

## HABITUATION AND ADDICTION

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To the man in the street the words "drug" and "narcotic" are often understood to mean drugs of addiction. In so far as this attitude creates a respect for drugs—even a healthy fear of them—this may be good. The use or misuse of drugs leading to habituation and addiction is an old problem to the doctor and the pharmacist. In Britain it is not a very large or serious problem and presents nothing comparable to the difficulties which arise from addiction to alcohol. These have led the Minister of Health (England) to issue a recent directive to Regional Hospital Boards on the setting up of special clinics for the treatment of alcoholism. In passing, while addiction to alcohol is often regarded as a problem quite apart from addiction to drugs, the two addictions can exist in the one person and complicate one another.

In 1958 an Interdepartmental Committee on Drug Addiction was set up by the Minister of Health and the Secretary of State for Scotland "to review the advice given by the Departmental Committee on Morphine and Heroin Addiction (the Rolleston Committee) in 1926, to consider whether any revised advice should also cover other drugs liable to produce addiction or to be habit-forming; to consider whether there is a medical need to provide special, including institutional, treatment outside the resources already available, for persons addicted to drugs; and to make recommendations, including proposals for any administrative measures that seem expedient." Before these problems can be discussed it is desirable that definitions be made which are generally, if not always, accepted. The Interdepartmental Committee in its report (1961) has slightly modified the WHO definitions of Addiction and Habituation, as follows.

1. *Drug Addiction* is a state of periodic or chronic intoxication produced by the repeated consumption of a drug (natural or synthetic); its characteristics include:

- (i) An overpowering desire or need (compulsion) to continue taking the drug and to obtain it by any means.

- (ii) A tendency to increase the dose, though some patients may remain indefinitely on a stationary dose.
  - (iii) A psychological and physical dependence on the effects of the drug.
  - (iv) The appearance of a characteristic abstinence syndrome in a subject from whom the drug is withdrawn.
  - (v) An effect detrimental to the individual and to society.
2. *Drug Habituation* (habit) is a condition resulting from the repeated consumption of a drug. Its characteristics include :

- (i) A desire (but not a compulsion) to continue taking the drug for the sense of improved well-being which it engenders.
- (ii) Little or no tendency to increase the dose.
- (iii) Some degree of psychological dependence on the effect of the drug, but absence of physical dependence and hence of an abstinence syndrome.
- (iv) Detrimental effects, if any, primarily on the individual.

It will be seen that addiction is differentiated from habituation in that in the latter there is less tendency to increase the dose and absence of physical dependence. This distinction is not absolute—the report accepts the existence of the stabilised addict and indeed gives brief case histories of six such people who take their share in the work of the world without increase of the dosage on which they are dependent for freedom from pain. Where drugs are used in this way for relief from chronic pain some authorities maintain that it is wrong to regard the sufferer as an addict. Again the habitue' may find that his intake of tranquilliser or barbiturate increases yet he may not suffer from physical dependence, or only to the extent to which the smoker exhibits such dependence when deprived of his cigarettes. "Habituation" is also used in another sense by Wikler (1961) as a synonym for relapse after cure, but such use of the word might lead to confusion.

#### TOLERANCE

The British National Formulary (1960) in referring briefly to habit-forming drugs gives the warning "In a susceptible person drug tolerance can readily develop and will reveal itself by a call for increased or more frequent dosage to obtain the required clinical effects". The nature of tolerance has been much disputed ; it is not primarily a question of the better or quicker metabolism or excretion of the drug, though Kato (1961) has demonstrated that meprobamate and phenobarbitone produce even within a day an increase of activity in the liver's drug-metabolising enzymes which break down mepro-

bamate. The fact that tolerance to morphine is developed to its depressant but not to its excitatory effects led to a hypothesis that addiction developed to mask the cumulative effect of residual excitation that persisted when the depression had worn off, but the phenomena of the abstinence syndrome does not support this theory.

While the precise nature of tolerance remains undetermined it is believed to be a cellular phenomenon—cells acquire the ability to survive and function in the presence of concentrations of morphine (or alcohol) which would ordinarily inactivate them, rather as trypanosomes can be accustomed to flavines. This must apply also to barbiturates and other hypnotics although the degree of tolerance that can be developed to opiates greatly exceeds that to most other narcotics.

