Drug Treatment of Disease

ADDICTION TO DRUGS: PART II*

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Treatment of Addiction

There are three underlying principles. The first is to wean the patient from the drug. The second is to persuade him of the necessity of forswearing it finally and for ever. The third is for both patient and therapist to try to understand the mode of life, the attitudes of mind and the "psychodynamics" that have led to the addiction, and, in the light of that understanding, to make adjustments in the mode of life and attitudes of mind, with the substitution of other sources of satisfaction. The first of these principles may be effected without much difficulty provided the patient agrees, but implementation of the second and third principles is never easy and may be very difficult indeed. It is, however, with the first principle that we are mainly concerned here.

It is almost always necessary for the patient to be removed from home and from the associations with which the addiction started, and placed in a controlled environment (i.e., hospital or nursing-home), away from sources of supply. Even so, many patients will cheat, and precautions must be taken accordingly. The patient should be kept in bed, on a full diet with extra glucose fluids and vitamins. Occupation should be encouraged as soon as the patient's condition allows. Daily charts should be kept.

The means by which the drug is withdrawn will depend upon the severity that may be expected of the withdrawal symptoms. Severe withdrawal symptoms may be expected in addiction to morphine and its derivatives, to methadone and phenadoxone, and to pethidine. Moderate withdrawal symptoms may be expected in gross barbiturate addiction. Otherwise the withdrawal symptoms will be mild. The milder the withdrawal symptoms, the stronger is the case for immediate withdrawal of the drug—for example, in alcoholism, and in addiction to cocaine, chloral, and amphetamine. As to the more severe addictions, it is sometimes argued that gradual withdrawal by tapering off the dose is only to prolong the agony, but, since few patients will agree to abrupt withdrawal and it is possible to conduct gradual withdrawal without agony, the latter seems the better course. At this point it may be borne in mind that the addict's usual tendency to understate the amount that he takes is now apt to be reversed, owing to fear of being cut off too soon. A plan is then formed by which the dose of the addictive drug is gradually reduced over a period of, say, five to six days until an exiguously small dose is reached, followed by none at all. Formerly, it was usual to substitute barbiturates, and to induce a light narcosis to mitigate the discomfort of withdrawal. Nowadays this can be more satisfactorily managed by the use of chlorpromazine ("largactil," "thorazine") or its relatives, promazine hydrochloride ("sparine") and

acetylpromazine ("notensil"). These substances are also useful in the treatment of barbiturate addiction itself.

For example, a patient with a combined addiction to morphine and pethidine had succeeded in reducing her consumption of the former to about 1/10 gr. (6.5 mg.) three times a day, and of the latter to about 400 mg. in the day, usually taken in about eight doses varying between 40 mg. and 100 mg. each. The regime outlined in Table I was successful in getting her off the admittedly small doses of both drugs over a period of eight days with virtually no discomfort at all.

Such plans must not be adhered to too rigidly. There should be elasticity and variation according to the needs of the case. Anorexia, for example, may be so marked that the patient cannot eat satisfactorily unless the drug of addiction is given in relation to meals. Much discomfort may call for increase in dosage of chlorpromazine or barbiturate. The former is to be preferred. It may be given intramuscularly if a rapid effect is required, otherwise by mouth, in doses of 50–100 mg., which may be repeated if necessary up to three, four, or more times in the day. In the dosage that is likely to be required for treating drug addiction, such untoward

