacy VI. Cambridge, Cambridge University Press, 1984.
54. Blum, R. & Kreitman, K. Factors affecting individual use of medicines. In: Blum, R. et al., ed., Pharmaceuticals and health policy, London, Croom Helm, 1981, p. 126-185.
55. Mazzullo, J. The non pharmacological basis of therapeutics. Clin. pharm. ther., 13: 157-158 (1972).
56. United States Department of Health, Education, and Welfare, Task Force on Prescription Drugs. The drug prescribers. Washington, 1968, p. 3.
57. Hemminki, E. Review of literature on the factors affecting drug prescribing. Social science and medicine, 9: 111-115 (1975).
58. Becker, M.H. et al. Differential education concerning therapeutics and resultant physician prescribing patterns. J. Med. Educ., 47: 118 (1972).
59. Hirschhorn, N. & Fabricant, S. Personal analysis (1983).
60. Worthen, D.B. British journal of medical education, 7: 109-117 (1973).

61. Hemminki, E. Op. cit., reference 56.
62. Berthoud, S. Profil de prescription en Suisse romande et au Tessin. Schweizerische Medizinische Wochenschrift, 109: 1194 (1979).
63. Marinker, M. The doctor role in prescribing. Journal of the Royal College of General Practitioners, 23 (suppl. 2): 26.9 (1973).
64. Avorn, J., Chen, M. & Hartley, R. Scientific versus commercial sources of influence on the prescribing behavior of physicians. American journal of medicine, 73: 4-8 (1982).
65. Lee, P.R. Op. cit. reference 25.
66. Christensen, D.B. & Bush, P.J. Drug prescribing: patterns, problems and proposals. Social science and medicine, 15 A: 343-355 (1981).
67. Stimson, G.V. British medical journal, 4: 508-509 (1975).
68. Helman, C. Culture, health and illness. London, Wright, 1984.
69. Bush, P.J. Psychosocial issues in prescribing. In: Morgan, J.P. & Kagan, D.R., eds., Society and medication: conflicting signals for prescribers and patients. Lexington, Lexington Books, 1983.
70. Myntti, C. Medicine in its social context. Ph.D. thesis for the London School of Economics, 1983.
71. Michel, J.M. Why do people like medicines? A perspective from Africa. Lancet, 1: 210 (1985).
72. Beird-Lambert, J. & Buchanan, I.V. Compliance with medication regimens in children, can it be improved? Medical journal of Australia, 142: 201-203 (1985).
73. Garrity, T.F. Medical compliance and the clinician-patient relationship. Social science & medicine, 15: 215-222 (1981).
74. Sackett, D.L. & Haynes, R.B. Compliance with therapeutic regimens. Baltimore, Johns Hopkins University Press, 1976, p. 36. Quoted in: Pharmaceutical sociology: issues in research education and service. Amer. j. pharm. educ., 43: 252-257 (1979).
75. Conrad, P. The meaning of medications: another look at compliance. Social science & medicine, 20: 29-37 (1985).
76. Helman, C. Culture, health and illness. London, Wright, 1984.
77. Stolley, P.D. The problem of drug utilization and the role of the World Health Organization. Geneva, World Health Organization, unpublished document. WHO/DEM/75.5, 1975.
78. WHO Technical Report Series, No. 685, 1983.
79. Moore, G.D. Essential drugs for Kenya's rural population. World health forum, 3 (2): 196-199 (1982).
80. Taylor, R.J. Towards better prescribing. Journal of the Royal College of General Practitioners, 28: 263-270 (1978).

81. Azarnoff, D.L. (1980) Monitoring and control of physician prescribing are needed. In: Controversies in therapeutics, reference 25, p. 534-541.
82. Tisseyre-Berry, M. & Soucaret, J.R. Op. cit., reference 26.
83. Huber, S.L. et al. Influencing drug use through prescribing restrictions. American journal of hospital pharmacy, 39 (11): 1898-1901 (1982).
84. Tisseyre-Berry, M. & Soucaret, J.R. Op. cit., reference 26.
85. Herxheimer, A. & Twycross, R. Continuing education in therapeutics: aids to discussions on prescribing. British medical journal, 1: 1198-1200 (1976).
86. Harris, C.M. et al. Prescribing a suitable case for treatment. London, Royal College of General Practitioners, 1984 (Occasional paper, No. 24).
87. Council of Europe. Op. cit., reference 27.
88. Avorn, J. & Soumerai, S.B. Improving drug therapy decisions through educational outreach. New England journal of medicine, 308: 1457-1463 (1983).
89. Stolley, P.D. Op. cit., reference 77.
90. Op. cit., reference 28.
91. Nightingale, S.L. Do physicians tell patients enough about prescription drugs?
92. LINFO, Läkemedelsinformation AB. Patient-Fass. Sweden, different years.
93. Blum, R. & Kreitman, K. Op. cit., reference 53.