been made to demonstrate the relevant arterial distribution by injecting methylene blue into the umbilical artery of a living anencephalic foetus, but without success. Experiments have been made elsewhere to reproduce the lesion in cats, but no positive result has been obtained. The difficulty of such experiments lies in the fact that the injection must be made against the full force of the neonatal blood pressure, and the fluid is thus unlikely to travel so far in a retrograde direction as it would when the subject was shocked or gravely asphyxiated. However, it is of some significance that after explanation of the danger of intra-arterial injection to the resident staff no further cases were recorded; and those who are uncomfortably aware of having themselves made such an injection testify to the extreme facility with which it may be made in moments of stress and shortage of sleep. There is no satisfactory explanation of the variable interval between injection and discovery of the lesion (6–60 hours), and an inexplicable fact is the sudden appearance of this series of cases in a hospital in which the use of nikethamide by injection into the umbilical cord has been an integral part of the routine for neonatal resuscitation for several years.

Summary

A new syndrome is described, comprising arterial lesions with occasional paralysis in the lower limb of the newborn.

Eight cases are recorded as having occurred in a period of 10 months at a busy maternity hospital.

The aetiology of the condition remains unproved. It is suspected that the lesions may be due to injection of drugs into an artery in the umbilical cord. The evidence in favour of this theory is discussed.

I am deeply indebted to Dr. Frances Braid for her interest in these babies and her stimulating encouragement. I wish to thank Dr. Hudson, of the Walton Hospital, Liverpool, for details of a similar series of cases, and the staff of the Birmingham Maternity Hospital, under whom the cases were admitted, for permission to publish.

A number of Government scholarships have hitherto been available to selected nurses who wished to train as nurse tutors. The assistance given has covered the training and examination fees and the cost of books, and provided an allowance of £150 for the period of training. The Ministry of Health has decided to end this arrangement and to substitute the following. Nurses, both male and female, who are accepted by training institutions for training as nurse tutors should be granted leave on full pay, including emoluments where appropriate, for the period of the training. The nurse would be required to pay the full cost of the training, including examination fees and books. The courses cover an academic year and begin in the latter part of September or early October. The recognized institutions which will be running courses next term are: Battersea Polytechnic, Battersea Park Road, London, S.W.11 (40 places); King's College of Household and Social Science, Campden Hill Road, London, W.8 (20 places); Royal College of Nursing, 1A, Henrietta Place, London, W.1 (36 places); University College, Hull (12 places). The fees for the courses vary from £20 to £50. Applicants must (a) be registered in the General Part of the State Register, or the Part of the Register for Male Nurses (General Trained); (b) have had at least three years' experience in nursing in hospital since registration in any Part of the Register, including at least one year as a ward sister (or corresponding rank in the case of a male nurse) in an approved training school; (c) satisfy the training institution that their general education is such as to justify taking up training. Where an applicant is registered both as a general trained nurse and as a mental nurse or nurse for mental defectives, but has not had a year's experience in charge of a ward, the applicant must have post-registration experience, satisfactory to the General Nursing Council, in an approved training school for a period of at least four years.

TETRAETHYLTHIURAMDISULPHIDE* IN THE TREATMENT OF ALCOHOLICS

BY

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So numerous have been the drugs and techniques used and abused in the age-long struggle against alcoholic excess that one naturally is wary about recommending any new preparation. Yet tetraethylthiuramdisulphide, with the structural formula of $(C_2H_5)_2N.C-S-S-CN(C_2H_5)_2$, recently

introduced by Dr. Erik Jacobsen, of Copenhagen, shows such promise that it merits extended trial so soon as it becomes readily available to the medical profession in this country. Adequate samples were placed at my disposal upon request, and the following preliminary report shows the advantages derivable from its administration.

The Drug's Action

Before relating these it will be of interest to expound the pharmacological basis of the drug's action. For many years it has been known that certain substances—e.g., cyanamide and the fungus *Coprinus atramentarius*—though innocuous to man when taken alone, yet gave rise to unpleasant symptoms when alcohol subsequently was consumed. Tetraethylthiuramdisulphide has a similar action, and the work of Dr. Jacobsen and his colleagues in Copenhagen has shown fairly conclusively that these characteristic effects are due to an interference with the normal metabolism of alcohol in the body, so that unusually high levels of acetaldehyde become present in the blood stream. Acetaldehyde is a normal intermediate stage in carbohydrate metabolism, and after alcohol its presence in the blood shows a temporary slight increase. When any member of the sensitizing group of substances now under discussion has been taken before the consumption of alcohol the blood acetaldehyde rises steeply (up to tenfold) and its elimination is slow.

