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Antabuse in the treatment of chronic alcoholism

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ANTABUSE IN THE TREATMENT OF CHRONIC ALCOHOLISM

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INTRODUCTION

For years the treatment of the chronic alcoholic has been studied from many angles. Recently our public press has led us to believe that at last a new drug, "Antabuse", has been discovered which is a cure for alcoholism.

It is clear that the etiology of chronic alcoholism is exceedingly complex involving both the make up of the individual and his adjustment to his environment. Many believe that the chronic use of alcohol is associated with a defective personality structure. Williams (31) is of the opinion that the prolonged use of alcohol results in the formation of a metabolic personality, or psychoses, which manifests itself by a craving for alcohol. And in his experience he has yet to know of a so called alcoholic who reverted to moderate drinking.

No claims are made that this new drug will correct this defective personality structure, but it will promote an abstinence from alcohol while psychotherapeutic measures are instituted to encourage him to continue medication and adjust himself socially.

DISCOVERY

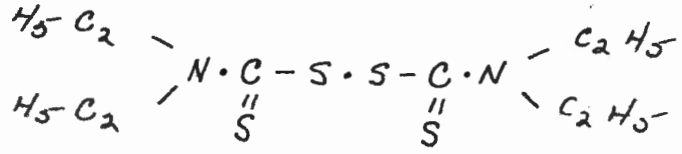
Chance led to the discovery of antabuse by Doctor's Erick Jacobsen and Jens Hald of Copenhagen, Denmark, in 1948. In search of an anthelminthic their attention was directed toward antabuse. Finding this substance to be relatively non-toxic for laboratory animals, they ingested several grams and no side effects were noted until they attended a cocktail party a few days later. Since both became quite ill and had to leave the party, it was considered more than coincidence, and the substance that they had been testing was suspected. (5) Subsequent experimentation indicated that persons who have ingested this substance showed symptoms after consumption of alcohol which differed from the common picture of alcohol intoxication. They then decided to submit antabuse as a possible remedy for alcoholism. (21)

Most of the work in the literature thus far has originated in Denmark, Sweden, Great Britian, and Canada.

Antabuse is being investigated in approximately one hundred universities and other institutions in the United States. In this country it is classified as a "new drug" under the Federal Food, Drug, and Cosmetic

Act of 1938, and is not yet available on a prescription basis. (12)

CHEMICAL FORMULA



PHYSICAL PROPERTIES

Antabuse, (tetraethylthiuramdisulphide), is a colorless or slighly yellowish crystalline substance with a melting point of 70-72°C, a violet like odor, a bitter taste, and is insoluble in water, but is readily soluble in ethyl ether and chloroform. (15)

CHEMICAL PROPERTIES

Little is known of the chemical properties of antabuse, however, intensive yellow colors are formed with cupric salts. (15)

ABSORPTION

Antabuse is rather slowly absorbed from the gastro-intestinal tract as its characteristic antabuse-alcohol effect is not seen unless the antabuse is

ingested at least 3 hours prior to the administration of alcohol, and 6-12 hours are required before the full effect is seen. (15)

About 20% is not absorbed and is eliminated in the feces. (5) (14) (15)

ELIMINATION

Elimination from the body is slow as can be seen from the duration of the effect of antabuse. Even when alcohol is administered several days after the intake of a single dose of antabuse, the characteristic clinical effect is seen. (15) The mechanism of elimination is as yet unknown. As has been stated previously, about 20% is not absorbed and is excreted in the feces. This has been traced for 7-8 days in man. (21) No antabuse is excreted in the urine. (14) (15)

SIMILAR SUBSTANCES

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, gave rise to unpleasant symptoms when alcohol subsequently was consumed. (6)

Following the taking of cyanamide, alcohol even in small amounts would cause such symptoms as transitory redness of the face, headache, accelerated and deepened respiration, accelerated pulse, and a feeling of giddiness. This was followed by tiredness and sleepiness. (15)