TABLE I

	Time	Pethidine	Morphine	Chlorpromazine	Barbiturates
1st day	0500	75 mg.	—	—	—
	0800	50 "	gr. 3/40 (5 mg.)	—	—
	1030	50 "	—	—	—
	1500	50 "	—	—	Amylobarbitone gr. 3/4 (50 mg.)
	1900	100 "	—	—	Sod. amylobarb. gr. 6 (400 mg.)
	2230	50 "	—	—	—
		375 "			
2nd day	0730	50 "	—	—	—
	1030	50 "	—	50 mg. i.m.*	—
	1500	25 "	—	—	—
	1900	75 "	—	50 mg. i.m.	—
	2230	50 "	—	—	Sod. amylobarb. gr. 6 (400 mg.)
		250 "			
3rd day	0730	50 "	—	—	—
	1030	25 "	—	50 mg. i.m.	—
	1500	25 "	—	—	—
	1900	50 "	—	50 mg. i.m.	—
	2230	50 "	—	—	Sod. amylobarb. gr. 6 (400 mg.)
		200 "			
4th day	0730	50 "	—	—	—
	1030	25 "	—	—	—
	1500	—	—	50 mg. i.m.	—
	1900	50 "	—	—	—
	2230	25 "	—	—	Sod. amylobarb. gr. 6 (400 mg.)
		150 "			
5th day	0730	25 "	—	50 mg. i.m.	—
	1030	25 "	—	—	—
	1500	—	—	50 mg. i.m.	—
	1900	25 "	—	—	—
	2230	25 "	—	—	Sod. amylobarb. gr. 6 (400 mg.)
		100 "			

The pethidine was then reduced to 25 mg. t.d.s. and 25 mg. b.d. on successive days before being stopped altogether on the eighth day, when chlorpromazine 50 mg. t.d.s. was substituted without complaint from the patient.

* i.m. = intramuscularly.

*Part I of this article was published last week at p. 850.

TABLE II

	Time	Heroin	Chlorpromazine	Barbiturate (Sod. Amylobarb.)	Paraldehyde
1st day	1600	gr. 2/3 (45 mg.) i.m.*	—	—	11 ml.
	1900	gr. 5/12 (27 mg.) i.m.	25 mg.	—	—
	2200	gr. 5/12 (27 mg.) i.m.	—	gr. 6 (400 mg.)	—
2nd day	0800	—	50 mg.	gr. 2 (130 mg.)	—
	0900	gr. 3/4 (50 mg.) i.m.	—	—	—
	1300	gr. 5/12 (27 mg.)	—	gr. 2 (130 mg.)	—
	1600	gr. 5/12 (27 mg.)	—	—	11 ml.
	1900	gr. 5/12 (27 mg.)	50 mg.	—	—
3rd day	0800	gr. 6/12 (32 mg.)	50 mg.	gr. 2 (130 mg.)	—
	1300	gr. 2/12 (11 mg.)	25 mg.	—	—
	1600	gr. 2/12 (11 mg.)	50 mg.	—	—
	1900	gr. 2/12 (11 mg.)	25 mg.	—	—
	2200	gr. 2/12 (11 mg.)	—	gr. 6 (400 mg.)	—
4th day	0700	gr. 4/12 (22 mg.)	—	—	—
	0800	—	50 mg.	gr. 2 (130 mg.)	—
	1300	gr. 2/12 (11 mg.)	25 mg.	—	—
	1600	gr. 2/12 (11 mg.)	50 mg.	—	—
	1900	gr. 2/12 (11 mg.)	25 mg.	—	—
5th day	0700	gr. 4/12 (22 mg.)	—	—	—
	0800	—	50 mg.	gr. 2 (130 mg.)	—
	1300	gr. 1/12 (5 mg.)	25 mg.	—	—
	1600	gr. 1/12 (5 mg.)	50 mg.	—	—
	1900	gr. 1/12 (5 mg.)	25 mg.	—	—
6th day	0700	gr. 3/12 (16 mg.)	—	—	—
	0800	—	50 mg.	gr. 2 (130 mg.)	—
	1300	gr. 1/12 (5 mg.)	25 mg.	—	—
	1600	—	50 mg.	—	—
	1800	gr. 1/12 (5 mg.)	—	gr. 2 (130 mg.)	—
	2200	gr. 1/12 (5 mg.)	—	gr. 6 (400 mg.)	—

The patient was off heroin by the eighth day without discomfort, but this withdrawal could have been achieved far more quickly if the doses of chlorpromazine had been doubled.