#### INTERIM REPORT

In November, 1959, the Interdepartmental Committee submitted an interim report on two problems specially referred to it by the Ministers. The first was the occasional misuse of carbromal and bromvaletone and mixtures containing these drugs. The Poisons Board had repeatedly reviewed their growing use but felt they were not more toxic than such drugs as aspirin. It was recommended that any drug which so affected the central nervous system as to be liable to produce physical or psychological deterioration should be supplied only on prescription and this led to the modifications in The Poisons Rules, 1960. It is hoped that when new drugs with comparable actions are introduced, they will quickly be similarly scheduled. Such delays as followed the introduction of pethidine might well be disastrous.

The second difficulty arose over anaesthetists who became addicted to the gases and vapours they use. Examples of such abuse which might endanger the lives of their charges had recently come before Courts of Law; and while anaesthetic experts regard a preliminary sniff at their mixtures as an indispensable precaution it was recommended that the addict should never be allowed to administer anaesthetics and that the anaesthetist's professional colleagues should intervene in any such case. Appropriate steps have been taken by the authorities to implement these recommendations.

#### SYNTHETIC ANALGESICS

The Rolleston Committee met before the problem had arisen with synthetic analgesics, apart from derivatives of morphine such as diamorphine, and experience has since shown it to be unlikely that a potent analgesic will be

free from addicting potentialities. Facilities for testing these on man are not available in Great Britain, but exist at Lexington in the U.S.A. There would appear to be degrees of danger of addiction even amongst very potent analgesics. For example, phenazocine has been introduced with the claim that it is less of a menace than morphine. The establishment of such a distinction is only possible after prolonged clinical trial, although the W.H. O. experts (1962) are studying both the experimental and clinical methods by which the addicting potentialities of a drug may be investigated and assessed.

In America there is strong opinion that the synthetic analgesics have now been so developed that the opiates can be dispensed with entirely—we in Great Britain do not subscribe to this and still pay homage to “the incomparable morphine” even if its addicting tendency is greater and the treatment of any such addiction more difficult than those of most synthetic substitutes. We can point with reasonable confidence to our Table of Addicts and without being smug say “Ours is not the problem with which you contend”.

TABLE I

*Extent, trends and nature of the problem in Great Britain. Addicts known to the Home Office*

Drug	1936	1950	1960
All drugs ... ..	616	226	454
Morphine ... ..	545 (88 per cent)	139 (61 per cent)	204 (45 per cent)
Pethidine ... ..	—	34 (15 per cent)	116 (26 per cent)
Methadone ... ..	—	5 ( 2 per cent)	51 (11 per cent)
Levorphanol ... ..	—	—	16 ( 4 per cent)
“Professional” addicts—doctors, dentists, veterinarians and pharmacists. ... ..	147 (24 per cent)	48 (21 per cent)	68 (15 per cent)

An examination of the figures available to the Interdepartmental Committee indicates something of the changes of the last 25 years (Table I). Much doubt has been cast on the accuracy of these Home Office figures—our transatlantic friends view them with envy not unmixed with frank disbelief. When Sir Russell Brain (1961)—now Lord Brain—discussed the report of his

committee at a meeting of the Society for the Study of Addiction last year he was taken to task for his optimism by a pharmacist who claimed he could "record 40 or 50 cocaine, heroin and morphine addicts in the London area alone" and told of one, unknown to the Home Office, who was presenting prescriptions supplied by a doctor "who was making every effort to treat these people" for "something like 30 grains of cocaine or 40 to 50 grains of heroin". He claimed that such consumption was evidence that this patient had "been obtaining supplies illicitly to get used to these quantities". There are, of course, likely to be a few addicts whose records have not yet attracted the attention of the authorities but the opinion is that they are few—possibly recent arrivals in this country—and it is feared that the treatment threatened or meted out to the addict in some countries may on occasion drive him to Britain. But the U.S.A. has 45,000 morphine and diamorphine addicts, 10,000 of whom are juveniles. We can be confident that there is no addiction on any comparable scale in Britain. The disparity may be accounted for by the British subject's law-abiding tendencies and respect for the law, the careful way in which the law has been interpreted and administered and of course the careful way in which these drugs are handled.