EFFECT OF ANTABUSE ON MAN

In man, antabuse has the property of producing an unpleasant effect when alcohol is taken after its administration. (4) (5) The effect depends somewhat on the amount of antabuse ingested and the amount of alcohol consumed. Sensitivity produced by a single dose of 0.5 gram lasted 3-4 days while that of a 1.5 gram dose lasted 7-8 days. (15)

Antabuse is not habit forming. (5) (14) (15)

In man, single doses up to 6 grams and smaller doses of 0.25 -0.75 gram per day for months are exceptionally well tolerated. (15) Similar results are reported by others. (14) (21)

Antabuse appears to have no effect on the hemopoetic system as the red blood cell count, white blood cell count, hemoglobin and differential white blood cell count appear to be unaffected. (11) (15)

TOXICOLOGY

In Martensen-Larsen's series of 83 patients no harmful effects were observed on the heart, liver, kidney, or blood forming organs. (26) No subjective or objective effects are noted in most persons. (15) (21) An occassional patient may complain of insomnia, somnolence, diarrhea, constipation, anorexia, increased appetite, headache, palpitation, dizziness, urinary frequency, enuresis, nocturia, and bad taste. However, these symptoms disappear in from one to six weeks. (4) (11)

Urticaria has been reported in a few instances. (11) (12) (21) (27). In these instances Gelbman and Epstein (11), recommend that 50 mgm. Pyribenzamine be given three times a day for 3-4 days without discontinuing antabus.

Most authors agree that antabus by itself is relatively non toxic. (4) (5) (11) (14) (15)

EFFECT ON EXPERIMENTAL ANIMALS OF ANTABUSE IN COMBINATION WITH ALCOHOL

Larsen (23) observed that small amounts of alcohol had no effect on a normal rabbit, however, when an experimental rabbit had previously received

antabuse even small amounts of alcohol produced markedly increased blood acetaldehyde levels, increased respiration in both rate and depth, slightly lowered body temperature, a rather deep narcosis, and occassionally death. These effects were not seen unless the antabuse was given at least three hours prior to the alcohol administration. (14) The organism can be saturated with antabuse so that increasing the dosage gives no further effect. (16) In animals saturated with antabuse, increasing blood alcohol concentration resulted in increased blood acetaldehyde levels and more severe symptoms. (16) (21) (23) An increased amount of acetaldehyde has been identified in the expired air of rabbits treated with antabuse and alcohol. (16)

Lubin and Westerfeld (25), indicate that the liver plays an important part in acetaldehyde metabolism, but they do not indicate the mechanism for this process.

Hald, Jacobsen, and Larsen (17), have stated that the maximum metabolic capacity of an averaged sized rabbit's liver is 6-7 mgm. of acetaldehyde per minute. Maximal capacity for acetaldehyde metabolism is the same for both treated and untreated rabbits. A marked

difference is seen when perfusion is made on livers from antabuse treated rabbits, i.e. when one mgm. of acetaldehyde was administered to both treated and untreated rabbits the resulting blood acetaldehyde concentration in the former was 30-40 times higher. Similar results were obtained when alcohol was used.

Larsen (23), noted that when alcohol infusion into the portal vein of a normal rabbit was slow, the liver was able to metabolize acetaldehyde so that only a small amount appeared in the blood. However, if the infusion was rapid, then higher blood acetaldehyde levels resulted.

In 1948, Hald, Jacobsen, and Larsen, (17) in perfusion experiments with isolated livers and hind limbs of rabbits have concluded that the increased acetaldehyde concentration from alcohol after antabuse administration can be explained as due to an effect on acetaldehyde metabolism. Metabolism of acetaldehyde is apparantly impaired. It is not known if antabuse influences a single or several of the metabolic processes of acetaldehye oxidation.