Aldehydes are derived from the simple oxidation of primary alcohols, as is shown by the following equation with structural formulae:

Exactly how tetraethylthiuramdisulphide interferes with the normal metabolism of alcohol is not yet known, but there is an interesting correlation between this and the course of events in vitamin B₁ deficiency. In the latter case pyruvic acid, not acetaldehyde, is the stage at which metabolism goes wrong. Aldehydes and ketones are closely allied, having the same general formulae $C_nH_{2n}O$. Similarly the aldehydic and ketonic acids are closely related, and pyruvic

acid, $\begin{array}{c} H \\ | \\ H-C-C \begin{array}{c} \nearrow O \\ \searrow OH \end{array} \end{array}$, is the simplest of the ketonic

acids. Later the relation between the mechanism of the two derangements in carbohydrate metabolism will probably be discovered. Possibly some similar if not identical inborn

*This drug has the proprietary names of "antabus," "antabuse," and "antanco."

error of metabolism will be found to account for the hypersensitivity of certain individuals to small doses of alcohol.

Tetraethylthiuramdisulphide has an advantage over other sensitizing drugs in that, though its action is prolonged, lasting several days, there is no evidence of cumulative toxic effects in the dosage usually employed. Moreover, it is easy to carry and to administer orally in tablet form. No symptoms arise unless and until alcohol also is ingested. Then typical symptoms begin with a burning sensation in the face. This is followed by injection of the conjunctival vessels and redness of the face. The loose tissue around the eyes becomes congested and the patient may have difficulty in keeping his eyes open. The pulse increases in frequency and may gradually rise to 150 a minute, but there is little if any change of blood pressure, though most patients complain of a pounding at the heart. Giddiness, hammering in the ears, and headache are next to appear, and the patient complains of a vague generalized anxiety and distress. Finally, if the doses of both substances have been large, he vomits and feels "thoroughly ill." Symptoms begin within a quarter of an hour of the intake of alcohol and last a variable time (up to five hours), then fade away gradually in sleep. On the following day the patient feels lackadaisical and listless, but is capable of carrying on his work.

These typical symptoms, of course, are subject to considerable individual variation in their march and severity, but the above recital affords a general picture of the average patient under close observation. Advantage has in two ways been taken of the disagreeable sequelae of this drug plus alcohol as an aid in the total treatment of excessive drinkers.

Method of Treatment

First, in a special institution for the rehabilitation of alcoholics those patients allowed out on parole receive a dose of 1 g. the previous day and 0.75 g. at breakfast on the morning of the day of *cong*. As a knowledge of the effects of the drug has not yet spread abroad patients do not know the consequences which a breaking of parole will entail. They think that the tablets received are merely vitamins, to which they are accustomed. Should a patient upon his return from an outing complain that queer things befell him his physician draws the obvious conclusion, but, instead of asking awkward questions, explains that the susceptibility of persons under treatment is such that any lapse to alcoholic beverages is likely to be fraught with not unmerited distress.

As patients and public become knowledgeable concerning the properties of these innocent-looking tablets this particular device will cease to have strategic value and the second method must be adopted.

This method is frankly to discuss with the patient the way in which tetraethylthiuramdisulphide can be used to contribute to a cure in his individual case. He is then free to decide whether to co-operate in the plan. Though there is no pretence that the drug of itself can rectify the defective personality structure of which alcoholism is a symptom, it can, by temporarily rendering the lure of alcohol easier to resist, gain a sober interval in which the process of reorientation can be begun. Possibly also, though this is at present not proved, a small daily dose in a patient of good will may establish a permanent distaste for alcohol. Even so, unless those underlying motivations which prompted the patient to excess be adjusted he cannot be regarded as cured. The largely unconscious urges which gained neurotic gratification via alcohol will, if this means of escape be denied to them by pharmacological force alone, break out in some other and possibly more objectionable form. This drug

is therefore not recommended as a quack cure, but as a powerful addition to our already existing therapeutic armamentarium.