* i.m. = intramuscularly.

side-effects as jaundice, skin rashes, and development of a Parkinsonian syndrome are unlikely to occur, but, if there is a history of previous jaundice or evidence of liver damage, the allegedly less toxic related compounds—for example, promazine hydrochloride—may be substituted in similar dosage.

The plan shown in Table II allowed a comfortable withdrawal in the case of a man addicted to upwards of 3 gr. (200 mg.) of heroin intravenously spread through the day.

A patient addicted to morphine for seven years and accustomed to between twenty and thirty tablets of $\frac{1}{4}$ gr. (16 mg.) each in the day, was given $\frac{1}{2}$ gr. (32 mg.) hypodermically with sodium amylobarbitone 6 gr. (400 mg.), when admitted late at night, and thereafter was weaned from the drug with practically no complaint, though she was a very querulous person (see Table III).

Apart from giving chlorpromazine or its related compounds together with barbiturates, a comparatively modern technique which may be combined with that is treatment with insulin. The patient may be given 20 units, increased to 30 and then 40 on successive days, subcutaneously at, say, 7 a.m. This is followed by a meal rich in carbohydrate three hours later. The procedure can be repeated in the afternoon. (The patient should be observed day and night for possible subsequent hypoglycaemic reactions, which will call for reduction of insulin dosage). If the patient shows any sign of slipping towards sleepiness before three hours have elapsed, the hypoglycaemia should be terminated by glucose fluids, if necessary by nasal tube or by 33% glucose intravenously. Again, the next dose of insulin should be smaller. This is known as modified insulin treatment.

When withdrawal symptoms can be expected to be moderate or mild—that is, cases of addiction to barbiturates, alcohol, cocaine, chloral, amphetamine, or paraldehyde—the administration of chlorpromazine or its related compounds in doses of, say, 50 mg. four times a day orally (with intramuscular injections periodically instead, if rapidity of effect is specially desired), should suffice to keep the patient comfortable, and can be reduced gradually over several days after the patient has been weaned from the addictive drug itself. The hazard of pre-existent liver damage should be borne in mind, however, especially in alcoholic patients, whose withdrawal symptoms are anyway unlikely to be so severe as to call for any substantial medication unless there is a serious threat of delirium tremens.

Alcoholic Addiction

The treatment of alcoholic addiction is in itself a large subject, but it is worth mentioning here that both chlorpromazine (or the allied promazine) and the so-called modified insulin treatment described above are of use in controlling delirium tremens, while modified insulin is also valuable for detoxicating the alcoholic patient who remains short of delirium. Apart from detoxication and the control of delirium tremens, the immediate treatment of chronic alcoholism is usually directed towards diminishing the craving for and setting up an aversion to alcohol. These are specialized techniques which have often been described in the textbooks.

What is comparatively new is the long-term treatment of the alcoholic with disulfiram ("antabuse," "cronetal"). This substance, taken by mouth, interferes with the normal metabolism of ingested alcohol, causing accumulation in the blood stream of acetaldehyde, with unpleasant toxic effect. In fact, it causes acetaldehyde poisoning, with symptoms of tightness in the chest, pounding in the neck, a burning flush, headache, profound malaise, sometimes with nausea and