The increased concentration of acetaldehyde following an increase in the concentration of blood alcohol is difficult to bring into line with the

theory of alcohol combustion; namely, that regardless of alcohol concentration, the same amount of alcohol is burned per unit time. This is true even after the administration of antabuse. (16)

No one yet seems to know the exact mode of action of antabuse. Analysis showed that very little, if any, antabuse was found in the liver or blood of animals even when heavily treated. This would indicate that some unknown metabolite of antabuse is responsible for the characteristic effect.(16)

One group of experimenters believed the antabuse-alcohol effect to be due to a delayed elimination of acetaldehyde rather than to an increased formation of acetaldehyde as had been previously been described. (18)

Hald and Jacobsen (13), conclude that only part of alcohol combustion under normal conditions goes through acetaldehyde as an intermediate, but after treatment with antabuse the normal route is partly or completely blocked, and a higher percentage of alcohol is oxidized to acetaldehyde by an alcohol dehydrogenase.

FORMATION OF ACETALDEHYDE AFTER INGESTION OF ANTABUSE AND ALCOHOL IN MAN

Acetaldehyde is a normal intermediate in carbo-

hydrate metabolism. (3) It is formed in normal humans and animals after the ingestion of alcohol. (13)

Lubin and Westerfeld (25), have shown that a few minutes after intravenous infusion of rather large amounts of acetaldehyde, only very small amounts of acetaldehyde can be found in the blood. They believe acetaldehyde to be eliminated from the organism by oxidation in the liver.

The normal blood acetaldehyde level is 0.020-0.040 mgm%. (29) This has been confirmed by Hald and Jacobsen. (6)

When the blood concentration of acetaldehyde is abnormally high, it may be excreted by the lungs. (22)

Acetaldehyde has been isolated and identified in the expired air of individuals treated with antabuse prior to receiving alcohol. (13)

Hald and Jacobsen (13), have noted that the symptoms which appeared after the ingestion of antabuse and alcohol are accompanied by the formation of acetaldehyde in far greater quantity than when alcohol alone is ingested. After the same dose of alcohol, 2 ounces, the increase in blood acetaldehyde

does not exceed 0.105 mgm% in the untreated, while in the treated individuals levels not less than 0.526 mgm% are noted.

From isolated liver perfusion experiments, Jacobsen and Larsen (20), conclude that the increased blood acetaldehyde levels in antabuse treated animals are due to the effect of antabuse on the function of the liver cells. They have also shown that acetaldehyde is eliminated at the same rate in treated and untreated animals following alcohol administration.

Hald and Jacobsen (13), have concluded that only part of alcohol combustion under normal conditions goes through acetald hyde as an intermediate, but that after treatment with antabuse, the normal route is partly or completely blocked and a higher percentage of alcohol is oxidized to acetaldehyde.

EFFECT OF ACETALDEHYDE ON MAN

Lubin and Westerfeld (25), have shown that normally acetaldehyde is rapidly eliminated from the body and produces no symptoms.

When alcohol is taken by individuals previously sensitized by antabuse, the formation of acetaldehyde

is considerably increased. (3)

When acetaldehyde is infused intravenously into normal human subjects, at blood concentrations of 0.2-0.7 mgm%, a marked increase in heart rate, ventilation, dead space, and a decrease in alveolar carbon dioxide are noted. Both respiratory rate and amplitude are increased. Through carotid artery ligation experiments on rabbits, the response was shown to be due to the effect on the chemoreceptors of the carotid body. Pulse acceleration was shown to be due to a direct effect on cardiac muscle. Vasodilatation of the face appeared to be the most sensitive symptom in humans occurring at blood acetaldehyde concentrations low enough to have no effect on respiration. (3)

The effect of intravenous acetaldehyde on the normal human body is like that of alcohol on an antabuse sensitized patient, namely, intense flushing, increased heart rate, and an increase in rate and depth of respiration. (3)

Experimental subjects say that they get the same characteristic "hang over" feeling following acetaldehyde infusion as they received when taking alcohol after antabuse sensitization. (3)

Jacobsen and Larsen (20), believe that the effect

of alcohol on an antabuse sensitized patient is consequently due to an increased formation of acetaldehyde.