This pharmacist's experience of a large number of addicts in London emphasises another trend. Addicts are generally found in large centres of population; Isbell emphasises that the addicts of U.S.A. are substantially concentrated in certain areas of New York, Philadelphia, Chicago and Los Angeles.

#### HABIT-FORMING DRUGS

Apart from a few individuals whose personalities may well be more responsible for their addictions than the drugs they take, we think of habituation rather than addiction to sedatives, hypnotics, tranquillisers and stimulants. There is also habituation to the milder analgesics—Fourneau's antalgiques—and especially where the coal-tar derivatives are combined with codeine. Codeine has recently been commented upon by the W.H.O. Expert Committee on Addiction-producing Drugs (1962). Consumption of codeine continues to increase and this is thought to be less due to its antitussive use, for many synthetic antitussives have been introduced lately, than to these compounded analgesic preparations (Analgin, Antoin, Cephacan, Codis, Dellipsoïds D-4, Dexocodene, Dolviron, Hypon, Nembudeine, Neurodyne, Pardale, S.A.C. Vagadil-Alk, Veganin).

Codeine has a relatively low addiction liability, we are assured, and "its use will be advantageous as long as it prevents the use of substances of higher

addiction liability. Its use will be hazardous if it leads to a habit of drug administration and induces substitution of a more dangerous drug". Self-medication can so easily become a habit. Much energy has been directed by the manufacturers to the evolution of something better than codeine and the compound codeine tablet and the use of tranquillisers outside of hospitals may be a matter of some anxiety, especially in view of the side-actions associated with these drugs. A few years ago there was an attempt to popularise the use of rauwalfia preparations as a drug for free sale—fortunately and perhaps partly on the advice of the Pharmaceutical Society's Council and the brave action of the lamented "Chemists' Federation" this was withdrawn before it was established and long before it was appropriately scheduled as a poison. No one can deny the value of reserpine when properly used and controlled, nor that of the numerous phenothiazines which have so much affected behaviour and prognosis amongst the mentally sick. The Report quotes the ten-fold increase in chlorpromazine consumption in nine selected mental hospitals over 5 years—fortunately most practitioners treat these drugs with a healthy respect, valuable though they are in psychiatry.

TABLE II  
*Barbituates prescribed in Britain*

Year	Tons prescribed	Known cases, approx. of barbiturate poisoning
1938	20	40
1953	40 under N.H.S.	2,500
1959	80 under N.H.S.	6,000 (10 per cent mortality)

The problem of habituation to barbiturates in Britain is a more serious one. Usage in England and Wales "has expanded both progressively and substantially so that in 1959 it was almost twice what it was in 1951". The barbiturate addict, well recognized in America, is still rare here but too many, especially amongst the elderly, drift into nightly dependence on their capsules or tablets and some acquire an almost new lease of life when weaned of their habit. Certain aspects of the problem should be noted:

1. An increasing number of barbiturate substitutes are being developed and advertised. Whether these represent any substantial therapeutic advances

remains to be established. Lasagna (1957) has cast grave doubts on the merit of many. One promising substitute, thalidomide, has had to be withdrawn because of side-actions which had not become apparent even in prolonged pharmacological and clinical trials.

2. The regular use of sedatives at night may be a factor in the increasing use, as a *corrigens*, of such stimulants as amphetamines and phenmetrazine. The combination of sedative and stimulant has also been recommended and formulated—and has been found useful in spite of its “pharmacological incompatibility”. Amphetamine addiction at one period reached alarming proportions in Japan but only 50 cases have been reported in this country. In an analysis of N.H.S. prescriptions numbering many millions, 1 in 40 was for these stimulants.
3. The increased consumption of barbiturates has led to a still increasing incidence of barbiturate poisoning to which much attention has been directed in the past decade. Many of these are cases of attempted suicide and probably not a few alleged accidental poisonings are suicidal rather than accidental. But there is no evidence that the possession of barbiturates is an encouragement to suicide; this country's suicide rate has not gone up even if barbiturates are now often preferred to coal gas or more dramatic, and more certain, methods.