TABLE III

	Time	Morphine	Chlorpromazine	Barbiturate (Sod. Amylobarb.)	Paraldehyde
1st day	0800	gr. $\frac{1}{4}$ (32 mg.)	50 mg. orally	—	—
	1200	gr. $\frac{1}{4}$ (32 mg.)	—	—	—
	1600	—	50 mg. i.m.*	—	—
	1800	gr. $\frac{1}{4}$ (16 mg.)	—	—	—
	2200	gr. $\frac{1}{4}$ (32 mg.)	—	gr. 6 (400 mg.)	—
2nd day	0800	gr. $\frac{1}{4}$ (16 mg.)	50 mg. i.m.	—	—
	1200	gr. $\frac{1}{4}$ (32 mg.)	—	—	—
	1600	—	50 mg. i.m.	—	—
	1800	gr. $\frac{1}{4}$ (16 mg.)	—	—	—
	2200	gr. $\frac{1}{4}$ (32 mg.)	—	gr. 6 (400 mg.)	—
3rd day	0800	gr. $\frac{1}{4}$ (16 mg.)	50 mg. i.m.	—	—
	1200	gr. $\frac{1}{4}$ (16 mg.)	25 mg. orally	—	—
	1600	—	50 mg. orally	—	—
	1800	gr. $\frac{1}{4}$ (16 mg.)	—	—	—
	2200	gr. $\frac{1}{4}$ (32 mg.)	—	gr. 6 (400 mg.)	—
4th day	0800	gr. $\frac{1}{4}$ (16 mg.)	50 mg. i.m.	—	—
	1200	gr. $\frac{1}{4}$ (16 mg.)	50 mg. orally	—	—
	1600	—	50 mg. orally	—	—
	1800	gr. $\frac{1}{4}$ (8 mg.)	—	—	—
	2200	gr. $\frac{1}{4}$ (16 mg.)	—	gr. 6 (400 mg.)	—
5th day	0800	gr. $\frac{1}{4}$ (16 mg.)	50 mg. orally	—	—
	1200	gr. $\frac{1}{4}$ (8 mg.)	25 mg. orally	—	—
	1600	—	50 mg. orally	—	—
	1800	gr. $\frac{1}{4}$ (8 mg.)	—	—	—
	2200	gr. $\frac{1}{4}$ (8 mg.)	—	gr. 6 (400 mg.)	—
6th day	0800	gr. $\frac{1}{4}$ (8 mg.)	50 mg. orally	—	—
	1200	—	50 mg. i.m.	—	—
	1600	—	—	—	—
	1800	gr. $\frac{1}{4}$ (8 mg.)	—	—	—
	2200	gr. $\frac{1}{4}$ (16 mg.)	—	gr. 6 (400 mg.)	6 ml. i.m.

Two days later the patient was morphine-free. Again, the withdrawal could have been achieved more quickly with larger doses of chlorpromazine.

* i.m. = intramuscularly.

vomiting. The rapidity and extent of these developments depend upon the rapidity of ingestion of alcohol and upon the amount of disulfiram taken. They may progress to orthostatic faintness and vasomotor collapse; coronary thrombosis has been known to occur. For these reasons disulfiram should never be given to an intoxicated patient, and introduction to the treatment is best given in hospital. It is usual to give 1-2 g. of disulfiram daily for three days, and to give the patient alcohol, in its preferred form, on the fourth day. A suitable dose is 2 fl. oz. (57 ml.) of gin or whisky, which may be repeated every 10-20 minutes according to the effect or lack of it. The flushing is usually replaced by pallor after about 45-60 minutes, and it is safest then to discontinue the alcohol, usually with the patient's ready agreement. The early development of pallor, with rising pulse rate and falling blood pressure, is a warning signal. As delayed reactions with vasomotor collapse and vomiting sometimes occur, the patient should be kept under observation for the rest of the day, and preferably in bed. If the effect is not severe enough to make much impression on the patient, the procedure can be repeated with larger and more frequent doses of alcohol. The patient is then encouraged to continue taking disulfiram (0.25 g.) daily in the hope that knowledge of its effects may help him to abstain from alcohol. No great reliance can be placed on this form of treatment except as a useful adjuvant to the more rigorous methods already referred to, designed to remove the craving and set up an aversion.