EFFECT OF ALCOHOL ON AN ANTABUSE SENSITIZED PATIENT

Gelbman and Epstein (11), in a study of 55 patients noted a rather typical sequence of events following the administration of 2-6 ounces of alcohol to antabuse sensitized patients. These effects occurred 2-15 minutes after the ingestion of the alcohol. Objective signs occurred in the following order:

1. Flushing of the head and neck, spreading downward, later sometimes covering most of the body.
2. Vasodilatation of the capillaries of the conjunctiva; later conjunctival edema.
3. Sweating.
4. Hyperpnea.
5. Dyspnea.
6. Tachycardia.
7. Decrease in blood pressure.
8. Odor of acetaldehyde on the breath.
9. Somnolence.
10. Sleep.
11. Vomiting in a majority of patients.

Subjective complaints occurred in the following order:

1. Warmth.
2. Dizziness.
3. Blurred vision.
4. Pressure on the top of the head.
5. Pounding headache, particularly in the temples or behind the ears.
6. Palpitation.

7. Difficulty in breathing.
8. Tightness in the throat.
9. Chest pain.
10. Numbness of the hands and feet.
11. Nausea.
12. Sleepiness.

Almost every patient fell asleep for 1-3 hours.

In addition to the above, Hald, Jacobsen, and Larsen (4), described a slight constriction in the neck, followed by irritation in the throat with slight cough, and a general uneasiness which was quite disagreeable. Many noted an inability to remain erect due to the sensation of impending collapse. When the symptoms began to fade, the patient generally felt exhausted and sleepy, however, after a few hours sleep he usually felt completely well again.

Other writers report similar findings. (2) (5) (4) (6) (8) (12) (14) (15) (21) (23) (26)

Intensity and duration of symptoms in an antabuse sensitized patient who has ingested alcohol depend on the dose of alcohol and the disposition of the individual, and are regardless of the type of alcoholic beverage used. (4)

The effect is the same in resting individuals and in individuals doing moderate muscular work. (2)

The severity of the cutaneous vasodilatation which follows the ingestion of a few ounces of whisky after a course of antabuse must be felt to be appreciated. (10)

The discomfort is so intense that, once experienced, it prevents the overwhelming majority of patients from further attempts at taking alcohol so long as they are influenced by antabuse. (21)

Normal people show little or no effect after taking 10-20 gram of alcohol. (14)

In an antabuse sensitized patient, alcohol taken orally or intravenously has the same effect. (2) (14) (15) The effect can be duplicated by the administration of intravenous acetaldehyde. (4)

It is necessary to administer antabuse at least three hours prior to the taking of alcohol for the characteristic effects to be seen. (5) (14) (21) The sensitizing effect of the antabuse will last 24-48 hours. (21)

Blood acetaldehyde is normally found in the blood at levels of 0.02-0.04 mgm%. (29)

The blood acetaldehyde level in not increased by the administration of antabuse alone. (14)

It is difficult to explain why antabuse causes

acetaldehyde to be formed in concentrations 2-5 times normal after the ingestion of alcohol. (14)

The elimination rate of acetaldehyde is the same in treated and untreated individuals. It is eliminated rapidly in both instances. (14)

Symptoms produced by alcohol after administration of antabuse are probably due to interference with the oxidation of alcohol so that abnormally high levels of acetaldehyde are produced in the body. (4) (14) (19)

Apparantly normally only part of the alcohol consumed is oxidized through an intermediate acetaldehyde stage. After the ingestion of alcohol and antabuse the normal elimination of alcohol is partially or completely blocked and increased amounts of acetaldehyde are formed. (14)

It may be assumed that alcohol oxidizing enzymes are affected by this drug. (19)

The antabuse plus alcohol effect is probably not due to the administration of a histamine like substance, in spite of the fact that histamine also gives an increase in pulmonary ventilation like that of alcohol on an antabuse sensitized patient. (2) (14) (15) However, no rise in blood histamine level

occurs. (14) The feeling of asthma is a common complaint of both, but in histamine sensitization a bronchoconstriction occurs and broncho dilatation occurs in the antabuse-alcohol reaction. The feeling of asthma in the latter is no doubt due to an increased irritability of the respiratory center. (2)

