

Drug Dependence: Some Research Issues*

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This paper examines some problems of drug dependence, stressing the importance of a balanced approach. Consideration must be given to the demand for, as well as the supply of, drugs. Without a demand, there would be no continuing supply of man-made agents and no need to control the availability of naturally occurring agents.

To achieve a balanced approach, increased research is needed into the effects on man of taking various dependence-producing drugs (particularly when these are used for long periods of time), the natural history of drug taking, the relative effectiveness of various preventive, therapeutic and restorative approaches and techniques, and means of identifying substances that, because of their dependence-producing properties, are apt to induce individual or public health problems. Attention is also called to some problems that may inhibit, but do not preclude, the initiation of studies in the field of drug dependence.

For many years, international organizations and governments have given considerable attention to the identification of dependence-producing drugs and to the control of their production and distribution. While such controls, when vigorously applied, have had an important limiting effect on the *supply* of certain dependence-producing drugs, the continuing presence of a very substantial *demand* for such drugs has resulted in their being quite readily available in many parts of the world. Although continuing efforts to control the supply of such drugs are important—and much remains to be done—it is clear that there is an urgent need to intensify markedly our current efforts to decrease the *demand* side of the “demand–supply balance”. As demand for drugs is created by existing and potential users, both regular and experimental, *increasing attention must be given to man, the drug taker, and to the environment in which he lives.*

I shall first comment briefly on some factors that appear to be associated with the initiation and perpetuation of the self-administration of dependence-producing drugs, i.e., factors associated with the demand for drugs. Secondly, some observations will be offered on the areas in which additional research

effort appears to be indicated. Finally, some of the attitudinal, ethical and methodological problems affecting research in these areas will be discussed.

DEFINITIONS

Drug dependence is defined by the WHO Expert Committee on Drug Dependence (1969 p. 6) as:

“A state, psychic and sometimes also physical, resulting from the interaction between a living organism and a drug, characterized by behavioural and other responses that always include a compulsion to take the drug on a continuous or periodic basis in order to experience its psychic effects, and sometimes to avoid the discomfort of its absence. Tolerance may or may not be present. A person may be dependent on more than one drug.”

It should be noted that this definition omits consideration of any possible need to control the production and distribution of a dependence-producing drug. The need for control of such a drug and the level of that control should be determined (WHO Expert Committee on Drug Dependence, 1969, p. 18) on the basis of “(a) the degree of risk to public health and (b) the usefulness of the drug in medical therapy”. A discussion of these and related matters, beyond the scope of this paper, will be found in the reports of the WHO Expert Committee on Drug Dependence (1969, 1970).

COMPLEX INTERACTIONS IN DRUG DEPENDENCE

Turning to the question of demand, persons “may become dependent upon a wide variety of chemical

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substances that produce central nervous system effects ranging from stimulation to depression" (Eddy et al., 1965) and often involving distortions of perception and/or judgement.

In endeavouring to understand a man-drug interaction of the type characterized in the preceding definition of drug dependence, attention must be given to three major variables: (1) the properties of the drug or drugs taken, (2) the characteristics of the person involved, and (3) the nature of his several environments. The varied properties of dependence-producing drugs are illustrated above. Also, not only do people vary, but the individual changes from moment to moment. Different persons who take dependence-producing drugs apparently do so for a variety of conscious and unconscious reasons; a given drug user may take the same or different drugs for differing reasons at various times. Socio-cultural pressures apparently favouring or discouraging drug-taking behaviour vary markedly between cultural and subcultural groups and these pressures change at various rates with the passage of time.

It may be useful to observe that one or more of the following personal "motives" often appear to be associated with drug-taking behaviour: (1) to escape from something, (2) to have a new experience, (3) to achieve improved "understanding" or "insight", (4) to achieve a sense of belonging, and (5) to express independence and sometimes hostility.

Among the socio-cultural factors that often appear to be associated with drug-taking behaviour are (1) rapid socio-economic change accompanied by modifications in the character of cultural controls, (2) readily available and rapid communications and transportation systems, and (3) the ever-increasing variety of different dependence-producing drugs (Cameron, 1971).

The complexities of the interrelation between a person, his environment and a drug may be glimpsed by noting that a barbiturate is often used to court slumber, but at other times to induce excitement. A cannabis smoker may experience little subjective effect when smoking in private, yet feel quite relaxed or stimulated when smoking comparable amounts of the same material in the company of convivial companions. The availability of a suitable setting, appropriate expectations, and a competent "guide" are generally regarded by LSD users as desirable in order to reduce to the minimum the possibilities of a "bad trip".