Before regular administration of tetraethylthiuramdisulphide is begun the patient should be put to a clinical test as follows. After sensitization has been established in the way about to be described, alcohol is administered to the patient according to his usual habit when drinking. His reactions then are carefully studied throughout. The detailed recital of a single typical but rather severe case will be more instructive than any attempt at statistics in illustrating the method adopted during a course of general and psychological treatment.

Illustrative Case

A married man aged 42, with no children, was first admitted in 1947. He was a Cambridge graduate and barrister-at-law, teetotaler until the age of 25, when he began drinking, which rapidly became excessive. His behaviour towards his wife became so brutal that he eventually consented to undergo institutional treatment. Under this he improved and gained considerable insight. He had, however, a suspicion, not altogether unfounded, that his wife meant to leave him when he got cured, and while he was undergoing treatment was only keeping in touch with him from a sense of her moral duty. He showed all the signs of an overcompensated inferiority complex with an overwhelming wish to be in the limelight and the "life and soul of every party."

On his return home renewed quarrels with his wife soon led to relapse. He thereupon left home and took up quarters in a public house at a port, where he drank heavily. While thus disporting himself he received a severe blow on the head in a drunken brawl. This necessitated trephining for removal of a blood clot. After discharge from hospital he went home and for a time refrained from alcohol. Then, without knowing why, he relapsed and kept drinking up to a bottle of gin a day and had superadded acute exacerbations associated with amnesia.

He insisted, however, that he had no real desire for alcohol but wanted to be cured of his uncontrollable habit. His history was already known in detail, as he had by request written an autobiography during his first admission, and this was brought up to date when he of his own wish returned for treatment early in 1949. The advantages derivable from tetraethylthiuramdisulphide were then explained to him, and he readily promised his whole-hearted co-operation. After a few days' rest, sedation, and detoxication a first test with the drug was performed to gauge his individual reactions. A dose of 0.75 g. was given one evening, and was repeated next morning. At 2.30 p.m. he was given a "double" gin (2 oz. (57 ml.) of 70% proof alcohol). Ten minutes later his face became hot and red. His conjunctivae were bloodshot and his lower eyelids puffy. His pulse went up from 68 to 120. Respiration also increased and he complained of a pounding at the heart and in the head. At 2.50 p.m. another double gin was given. Within a few minutes the patient's distress increased, his pulse rose to 130, and he felt so squeamish that he was sure any more gin would make him sick. These symptoms gradually subsided and he felt normal in just over two hours.

That night 1 g. of the drug was taken, and again at 10 a.m. the next day. At 3.45 p.m. he was given 2 oz. of gin. Symptoms as previously described came on more quickly than on the first occasion. A second 2 oz. of gin was given at 3.55 p.m. By 4 p.m. he felt extremely uncomfortable, with all symptoms increasing in severity. He next complained of seeing double and feeling generally ill and confused. At 4.05 p.m. a third 2 oz. of gin was given. (This order of drinking was the man's usual, and without the drug did not upset him, but led to more drinks.) After this third gin he became rapidly confused and felt desperately ill and anxious; pulse 150, respirations 36. Tingling followed by anaesthesia of the left hand developed and he could not move his left ring-finger and little finger. (These latter unusual symptoms probably are associated with his cranial operation.) At this point his face became pale instead of red, and he complained of feeling cold. At 4.25 p.m.

he vomited and asked to be allowed to go to bed. He complained of "noises in his head as if an engine were pumping away outside." At 5 p.m. he became sleepy and refused a proffered cup of tea and a cigarette. At 5.40, 5.45, and 6 p.m. he again vomited and complained that the vomit tasted unusually acid. He also felt "icy cold" but otherwise better. At 8 p.m. he vomited for the last time, and thereafter slept fitfully through the night.

Next morning he "felt a bit washed out" and "uneasy in the stomach," but he worked in the garden for two hours, morning and afternoon, as usual. Three days later, according to a previous arrangement, he travelled home (a long journey with two changes and waits, involving a three-days absence) to attend a meeting of directors, before, during, and after which he used on former occasions to indulge freely in drink. On this occasion he was primed with tetraethylthiuramdisulphide, 0.75 g. night and morning over the period. He did not experience any disagreeable symptoms and did not have any inclination to drink. His institutional treatment will shortly be terminated. Then, as an added precaution when in the outer world, a daily dose of 0.25 g. will be prescribed for a month or two with a view to giving him an added sense of security, as it has done to others.