Flushing is the most sensitive symptom, and is seen at blood alcohol levels of 15-20 mgm%. Increase in ventilation and pulse rate are not noted until the blood alcohol level reaches 25-40 mgm%. (14)

It seems obvious that in antabuse prepared subjects, alcohol produces a substance which directly or indirectly increases the irritability of the respiratory center. (2) This effect is no doubt due to an effect on the chemoreceptors of the carotid body.

A slight increase in cardiac output and oxygen consumption is seen, and this is easily explained on a hyperventilation basis. This comparatively slight increase in cardiac output shows that there is no serious risk of too heavy a load on the heart after clinical application of antabuse eventhough patients

often complain of serious palpitation and dyspnea. (2)

Acetaldehyde is excreted through the lungs and gives the expired air a characteristic acetaldehyde odor. (21)

RECOMMENDED PROCEDURE

Martensen-Larsen (21), believes that the best results are obtained when the treatment is given in small sanitariums and to groups of not more than 15-20.

Glud (12), recommends hospitalization for the first two clinical trials. However, other authors have conducted trials on an outpatient basis. (11) (21) (26)

For the first consultation, the patient is advised to bring a second party, a friend or relative, in order to get a clear view of the patient's drinking habits, personal and family history; two sources of information being better than one. (11) (12)

Carver (6), describes an outpatient method in which the patient is sensitized by telling him that the antabuse tablets are only vitamins, and he is not told of the effect that may occur if he drinks alcohol. Glud (12) and Martensen-Larsen (26) are not in favor

of this method of treatment.

The patients are encouraged to believe that their excessive use of alcohol is a disease for which treatment is indicated. It is likened to diabetes in which sugar must be avoided, and patients are advised that the taking of antabuse for an alcohol intolerant patient is just as necessary as is insulin for the diabetic. (12) (21)

The patient is then told how the treatment is given, and something of how the drug will affect him. He is then advised to go home and talk the situation over with this second person. During this time he is to stay sober, and is to return in 3 days. (12)

At this time a careful history is done. This includes a careful medical history as well as a psychiatric history, and it is important to become familiar with the patients background, his drinking habits, and if possible, determine the cause of his excessive drinking. (23)

Then a careful physical and neurological examination is advised. Special emphasis is placed on the cardiac picture and the blood pressure. (23)

Certain positive findings in the history and physical examination may warrant specific laboratory

studies. The following laboratory procedures are recommended: (12) (23)

1. Complete blood count (rbc, wbc, hemoglobin, and differential white blood cell counts).
2. Routine urinalysis.
3. Electrocardiogram.
4. Liver function tests; the bromsulfalein test is recommended.
5. Kidney function tests; a concentration test is suggested.
6. Blood sugar.
7. Glucose tolerance test.
* 8. Blood acetaldehyde.
9. Basal metabolic rate.
10. Carbon dioxide combining power.
11. Electroencephalogram.
12. Rorschach test.

* Blood acetaldehyde is determined by the method of Stotz. (29)

The first six tests are no doubt the most important.

Following an evaluation of history, physical, neurological, psychiatric and laboratory examinations, and the patient is found to be reasonably healthy, free from concurrent infection, and not psychotic, it is then advisable to get the patient in as good physical condition as possible. (11) (23) The use of a well balanced high vitamin diet and insulin stimulation are recommended. (23)

During this time, usually about one week, further study of the patients back-ground is made. In addition he receives further instruction in individual and also

in group conferences, and also intensive psychotherapy which is aimed at mental and social rehabilitation. He is told again that his excessive use of alcohol is a disease for which he must receive treatment. It is likened to diabetes; antabuse is to be his insulin. He is further instructed in the manner of treatment and how it will affect him. He is also advised that he will have to refrain from the taking of any type of alcoholic beverage, as well as any type of drug containing alcohol such as a cough syrup. He is also told that he will be closely supervised in the treatment by his physician. Regular intake of antabuse is advised as essential to successful treatment, and it is stressed that taking antabuse should be as regular as the morning cup of coffee. Here the role of a second person is very important. (21)