DRUG USE AS A COMMUNICABLE DISORDER

There is an element of communicability associated with the initiation of self-administration of dependence-producing drugs. Initial interest in taking various drugs of this type often appears to be communicated directly or indirectly from a user to a non-user. This characteristic appears to be particularly relevant to experimental or recreational use of drugs by adolescents and young adults and especially to use of drugs of the hallucinogen, cannabis and amphetamine types.

There is clearly a strong element of communicability in the spread of experimental and regular use of dependence-producing drugs, just as communicability is an important factor in the spread of infectious diseases. There are, of course, differences in the mechanisms of communication in these two situations. In the case of drug use, the host more often than not actively seeks out and voluntarily takes a drug. With infectious diseases, the host ordinarily does not seek the agent of infection. He may, of course, contribute to his exposure because of ignorance or carelessness. Only in the case of venereal diseases does the potential host indulge in a form of seeking behaviour that tends to bring him into contact with the agent of infection. Another difference in the mechanism of communicability of drug use and infectious diseases has to do with the nature of the agent of "infection". Dependence-producing drugs are not living organisms that propagate themselves. Rather, they are made or processed by man and are consciously and purposefully distributed by him.

Beyond the differences just noted, it is perhaps reasonable to observe that there are many similarities between drug dependence and the infectious-disease model of certain illnesses.

"There is an agent of 'infection' or abuse (the drug) that affects the host (the actually or potentially drug-dependent person) who lives in and is influenced by his environment. There is a mode of transmission of the disorder. . . a vector (pusher) may or may not be involved, and the method of transmission may differ with different agents and different groups of hosts" (Cameron, 1968).

With a model of a communicable disorder in mind, it may be suggested that the degree of risk of exposure to drug dependence (i.e., trying a drug) may depend upon at least the following factors: (1) the personality characteristics and the interests of the potential experimenter, (2) peer pressures, (3) cultural mores and moral attitudes, (4) the extent and accuracy of the prospective user's knowledge

about drug effects, (5) the availability of the drug, and (6) legal rules and regulations. Other factors are doubtless involved. Once he has tried a given drug (been exposed), the likelihood of a person repeating the experience until psychic and possibly physical dependence have been established will be affected by these factors and also by at least two other sets of factors: (1) his perception of his own emotional, intellectual and physical responses to the experience, and (2) the responses of persons about him.

BELIEFS INFLUENCE PROGRAMMES

The nature of any preventive, treatment, rehabilitation and follow-up services established in the field of drug dependence will depend on the character of prevailing conscious and unconscious beliefs and assumptions about (1) the causes of drug dependence, and (2) the immediate and long-term effects of taking drugs. The beliefs and assumptions about drug taking have to do with the nature of direct and indirect effects on the user himself, on the persons with whom he has contact, and on the social institutions of which he is a part. In the final analysis, however, conscious and unconscious beliefs and assumptions about causes and effects of drug dependence and the characteristics of any programmes developed in this field are profoundly influenced by the much broader system of values prevailing in a particular community. This broad system of values has to do with such matters as (1) the relative worth of material possessions and of spiritual, cultural or traditional beliefs and experiences, (2) the respective importance of individual rights, prerogatives and responsibilities and those of the society, (3) the nature of practices which are considered to be "good" or "evil", and (4) the meaning and value of life itself.

The health problems associated with the taking of dependence-producing drugs are thus complicated by moral judgements and cultural attitudes.

RESEARCH NEEDS

Differences of opinion on the causes and effects of drug taking and on the relative usefulness of various preventive, treatment, and rehabilitation activities help to identify areas requiring intensified research efforts. However, even where there is general agreement on a proposition, further research may well be indicated. It is frequently evident that a consensus stems more from the intellectual or

other attractiveness of an hypothesis than from objective evidence of its validity and usefulness. Propositions and assumptions are, and of course must be, developed and utilized as a basis for the provision of essential services when objectively validated data are not available. Unfortunately, when such operating assumptions are utilized for some time they may come to be accepted as proven facts rather than to be regarded as the unproven hypotheses they continue to be. Operating assumptions should be queried at frequent intervals.