Finally, since all addictions, and especially alcoholism, are apt to lead to dietary neglect, vitamins will have a part to play in treatment. Although I am less impressed than many by the effect of massive vitamin dosage in controlling or aborting delirium tremens, this may confer benefit and appears to do no harm. Recommended doses are: aneurine 1,000 mg., riboflavine 10 mg., pyridoxine 400 mg., nicotinic acid amide 200 mg., ascorbic acid 1,500 mg. These are best given intravenously, and, if the patient can be kept quiet enough, can be added to an intravenous infusion of 1,000-2,000 ml. of 10% dextrose in normal saline containing also 30 units of insulin. Except in cases of delirium tremens, a suitable preparation of vitamins for correcting dietary deficiency and stimulating appetite during the withdrawal phase is "parentrovite." This is prepared in ampoules for intravenous injection. One or more ampoules a day may be given according to the nutritional state.

FROM SCHOOL TO UNIVERSITY EDUCATIONISTS CONFER AT LEEDS

A conference on "School and University Relationships, with Particular Reference to Medicine," was held last week at Leeds under the auspices of the Institute of Education of the University of Leeds. About seventy headmasters, headmistresses, and members of the faculty of medicine attended.

The conference was opened by Professor P. J. MOIR, dean of the faculty of medicine, who gave a brief account of the landmarks of medical training, the opportunities available to medical graduates, and the current distribution of medical graduates in the different

branches of the profession. Figures relating to women were given, based on a report of the British Medical Women's Federation.

Professor A. HEMINGWAY, professor of physiology, stressed the unique feature of medical training, in that it combined both university education and vocational training. Explaining the role of the General Medical Council in the control of medical education, he stressed that the G.M.C. made recommendations and that these were not to be interpreted as regulations. The recent report of the G.M.C. was couched in general terms and gave the universities much greater freedom to plan courses. A new development, resulting from the passing of the Medical Act of 1951, had been the power of the G.M.C. to inspect medical schools and to report upon the courses, teaching, and equipment.

The speaker then passed to the requirements for entry into medical faculties. In 1957 2,192 medical students were admitted to the medical schools of Great Britain, and of these 1,456 took a 1st M.B. course. Therefore, roughly one-third of those admitted were exempted from the 1st M.B. The new entrance requirements of London University—three subjects at the advanced level in the G.C.E. (chemistry, physics, and zoology in the case of medicine)—had had a profound effect upon the policy of other universities. Professor Hemingway himself did not personally approve of modern tendencies, nor in the partial disappearance of the 1st M.B. in the universities. In discussing university entrance requirements, he thought that there was the tendency to neglect the quantitative approach to medicine, and he hoped that schoolmasters would realize that a good grounding in mathematics and physics provided a useful basis upon which to build a medical course.

A Schoolmaster's View

Mr. J. DRONFIELD, headmaster of St. Peter's School, York, spoke as a schoolmaster concerned with the problem of advising boys upon medicine as a career and then with getting them into medical schools. He held the profession in high regard, as in his view did the public. Even the hardened businessman was not altogether disappointed if one of his sons, not wishing to enter the business, was prepared to take up medicine. He had been interested in the recent return to popularity of medicine as a career for doctors' sons.

The qualities he looked for in advising a boy to study medicine were (1) a good intelligence, (2) an interest in people, and (3) that he was a good mixer. He took notice of a sense of vocation, but in a boy of 16 or 17 this could often be misleading, and one had to be very careful in interpreting the significance of a boy's so-called sense of vocation. The schools wanted to know how much science a boy ought to know before beginning the study of medicine and how much time should be spent on non-vocational subjects.

Women in Medicine

Miss M. M. BLACK, headmistress of Bradford Girls' Grammar School, opened the discussion from the woman's point of view. Medicine was a very long course for a woman to undertake. When the average age of marriage was lower, there was a tendency for girls to feel they were "on the shelf" if they were not engaged by the age of 19. This often meant that they married during the medical course, which was far from being an ideal situation. Miss Black asked if the supposed equality of men and women in medicine really was a fact when it came to appointments. She would like to know whether women gravitated towards