Glud (12), recommends the following dosage schedule:

1st day	2	grams
2d "	1.5	"
3d "	1.0	"
4th "	0.75	"

Thereafter 0.75 gram per day will serve as an adequate maintenance dosage in most cases. It is important that the complete dose be taken each day and

preferably in the morning. Other authors recommend similar dosage schedules. (5) (8) (9) (11) (21) (25) (26)

Glud (12), recommends that clinical trials with alcohol be tried on the 4th and 8th days. He believes that the first two trials should be conducted in a hospital or sanitarium. For the first trial he advises 40-50 cc of whisky or its equivalent in other alcoholic beverage. For the second trial he advises 30-40 cc of whisky or its equivalent.

Most authors agree that the patient may choose his type of beverage and that he may drink in his accustomed manner, but is to be allowed no more than 8 ounces of whisky or its equivalent. No one is urged to drink more than he desires. Experience has shown that it is advisable to slow the rate of drinking. (11)

The typical reaction usually occurs in 2-15 minutes and is described elsewhere in this paper.

Glud (12), advises a second clinical trial on the 8th day. Frequently, however, patients will refuse a second clinical trial. If possible they should be persuaded to repeat the trial. The reason for a second trial should be carefully explained to

them.

Following the second clinical trial, the patient is dismissed from the hospital and placed on a maintenance dosage of 0.75 gram of antabuse per day. (12) Others recommend a maintenance dosage of 0.25-0.5 gram per day. (21)

It is important to bring the patient back to his normal surroundings as soon as possible so that he may learn to live a non-alcoholic life among normal drinkers. (21)

Five to eight clinical trials are recommended over a two month period. These trials will serve to show the patient how he reacts to alcohol, will allow him to develope an aversion for alcohol, and will serve to adjust the maintanance dosage of antabuse. (12) (21)

Glud (12), has described a method whereby a minimal maintenance dosage may be determined clinically. An effort is made to adjust the maintenance dosage of antabuse so that the consumption of 15-20cc of whisky will produce a slight flushing of the face, slight increase in pulse rate, and a mild dyspnea. This seems unnecessary when it is known that a maintenance dose of antabuse of 0.5 gram, will of itself cause no discomfort, and is adequate to produce

marked clinical symptoms when alcohol is ingested.

The patient is encouraged to join some group organization such as Alcoholics Anonymous, or some other similar organization. Mutual support is of paramount importance, and group therapy of this type has proved to be effective. (21)

It may be necessary to change the patients environment.

The physician must see the patient at regular intervals to discuss the patients course, regulate the maintenance dosage, and issue antabuse. The date of the next interview should be set at this time. For the first few months interviews should occur weekly or bimonthly; later monthly interviews will be adequate. Should the patient break an appointment the physician must call on him and stress the importance of regulation. (21)

Alstrup (1) recommends that the patient receive no more than enough tablets to last him to the next scheduled interview. This will serve to promote regular return visits to the physician.

Naturally the question of how long the antabuse therapy should continue arises. As yet there is no satisfactory single answer. This must be adjusted

for each individual patient.

Many patients will say that they have lost their taste for alcohol and desire to cease the taking of antabuse. These patients should be advised to continue antabuse lest they fall back into their old habits. They should be advised to stop medication in these instances only after careful evaluation. (21)

Should a patient cease to take antabuse regularly for some time, on reinstitution of treatment it is not necessary to start him off with 2 grams, merely reinstate the maintenance dosage. (12)

However should a patient lapse, Martensen-Larsen (26) believes that another trial with alcohol is indicated. In those patients who seem liable to lapse a clinical trial every third month is advised.