These considerations suggest that there is an urgent need for intensified research efforts in the following important areas: (1) the effects on man of taking dependence-producing drugs, (2) the natural history of drug taking, (3) the effectiveness of various preventive, treatment, and rehabilitation measures, and (4) means of identifying substances that, because of their dependence-producing properties, are apt to lead to sufficiently adverse effects in man as to constitute individual or public health problems. Other, more complete listings of areas requiring substantial additional research are to be found in a number of publications, for example, the reports of the WHO Expert Committee on Dependence-Producing Drugs (1966) and of the WHO Expert Committee on Mental Health (1967, p. 44).

Effects on man of taking drugs

The first general area, concerned with the effects on man of taking drugs, is chosen because it is self-evident that there should be no particular reason for concern about persons taking a drug capable of producing even substantial psychic or physical dependence if such use were not apt to result in significant public health and related social problems or to produce appreciable adverse effects in a substantial number of users. In these circumstances, there would be no practical need to prevent or otherwise minimize use of a dependence-producing drug. Conversely, if it were demonstrated that a particular drug of this type were apt to produce very serious adverse effects, especially on the public health, great effort would be justified to minimize the demand for it, and possibly to control its availability. A lesser effort might be warranted in the case of a less noxious substance.

Within this broad area, we are concerned with studying the consequences of drug use when the drug has been taken because of its dependence-producing properties, but not the problems associated with the accidental or intentional taking of

drugs for other reasons. For example, we are not here concerned with the suicidal use of poisons, whether or not they possess dependence-producing properties, or with the use of sedatives or stimulants, of whatever nature, in the doping of human or animal athletes. On the other hand, we are concerned with an area of inquiry that is not limited to the pharmacodynamics of particular man-drug interactions. The latter is but a single, though very important, segment to be studied within a broad spectrum of consequences that is influenced not only by the numerous characteristics of the man and of the drug involved, but also by related moral and cultural attitudes, expectations and sanctions within peer and other social groups.

Significant events that occur after taking dependence-producing drugs are, of course, not necessarily related to the man-drug interactions, nor even to the man-society interactions that can stem from being involved in a socially disapproved activity. Beyond this, it would be prudent to be certain that a significant event or phenomenon had indeed occurred before attributing its cause to drug taking or anything else. This is not so obvious as it might appear. Not too many years ago it was being asserted that the use of marijuana led directly to criminal behaviour (Wolff, 1949). To the best of my knowledge there were then, and still are, no data to support this assertion. Of course, the absence of data about the existence of a phenomenon is no proof that it does not exist; for example, in 1930 lung cancer was presumably more prevalent among heavy cigarette smokers than among non-smokers, even though the phenomenon was not demonstrated until many years later.

Influencing factors. Many factors influence the character of the events related in some way to the taking of dependence-producing drugs. As has been previously noted, the influencing factors have to do with the drug, the drug taker and his environment. They must be taken into account in endeavouring to understand any cause and effect relationships that may be postulated to exist between the act of drug taking and subsequent events.

Influencing factors associated with the *drug* include not only its pharmacodynamic properties, but also (1) the form of dosage, (2) potency, (3) dose taken, (4) route of administration, and (5) frequency and duration of use. Hashish is more potent than marijuana and the taking of 20 mg–30 mg of amphetamine by mouth is a very different matter from taking 500 mg intravenously. One of the difficulties

in studying even the immediate effects of cannabis has been the enormous variability in the potency of materials available for study. This difficulty is now being partially overcome, but it will remain a serious problem, especially with regard to the effects of long-term use of natural materials by man.

Influencing factors associated with the *host* may include (1) genetic endowment, (2) general state of health and nutrition, (3) presence of intercurrent illnesses or disorders, (4) previous personal and interpersonal experiences, (5) the degree to which cultural and peer attitudes have been internalized, (6) the intensity of conscious and unconscious needs for emotional security, independence, satisfaction and recognition, and the patterns usually employed in satisfying such needs, (7) self-concept, including the extent to which the host believes it will be possible for him to achieve his aspirations and (8) the host's intellectual and emotional set or expectations. The importance of his attitude or expectations may be appreciated when it is recognized that numerous studies have shown a placebo to be about 40% as effective as a therapeutic dose of morphine in the relief of postoperative pain.

Influencing factors associated with *environment* include (1) the character, strength and stability of family, peer and cultural attitudes and mores, (2) the availability of drugs and of information about the effects of taking them and, perhaps, (3) the general level of tensions, particularly of an unstructured nature, within and between social groups.