Comment

There is a hope that in milder cases, with the help of tetraethylthiuramdisulphide, the patient may receive enough help and understanding from his environment to dispense with specialized institutional treatment, or at any rate to shorten its duration. This, however, will require careful judgment, and remains for future experience to evaluate. At present one is justified in considering that tetraethylthiuramdisulphide seems likely to occupy a useful place in the treatment of alcoholics, and that it merits extensive but cautious investigation. The reactions of each individual patient under his usual drinking habit should be carefully tested the day after an initial sensitizing dose of the drug. Under out-patient conditions vigilance is required to see that a patient who has been placed on a small regular dose of the drug is not also managing to consume some alcoholic beverage. Should he do so the dose ought immediately to be quadrupled.

Summary and Conclusions

The use of tetraethylthiuramdisulphide is recommended as a useful ancillary, but not as a substitute for, general and psychological methods in the treatment of alcoholics.

The pharmacological action of the drug is discussed. It is innocuous to man unless followed by alcohol, but certain precautions in its administration are advocated.

Details in a severe case of alcoholic addiction are related in order to illustrate the symptoms and technique in treatment.

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Among developments that Governor Dewey has recently announced will be carried out in the New York State mental hygiene programme (*New York Times*, July 20) is the establishment of a new relationship between voluntary hospitals and State mental hospitals; the former will provide preliminary treatment for patients before they become State charges. A second innovation that he described as "my own private brain child" is the creation of a new intern system in which 200 men yearly will serve for two years as interns in every State mental hospital, which would pay interns more than the voluntary hospitals do. "This is a system of which I vigorously disapprove," he said, "unless it is a public necessity, and I think this is a public necessity."

INCIDENCE OF PHYSICAL DISORDERS AMONG PSYCHIATRIC IN-PATIENTS

A STUDY OF 175 CASES

BY

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During my period of duty as resident medical officer to the psychiatric unit I was so impressed by the number of patients needing attention for physical conditions that I reviewed the case records of all those admitted to the unit in 1948 in order to estimate the frequency of such conditions among the patients treated and the relevance of these to their psychiatric conditions.

Material Studied

During 1948 the unit had the use of 28 beds—22 for females and six for males, though, owing to redecorations, not all the former were continuously available. A total of 179 patients were admitted, of whom four did not stay long enough to allow of full examination and so are excluded from this series. The number of patients studied was 175, comprising 124 women and 51 men. All were in need of psychiatric attention, and no purely physical criterion entered into their selection.

The predominant features of the psychiatric conditions found were as follows: affective reactions, 108 (endogenous depression 51, reactive depression 35, anxiety states 16, cyclothymic reactions six); hysterical reactions, 22; schizophrenic reactions, 20; obsessional reactions, 16; organic reactions, five; hypochondriasis, neurasthenia, behaviour disorder, and drug addiction, one each.

Abnormal Physical Conditions

In no fewer than 77 patients (44%) some physical condition needing attention was found. As might be expected, the incidence was higher in those over 40 than in younger patients (61% against 35%).

In four patients serious physical disorders were first discovered during examination in the unit, their presence not having been previously suspected; these comprised one case each of pulmonary tuberculosis, bronchial carcinoma, glioma, and major epilepsy. In two other patients serious physical disorders, not related to the psychiatric condition, developed during their stay in hospital; these comprised one case each of cerebral thrombosis and thrombophlebitis.

In the accompanying tables the various physical conditions found are analysed according to their apparent relevance to the psychiatric conditions for which treatment was required.

TABLE 1.—Physical Conditions Contributing to the Onset of Psychological Illness

	No. of Patients
Gynaecological conditions (menopause, 6; pregnancy, 4; eclampsia, abortion, sterilization, puberty, 1 each)	14
Disorders of central nervous system (epilepsy, 3; cerebral contusion, glioma, internal carotid aneurysm, poliomyelitis, encephalitis lethargica, 1 each)	8
Disorders of respiratory tract (influenza, maxillary sinusitis, asthma, pulmonary tuberculosis, bronchial carcinoma, 1 each)	5
Orthopaedic conditions (prolapsed intervertebral disk, 2; fracture of tibia, 1)	3
Disorders of vision (cataract, Leber's atrophy, 1 each)	2
Endocrine disorders (acromegaly, hypothyroidism, 1 each)	1
Arteriosclerosis	1
Chronic nephritis	1
Intestinal obstruction	1
Otosclerosis	1