Since there is no evidence that antabuse has cumulative toxic effects, and no symptoms occur unless alcohol is taken the physician may seem justified in prescribing it for a longer period than appears necessary. (6)

PRECAUTIONS

Patients under the influence of alcohol should not receive antabuse. Deaths have occurred in this

type of combination in several instances. (12) (26)

Paraldehyde should not be administered to an antabuse sensitized patient, as it may be metabolized through an acetaldehyde stage. And conversely a patient who has recently been sedated with paraldehyde should not receive antabuse. (12)

Liver function whould be at least 85% of normal before a patient is allowed to have an antabuse-alcohol reaction. (12)

Great care should be taken when antabuse is administered in the following conditions: epilepsy, goiter, acute or chronic nephritis, diabetes, asthma, myocardial failure or coronary artery disease. The above conditions should be well controlled before antabuse is administered, and then smaller doses of alcohol should be used in initial clinical trials. (12)

Medications with an alcoholic base must be avoided. (11)

ADVERSE REACTIONS

Martensen-Larsen (21), from a study of 550 patients has noted that about 20% complain of tiredness for the first 1-2 months of treatment, but this soon wears off. A few noted decreased sexual

potency, but this was only transient. One patient developed a manic state during the first few weeks of treatment and it was necessary to discontinue the drug. Following withdrawal he quickly recovered.

Some patients will complain of insomnia, somnolence, anorexia, increased appetite, diarrhea, constipation, headache, palpitation, dizziness, urinary frequency, enuresis, nocturia, and bad taste. These effects are only transient however and will disappear in 1-6 weeks. (4) (11) Hald (13) has suggested that these symptoms may be due to the withdrawal of alcohol and not to antabuse.

Several authors have reported urticaria. (11) (12) (21) (27)

Deaths have occurred when antabuse was given to patients during a heavy drinking period. (21)

Severe vomiting, severe throbbing headache, peripheral vascular collapse, and cessation of respiration have been reported. (4) (21) (27)

Convulsions have been seen in a few instances and were believed due to hyperventilation. (21)

The severe reactions are usually seen after large doses of alcohol have been ingested. (21)

Deaths have occurred in several patients on

only small doses of alcohol indicating that a few patients at least are abnormally sensitive to the antabuse-alcohol reaction. As yet there is no explanation as to why some patients should show very severe reactions. (22)

Linden (24), has reported a heart attack during the course of an antabuse-alcohol reaction.

Jones (24), has made a rather thorough study of a death that occurred in Canada during an antabuse-alcohol reaction in which case autopsy indicated that death was due to a right-sided heart failure.

Once a reaction is established, there is no means of controlling it. (4)

Because of these occassional severe reactions, Jones (22) and Ferguson (10), are of the opinion that initial treatments should be conducted in a hospital, and not on an outpatient basis.

It must be recognized that the antabuse-alcohol reaction is a potential danger to life.

CONTRAINDICATIONS

Jacobsen and Martensen-Larsen (21), have seen no absolute contraindications thus far, having treated

patients with cirrhosis, arteriosclerosis, diabetes, and stomach ulcers without serious complication. Other authors take a more conservative attitude and state that cardiovascular disease is a contraindication. (5) (11) One author believes that the drug should not be used in cases of diabetes and extreme obesity. (11)

Without exception, antabuse should not be given to anyone under the influence of alcohol. (It should not be given to sober up an alcoholic). (4) (5) (11)

Jacobsen and Martensen-Larsen (21), have treated pregnant women successfully and without complication, but Glud (12), believes that until further information is gathered they should not be treated. Westerfeld and Richert (30), have indicated that enzyme systems involved in the normal metabolism of acetaldehyde may be inadequately developed in fetuses, and thus dangerously high blood acetaldehyde levels might result.