Let us turn now to the nature or *character* of events related in some way to drug taking. These events involve not only the drug taker himself, but also persons with whom he comes in contact and a number of social groups and institutions. For example, drug takers may present evidence of such things as alterations in perception or judgement, impaired neuromuscular co-ordination and changes in the central nervous or other organ systems. An injured motorist whose car has been hit by an intoxicated drug taker is a person affected by contact with a drug taker. And, of course, there is often a cost to society for medical care afforded to an incapacitated drug taker or for welfare payments to the family he no longer supports.

The consequences of drug taking may usefully be looked at from two points of view. An event may be the direct or the indirect consequence of taking a drug, while the time relation between the event and the drug taking may be immediate (measured in minutes or hours or possibly days), intermediate

(measured in weeks or months), or long-term (measured in months and years). Intoxication would be seen as an immediate, direct consequence of drug taking. Malnutrition could be the indirect, intermediate or long-term result of taking drugs, the effects and/or cost of which caused the drug taker to fail to obtain a balanced diet. Infectious hepatitis, acquired in the course of utilizing contaminated equipment for the intravenous injection of a dependence-producing drug, might be seen as the immediate and potentially long-term, indirect, but accidental, result of self-administration of a drug. On the other hand, death resulting from an unwitting overdose of heroin would be the immediate, direct, but accidental, result of drug taking. The consequences to society may be immediate and direct, as in the case of providing medical services to an intoxicated drug taker, or long-term and indirect, stemming, for example, from his loss of productivity (intellectual, artistic, economic, etc.). The legal and other social sanctions imposed on a drug taker because of his involvement in a disapproved activity (drug taking) may be immediate, but are more often intermediate and long-term.

These several, rather obvious ways of regarding possible relationships between the act of taking a drug and a subsequent event are mentioned only because it appears that some of the difficulties of communication between persons holding apparently differing views on these relationships may stem from their mutual failure to make clear the character of the relationships they are postulating. Sweeping generalizations seem often to take the place of more precise formulations.

Some of the more important research questions in this area that merit greatly intensified study have to do with the direct pharmacological and toxicological effects on man of the long-term use of drugs of various types, particularly those of the cannabis, hallucinogen and morphine types. Data related to drugs of these types are remarkably sparse. For example, it would be important to learn if there is any relation between cannabis taking and suggestibility or intellectual deterioration, as postulated by Zinberg & Weil (1970). The same questions are particularly pertinent for LSD and other hallucinogens. Is there an association between the taking of drugs of various types and a sense of apathy, estrangement or hostility toward society? If so, what is the relationship? If such a sense occurs primarily after taking drugs, is it a pharmacodynamic effect, one largely determined by

socio-cultural influences and attitudes, or is it related to either? The existence in different parts of the world of varying socio-cultural attitudes toward the use of a given drug will facilitate the design of projects addressed to the study of these questions.

Natural history of drug taking

Far too little is known about the natural history of various types of drug dependence in a given culture, let alone the variations in patterns to be found in differing cultures. As an example, only relatively recently have data been presented suggesting that among North American narcotics users there may be a tendency for some spontaneously to stop taking narcotics as they reach the ages of 35-45 (Winick, 1964; Richmann, 1966). We do not know if this is true in other settings or if comparable patterns are to be found with regard to dependence of the amphetamine and other types.

More information is needed on such matters as the modes of initiation to use of various types of drugs and the methods and patterns of their continued use. For example, what is the contribution of word-of-mouth relative to mass-media communication in arousing initial interest in the experimental or recreational use of drugs. Clearly, knowledge of such matters would be helpful in endeavouring to increase the effectiveness of treatment, and particularly preventive, services. Improved data on the prevalence and incidence of drug dependence of various types is necessary if authorities are to attempt to foster a volume of services commensurate with needs (WHO Expert Committee on Mental Health, 1967, p. 19). More studies are also needed "that would shed light on why it is that, among a group of persons with apparently comparable personality structures and psychic needs and subjected to common socio-cultural forces, some adopt and others reject drug taking as a way of life" (Cameron, 1971). To approach these "why" questions, it is necessary that one first learn *what* experiential and other events appear to be associated with these different types of behaviour.

As noted earlier, such studies need to be carried out in a variety of cultural settings. The collection of data based on reasonably comparable parameters in differing cultures will help to distinguish between consequences of drug taking that are largely socio-culturally determined as contrasted with those more directly related to the pharmacodynamics of the man-drug interaction. This is particularly true in relation to the consequences of long-term drug use.