#### THE FUTURE

What is to be done? After spending 2 years in reviewing a great deal of evidence, the Interdepartmental Committee may not appear to be very far-reaching in its recommendations. Perhaps the most important of these was that of the interim report—that any drug which is liable so to effect the nervous system as to produce physical or psychological deterioration should be supplied only on prescription. This puts the responsibility on the doctor.

#### TREATMENT AND THE DOCTOR

The doctor is often blamed for starting the addict on his drug. American analysis of “how it all started” puts more emphasis on the influence of the company of other addicts, on curiosity, on the desire for “kicks”. It also indicates the high incidence of some personality disorder—the administration of potentially addicting medicaments to the psychopathic patient is clearly to be avoided if possible. The diagnosis of addiction is often difficult, often delayed unless suspected. The treatment recommended by the Interdepartmental Committee is gradual withdrawal in an institution, usually after substitution of some orally-active alternative such as methadone, combined

with rehabilitation both physical and mental, occupational and recreational therapy. In American cities with a high incidence of addiction, there is increasing conviction that the addict should be treated as a very sick man rather than as a criminal. In New York 450 hospital beds are set aside for the use of male addicts (the female addict is relatively unusual), and much attention is focussed on prevention by education, on the after-care and social rehabilitation. Yet relapses are common—most addicts come to hospital not to be cured but to escape from pressing problems or to have their tolerance reduced so that they can afford to return to their drug. Forty-one per cent of voluntary admissions leave one hospital within 8 days, 83 per cent within 25 days and out-patient appointments for further treatment are rarely kept. In Israel it is estimated that 20 per cent of treated addicts safely survive the first year but only 2-3 per cent do not relapse within five years. There, as in America, the problems of the association of drug addicts with other occupants of psychiatric wards and the difficulties of staff attitudes at all levels are very great and it is argued that the majority of drug addicts need three to five years under strict supervision on a work camp or farm if they are to be cured.

The doctor is advised to seek a second opinion if he feels that he must prescribe a prolonged course of dangerous drugs and to give only a limited supply of such to a patient temporarily under his care unless he has been in correspondence with the patient's own doctor. After weighing the pros and cons, proposals for the establishment of specialised institutions, compulsory committal of addicts to such, systems of registration of addicts, the use of special distinctive prescription forms for dangerous drugs, further statutory powers to control new analgesic drugs, or to cope with irregularities in prescribing, are not regarded as necessary or desirable. The substantial increase in the use of drugs which are potentially habit-forming is regarded as something which requires careful watching but, at present, no further statutory control.

#### THE PHARMACIST

The pharmacist is the man who knows all about drugs and increasingly the doctor will lean upon him for guidance and be grateful for his advice. With the insistence on prescriptions for all drugs that are potentially habit-forming it may seem that the burden of responsibility is placed upon the doctor rather than the pharmacist. But the scrutiny of prescriptions for dangerous drugs has often led to the detection of errors, of wrong doses, of alterations made by the patient to increase supplies. No less important is the co-operation between doctor and pharmacist as two professional men, both part of the Health Service, both concerned with the welfare of those who



seek their aid. Knowing the miseries that addiction can produce, both are concerned with avoiding the risk but this does not mean that they are unprepared to use dangerous drugs as necessary for the relief of pain. Provided the physician and pharmacist meet they will find ways and means of helping each other.

The responsibility is not limited to the retail pharmacist. The hospital pharmacist may have difficulties over the authority held by sisters and acting-sisters in charge of wards to hold stocks which the pharmacist has to check from time to time. True, the sister only supplies these drugs to patients "in accordance with the instructions of the doctor in charge" but drugs are not always checked as regularly as might be desirable. On the other hand some sisters insist on a daily personal check of their Dangerous Drugs cupboards.

The manufacturing pharmacist who may be concerned with the introduction of a new drug of potential addiction clearly has a great responsibility. If its dangers are not recognised and its distribution safeguarded from the first, great harm may be done. Much attention has recently been focussed on adequate clinical trials for new products. If the product be possibly addicting, suitable tests are the more necessary. Such have been devised and used at Lexington. We may have to refer our questions to such a centre.

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