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SYMPOSIUM
DRUG ADDICTION
FIRST INTRODUCTORY ADDRESS

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The use or misuse of drugs leading to habit and addiction is an old problem to the doctor and the pharmacist. In Britain it is not a very large or serious one and certainly not to be compared in size to the problems arising from addiction to alcohol. But drug fashions and habits change and a one-time serious danger disappears or is dwarfed by a new difficulty. In particular, the development of synthetic substitutes for morphine in the last 25 years has modified the opium problem, while the increase in the use of barbiturates and the so-called tranquillisers is disquieting.

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." I had the honour of serving upon that Committee and have for some years had close contact with the Society for the Study of Addiction and as a member till recently of the Council of the P.S.G.B. have some experience of how pharmacists are involved in the problems that addiction to drugs can raise.

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.

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

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

* The Chairman's Address entitled "The Role of the Pharmaceutical Sciences in Medicine" is published in the *Pharmaceutical Journal*, 1962, **189**, 243–246.

2. A tendency to increase the dose, though some patients may remain indefinitely on a stationary dose.

3. A psychological and physical dependence on the effects of the drug.

4. The appearance of a characteristic abstinence syndrome in a subject from whom the drug is withdrawn.

5. An effect detrimental to the individual and to society.

Drug Habituation (habit) is a condition resulting from the repeated consumption of a drug. Its characteristics include:

1. A desire (but not a compulsion) to continue taking the drug for the sense of improved well-being which it engenders.

2. Little or no tendency to increase the dose.

3. Some degree of psychological dependence on the effect of the drug, but absence of physical dependence and hence of an abstinence syndrome.

4. Detrimental effects, if any, primarily on the individual."

It has also defined sedative, hypnotic, tranquilliser and stimulant drugs but gives both pharmacological and popular conceptions of the term "narcotic"—to the man in the street "drug" and "narcotic" are often understood as drugs of addiction.

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 habitué 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 effect". 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 meprobamate. 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 do 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. We 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 we 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 of synthetic analgesics had arisen, apart from derivatives of morphine such as diamorphine. 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 dangers 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 be 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, in America, contend".

TABLE I

EXTENT, TRENDS AND NATURE OF THE ADDICTION 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) 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 50,000 morphine 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. He also maintains that these unfortunates are mostly

psychopaths from the depressed strata of society. It would therefore seem specially important that the psychopath should never be introduced to potential drugs of addiction where this can be avoided.

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 compounded analgesic preparations (Analgin, Antoin, Cephacan, Codis, Dellipsoids D-4, Dexocodene, Dolviron, Hypon, Nembudeine, Neurodyne, Pardale, S.A.C., Vagadil-Alk, Veganin).

TABLE II

Relative consumptions of pethidine and morphine in selected countries

	Pethidine used (in kg.) in 1960	Ratio (per cent) of pethidine to morphine used in 1960
U.S.A.	10,758	0·63
United Kingdom	2,745	0·16
Germany	1,497	0·13
Canada	638	15
France	500	0·05
Ireland	66	5
Mexico	56	19

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 rauwolfia 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.

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 recognised 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, 1962) 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 and thorough 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 affect the nervous system as to produce physical or psychological deterioration should be supplied only on prescription. This puts the responsibility on the doctor. 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.

TABLE III

BARBITURATES PRESCRIBED AND INCIDENCE OF POISONING IN ENGLAND

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

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 and such have been devised and used at Lexington. We may have to refer our questions to such a centre.

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SUMMARY OF

SECOND INTRODUCTORY ADDRESS

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THERE is no agreed scientific definition of addiction. There is a popular definition and it works: The patient says "I can't do without it."

There is an absence of precise scientific knowledge about addiction. From the pharmacological and clinical aspects, drug tolerance, habituation and addiction are part of a spectrum, and it depends where the dividing line is drawn as to whether one is dealing with an habituate, an addict, or merely one who had a tolerance. It is extremely difficult to say that one individual is habituated and another is addicted. More knowledge of enzyme reactions might provide a clue to the situation.

With addiction there is a tendency to increase the dose: with habituation, little tendency. There is also a psychological and physical dependence in addiction but psychological dependence only in habituation. The occurrence of an abstinence syndrome depends on the patient, on the amount of the drug, and on the duration of treatment.

In the range of habituation and addiction, the patient's symptoms remain unabated and his demands increase. Experience suggests that that state of affairs arises from an inability to cope with life—a form of escape from reality. There follows a depression of moral standards, and then a swift depression of morale.

Drugs which may lead to addiction are those which relieve anxiety, or tension, or fear, or all three. Morphine, heroin, pethidine and, perhaps, certain barbiturates, in proper hands, were most beneficient drugs but lead to addiction if misused by the patient or by the prescriber. New sedative, hypnotic, or tranquillising drugs might prove sooner or later to be addictive; it is not always possible to uncover these properties until some years have elapsed.