A number of high-drug-use groups have been identified in widely separated locations in the world. Research-oriented personnel have gained entry to a number of these groups and are reporting on their observations. Doubtless, the time has come to seek ways of providing an increasing number of formal opportunities for small groups of these and other observers and research personnel, representing several different professional disciplines, to discuss at first hand their experiences in obtaining data in this broad area and to exchange views on the feasibility of collecting reliable data based on reasonably comparable parameters.

In connexion with this, a resolution (WHA23.42) on drug dependence was adopted at the Twenty-third World Health Assembly in May 1970 (*Off. Rec. Wld Hlth Org.*, 1970). It makes the following points, among others:

“Noting with great concern the extensive and serious public health problems resulting from the self-administration of dependence-producing drugs, in particular among the younger age-group;

.....

“Convinced that there is an urgent need at local, national and international levels to implement improved preventive, treatment and rehabilitation measures,

- “1. RECOMMENDS that the World Health Organization should encourage and assist the development of improved preventive, treatment and rehabilitation programmes and the pursuit of needed knowledge in the field of drug dependence;
- “2. URGES Member States to promote preventive, therapeutic, rehabilitative and research programmes in this field; and
- “3. REQUESTS the Director-General:
 - (i) to develop means for the international collection and exchange of data on the prevalence and incidence of drug dependence, and on the human and environmental factors associated therewith . . . ”

Effectiveness of services

There is an urgent need to evaluate the relative effectiveness of various approaches and techniques used (1) in the prevention and control of drug dependence, and (2) in the treatment, rehabilitation and follow-up of drug-dependent persons. Particularly is this so in view of the facts that many of the methods presently used are costly in time and money, and that their superiority over the absence of formal preventive and treatment activities has not always been demonstrated. Indeed, as in other fields (Todd, 1970), the validity of the theories and

operating assumptions on which *some* of these activities are based have not been established.

In carrying out research on the effectiveness of treatment or rehabilitation activities, it is first necessary to establish suitable criteria against which the various services are to be measured. The usual, and often the sole, criterion utilized for the evaluation of treatment, rehabilitation and follow-up services for drug-dependent persons has been the presence or absence of drug taking. This obvious criterion is not always as easy to determine as some might at first believe. Besides, there clearly are other very crucial criteria that should be considered in studying treatment effectiveness. Among these are the extent of drug taking, if it still continues. Further criteria involve occupational performance, relations with others and the patient's emotional stability. Is the patient working or going to school? If so, what is the quantity and quality of his work as seen by his employer or teachers, his peers, family and himself? Has any presenting asocial, antisocial or unlawful activity been modified during the course of treatment and rehabilitation? Have his interpersonal relations with his family, or others important to his daily activities, been modified? If so, in what ways? It is possible that a man might have stopped taking a particular drug, only to increase his use of another. Or he might have discontinued all dependence-producing drugs only to develop manifestations of some severely crippling mental disorder. Perhaps without the impediments of drugs, a former user may have become a more skilful thief. It is emphasized that in studying the outcome of various treatment and rehabilitation techniques, account must be taken of many significant life events beyond the single, “all-or-none” criterion of drug taking. Few treatments of any malady can be successfully judged by a single criterion; even persons who eventually die of a terminal illness may have been rendered more comfortable in their last days by a treatment that did not succeed in averting their eventual death.

Beyond the question of criterion measures is the matter of making meaningful comparisons between different measures or techniques, including comparisons between treatment and no treatment. In some situations such meaningful comparisons can be made by utilizing a patient as his own control. An example is seen in the double-blind assessment of the degree of pain relief resulting from the administration to a given patient of analgesics of known effectiveness, candidate analgesics and a

placebo. To assess the effectiveness of some other treatment procedures, it is necessary that each technique be applied to a different group of comparable patients. While there are too few studies of treatment effectiveness, some of those still being reported might well not have been undertaken because of their failure to provide for meaningful comparisons.

Having said this, may I note the special difficulties of assessing the relative contributions made by particular medicaments or other treatment measures within a total therapeutic regime of demonstrated usefulness? For example, among alcoholics in a given setting and having designated characteristics, are *sensitizing* medicaments (Glatt, 1970), such as disulfiram, more or less effective than certain forms of insight or supportive therapy? Is the combination better than either alone? Are the same relationships to be found in treating alcoholics possessing different attributes? Or again, what is the relative effectiveness of a *blocking* agent, such as naloxone or cyclazocine, and of a *substitutive* agent, such as methadone, in the treatment of narcotic-dependent persons? What is the relative contribution of such agents as compared with group therapy or peer support? What is the relative effectiveness of these and other treatment measures among so-called voluntary patients as compared with comparable patients undergoing compulsory treatment? There is a fairly widely held view that only voluntary treatment of drug-dependent persons will be effective. Presumably this view stems from the need for a patient's co-operation during the course of therapy. Despite this, there is evidence (Vaillant, 1969) to indicate that some forms of compulsory treatment are more effective than many voluntary programmes that have been utilized. This, of course, does not mean that future, improved methods for treating voluntary patients might not prove superior to past, compulsory methods—assuming that comparable groups can be marshalled for comparison.

Clearly, there is much difficult research remaining to be done in the area of assessing the effectiveness of treatment and rehabilitation services. And the problems of assessing the effectiveness of educational and other preventive programmes are perhaps even more difficult. Preventive efforts are of two types. The first has to do with the *supply* side of the demand-supply balance and consists of efforts to control the production and distribution of drugs. More study is needed on the relative effectiveness of various policies and techniques designed to control the

availability of drugs. The second has to do with the *demand* side of the balance. Active educational efforts are carried out to communicate information and attitudes intended to minimize demand. All of us recognize the need for additional research into the effects achieved by communicating different types of material and utilizing different modes of communication. But of perhaps even greater importance is the need for research on the effect of *not* communicating certain other types of information. I am reminded of a story about a perhaps apocryphal entrepreneur, active in the United States of America during the alcohol prohibition era, who marketed, as least temporarily, a packet containing sugar and a fruit flavour. The label read somewhat as follows: "Instructions: Use only for the preparation of syrup! Warning: Do *not* place in an earthenware jar with yeast and cover with two gallons of water. To do so might result in the production of an alcoholic beverage, which is unlawful".

Would it be possible to determine if there may have been an association between the rapidity of spread of abuse of certain drugs in a given locality and the appearance of material in the mass media which might have carried "warnings" which were only sometimes as accurate, but perhaps even more attractive than that of our enterprising entrepreneur? Could observations be made during future outbreaks relative to the rapidity and character of spread and the nature and volume of related material transmitted by the mass media? If an association were found, it would still remain to determine the nature of the association. Of course, *if* it were learned that certain types of data communicated *via* mass and perhaps other media tended to encourage the rapid spread of experimental and recreational use of drugs, new but difficult avenues for preventive activity would have been identified. Perhaps the news media in selected areas will be interested in joining in studies of the effects on drug use of various forms of journalism.

Identification of dependence-producing substances

Since the self-administration of certain dependence-producing substances *may* result in individual and/or public health problems, it is important that substances with these properties be identified as early as possible. Once identified, it does not necessarily follow that they should automatically be recommended for control. But their identification is crucial to the prevention of possible future problems. Quite good techniques have been evolved for

the identification of substances possessing significant physical-dependence liability, but equal progress has not been made with regard to psychic-dependence liability (WHO Scientific Group on the Evaluation of Dependence-Producing Drugs, 1964; WHO Expert Committee on Drug Dependence, 1969, sections 1.3.1 and 1.3.2). Psychic dependence is to be found in connexion with all forms of drug dependence, while physical dependence occurs only in relation to three types. There is thus an evident need for additional research looking to the development of techniques that will readily and reliably allow the prediction of the psychic-dependence liability of a drug in man. Some of the avenues that appear to be most fruitful have to do with self-administration techniques adapted for use in drug-naïve and drug-experienced animals. The ratings of drugs by experienced human volunteers is also very promising, but has some rather obvious difficulties.

SPECIAL IMPEDIMENTS TO RESEARCH

Several impediments beset the initiation of research involving questions pertaining to (1) the effectiveness of public and other policies, programmes and methods in general, and (2) the effectiveness of certain medical techniques in particular. These go beyond the difficulties of developing testable hypotheses in such disparate areas as, for example, (1) the effects produced by the establishment of a given broad public policy or law, or (2) the validity of many aspects of psychoanalytic theory, and also the difficulties of establishing valid comparison groups and of isolating the influences of one variable from those of another—difficulties that, in themselves, are often very substantial. Studies in the field of drug dependence carry with them their own set of additional difficulties stemming from the strong moral and emotional overtones that often tend to obfuscate basic issues. By drawing attention to the nature of some of these special impediments to research, it is hoped that further studies in this may be stimulated and even facilitated.

Uncritical acceptance of assumptions

As was noted earlier, when validated data are not available it is often necessary to develop working assumptions as a basis for establishing programmes that are believed to be necessary. Indeed, programmes have more than occasionally been founded on a given set of assumptions or beliefs despite the

existence of evidence suggesting that the assumptions were incorrect. In any case, the programme may have appeared to be effective. Three examples may be cited:

(1) A programme or treatment carried out to prevent a non-existent phenomenon may be judged, particularly by its originators, to have been effective. Persons with ample supplies of vitamins in their regular diet may take supplementary amounts to ward off various ailments which were not manifest before, or after, taking the additional vitamins.

(2) The establishment of a programme or treatment designed to prevent or relieve a phenomenon whose existence has been clearly demonstrated may be followed by a reduction in the unwanted phenomenon, but for reasons other than the newly established activity. In a laboratory where studies were being carried out on the relative effectiveness of antitussive agents, a cat was caused to inhale sulfur dioxide fumes in sufficient concentration to produce an experimental cough. After treatment with an antitussive, the same concentration of sulfur dioxide did not result in coughing. The drug was, at first, presumed to be an effective cough suppressant. However, it was subsequently noted that by the time the drug trials were run the cat was breathing in a very shallow, restrained fashion, apparently having learned to breathe in this way to avoid inhaling sufficient sulfur dioxide to cause an unpleasant cough. The cough was suppressed whether or not an antitussive was given.

(3) The programme activities may have produced the desired and expected result, but only because it brought into play forces unrelated to the beliefs or postulates on which the programme was founded. Recently a particular oral medication was withdrawn from the market in the United States of America because it was shown not to be effective. Included in the evidence that it was ineffective was the fact that it was quite insoluble when taken by mouth as prescribed. When it was taken off the market some physicians and more of their patients objected to the loss of a medication they believed to be effective. Mention was made earlier of the importance of psychological expectations and of placebo effects.

In circumstances such as these three, and particularly when the beliefs or assumptions underlying the programme have not been explicitly stated, the assumptions involved may inappropriately come to be accepted as valid. And, if an hypothesis is believed to have been validated, there is little incentive to test

it. Thus, some needed research fails to be proposed, or if it is, fails to receive necessary support. The problem of unwarranted assumptions is particularly common where the subject is burdened by strong moral and emotional overtones. Drug dependence is such a subject.

Threat to self-concept

Most persons do not consciously set about asking, let alone studying, questions which might imply that what they have been doing much of their lives may not have been worth while, nor that what they currently believe may be inappropriate. Indeed, they may even resent such questions being raised by others. Questions of the effectiveness of some legislative enactments or certain therapeutic techniques are sometimes encumbered by such considerations. In countries having a representative form of government, to suggest studies on the effectiveness of a law has the added difficulty of appearing to question an action agreed upon by a majority of the representatives of the people. Particularly is this the case where a law was enacted primarily because it was believed to be the "right" or moral thing to do as contrasted with a "necessary" action. For example, it appears to have been more difficult to initiate studies on the effectiveness of heavy penalties as a deterrent to unlawful possession of a drug—the self-administration of which is considered by many to be "evil"—than to initiate studies on the effectiveness of certain measures designed to regulate the flow of automobile traffic in the interests of safety.

Consider the attitude likely to be taken by a legislator who, out of a sincere conviction that all wrong-doers should be punished, has just voted to increase the penalties for the unlawful possession of a given drug, if he is then asked to approve the use of funds to study the usefulness of the law he supported. It might also be interesting to speculate on the likely reaction of a physician who, after devoting about a quarter of a century to acquiring a formal education and another twenty-five years to the practice of his chosen profession, is asked to undertake or at least to collaborate in a study to determine if a particular treatment he has come to value is any more effective than a placebo.

Thus, some much needed research in the field of drug dependence fails to be proposed, or if it is proposed, fails to receive necessary support. This is said despite the recognition (1) that numerous very well controlled studies are being carried out on the therapeutic effectiveness of many psychoactive drugs, some of which are dependence-producing, and (2) that some efforts have been undertaken to study the relative effectiveness of various treatment approaches to the problems of drug dependence.

Ethical and legal problems

There are numerous ethical and sometimes legal problems that arise in connexion with experimental studies that are to involve human subjects, whether or not the studies have to do with drug dependence. These problems, which include such matters as risk-benefit ratios, withholding treatments of known effectiveness, informed consent and the liability of investigators will not be discussed. Instead, I wish only to mention two special problems in this area.

An ethical problem peculiar to studies involving dependence-producing drugs has to do with the extent to which it may be appropriate to administer such substances to drug-naïve subjects, assuming of course they have given informed consent. This is a special issue involving a risk-benefit ratio. While finding answers in situations involving polar values of this ratio may present few difficulties, the problems are much more pronounced in situations resulting in less extreme risk-benefit ratios.

Another special problem peculiar to dependence-producing drugs has to do with obtaining supplies of such a drug for *bona fide* research purposes where legislative and/or administrative barriers have been established, quite appropriately, to prevent diversion of a drug from licit to illicit channels. It is difficult to understand how competent and ethical scientists could seriously object to appropriate safeguards of this kind. They frequently do object, however, to what they consider inappropriate inquiry into their research methodology. These difficulties may even be more apparent than real and still constitute a psychological barrier to research in this area. In order to facilitate the distribution of drugs for legitimate research, it is necessary that mechanisms be established which have the mutual understanding and respect of researchers and those responsible for preventing diversion of drugs to illicit channels.

RÉSUMÉ

PHARMACODÉPENDANCE: QUELQUES DOMAINES DE RECHERCHE

Depuis de nombreuses années, les organisations internationales et les gouvernements accordent une attention particulière à l'identification et au contrôle des médicaments qui engendrent la dépendance. Cependant, bien que leurs efforts aient contribué à réduire la *production* de substances de ce genre, il importe de se préoccuper toujours davantage des moyens à mettre en œuvre pour restreindre ou contrôler la *demande* née des besoins des utilisateurs actuels ou en puissance. Une approche pondérée est indispensable à la solution de ces deux aspects du problème.

La dépendance à l'égard des médicaments résulte d'une interaction complexe entre: a) les caractéristiques individuelles des consommateurs; b) la nature des facteurs de milieu auxquels ils sont soumis; c) les propriétés des médicaments dont il est fait usage. L'élément « communication » joue un rôle important dans l'initiation à l'usage de la drogue et dans sa propagation. Les consommateurs sont enclins à recruter et à persuader de nouveaux adeptes, mais ces derniers, de leur côté, sont souvent à l'affût d'une occasion d'expérimenter les effets de la drogue.

En matière de pharmacodépendance, le caractère des services de prévention, de traitement, de réadaptation et de surveillance sera influencé par les concepts relatifs aux causes et aux effets de l'usage de la drogue et, en dernière analyse, par l'ensemble beaucoup plus vaste des valeurs admises dans une collectivité donnée: importance respective des droits et des responsabilités de l'individu au regard de ceux de la société, notions du « bien » et du « mal », opinions concernant la signification de l'existence elle-même.

Il convient de réunir d'urgence de nouvelles données si

l'on veut maintenir un équilibre raisonnable entre, d'une part, la nécessité de réduire la demande de médicaments engendrant la dépendance et, d'autre part, les exigences du contrôle de la production des drogues. Quatre secteurs de recherche devraient être explorés avec le maximum d'intensité. Le premier concerne les effets de l'usage de la drogue sur l'homme. La distinction est à faire à cet égard entre les effets dus à l'interaction entre le sujet et le médicament et les effets liés à la réaction de la société envers un de ses membres dont le comportement est jugé inacceptable. En deuxième lieu, il faudrait accroître notre connaissance de l'« histoire naturelle » de la pharmacodépendance, les investigations portant aussi bien sur les raisons pour lesquelles certaines personnes ne font pas usage de drogues que sur les motifs qui incitent d'autres à en consommer. Un troisième domaine de recherche est celui de l'évaluation de l'efficacité des mesures de prévention, de traitement et de réadaptation, étude qui recueillerait des bénéfices certains de comparaisons entre groupes. Enfin, la mise au point de méthodes plus précises est indispensable en vue de l'identification des médicaments engendrant la dépendance et en particulier de ceux qui suscitent une dépendance psychique sans dépendance physique.

En raison des incidences morales et affectives du problème de la pharmacodépendance, diverses hypothèses relatives à ce comportement risquent d'être acceptées sans avoir fait l'objet d'un examen critique suffisant. Certaines d'entre elles, de même que les aspects éthiques et légaux de la pharmacodépendance, sont autant d'obstacles potentiels à la recherche, mais ces difficultés ne doivent pas entraver les études nécessaires.

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