When chronic alcoholism is complicated by drug addiction, the latter condition should be treated first. (12)

Antabuse should not be administered unless the patient has 85% of normal liver function. (12)

Antabuse should not be administered to a patient

who has recently received paraldehyde or medications containing alcohol. (12)

RESULTS OF SERIES STUDIES

Gelbman and Epstein (11), have reported a series of 55 cases. Two patients failed to return for the first controlled experience session and four failed to return for the second controlled experience session. Their course beyond this is unknown. Four other patients are known to have discontinued antabuse and reverted to their old drinking habits. Of the remaining 45, four have remained sober without taking further antabuse, and 41 are continuing on antabuse. Of this number 4 are known to have tried drinking, but were not successful and had typical reactions on rather small amounts of alcohol.

Martensen-Larsen (26), has made a comprehensive study of 83 patients. In 9 cases the treatment failed. In 32 cases the treatment was considered very successful, these patients could be controlled by telephone. Twenty-nine met the doctor in his consulting room at regular intervals, and required encouragement to continue therapy. In 13 patients who were definitely psychoneurotic, treatment was difficult to follow and

required a great deal of psychotherapy. (In these instances treatment would be still more effective if legal measures could be taken.)

It appears that the emotional adjustment that patients make along with antabuse therapy is well correlated with the success of the therapy. Gelbman and Epstein (11), have divided this into 5 major groups:

1. Those people in whom alcohol seems to be the only major difficulty respond extremely well to antabuse therapy. There is little need for psychotherapy in these patients.

2. Those in whom there is an initial period of anxiety following the first clinical treatment usually make a satisfactory recovery with support and guidance.

3. Those who have a mild psychoneurosis and have a struggle to continue therapy, but will adjust with further antabuse treatment andpsychotherapy.

4. Those in whom there is a markdd psychoneurosis and will discontinue therapy and revert to their old drinking habits without deeper psychotherapy.

5. Those who are psychotic and are incapable of adjusting to sobriety. In spite of their promises this group will be unfaithful and not continue treatment. These people may recover with intensive psychotherapy and close supervision. This group offers the poorest prognosis.

Jacobsen and Martensen-Larsen (21), in a study of 99 patients over a six months period found that 52 were "socially recovered", 19 were "much better",

and 16 showed no improvement. Relapses were frequently seen when patients stopped taking the medication. In patients who had previously been treated by the aversion method similar results were recorded. Of the 50 patients studied in this latter group, 23 were considered "socially recovered", 10 "much better", 8 "somewhat better", and 9 patients made no improvement.

CONCLUSIONS

First of all, antabuse is not a cure for alcoholism as has been erroneously reported in the non-scientific press.

That antabuse itself is the answer to the treatment of alcoholism is extremely unlikely. When taken regularly it will prevent the individual from taking more than very small amounts of alcohol, and thus provide a period of sobriety in which he may be amenable to psychotherapy.

Antabuse when given in adequate dosage will cause the individual to have a very unpleasant reaction when he consumes even small amounts of alcohol.

The unpleasant effects of the antabuse-alcohol reaction are attributed to formation of increased

amounts of acetaldehyde within the body.

Antabuse apparantly upsets the normal alcohol-acetaldehyde metabolism.

The effect of antabuse lasts from 6-12 days after the patient stops taking the drug.

No habituation to the drug occurs; on the contrary sensitivity to alcohol seems to increase.

No serious reactions have been reported following the taking of antabuse over long periods of time.

Antabuse is a relatively safe drug to use, but with care and full appreciation of its dangers.

Antabuse should definitely not be administered to an individual under the influence of alcohol. Deaths have occurred in this condition.

Antabuse is contraindicated in pregnancy, marked cirrhosis of the liver, and coronary insufficiency.

Antabuse is easily administered, being taken orally in tablets.

Treatment may be unsuccessful unless the patient desires to be treated.

It is recommended that the first and second clinical trials be conducted in a hospital or in a sanitarium.

There is no means of controlling a reaction

once it has been established.

Treatment should be undertaken only by physicians who have enough time and interest to follow through with rehabilitation of the patient both psychologically and somatically. Regular follow-up visits and supervision of antabuse administration are essential.

Group therapy and membership in organizations similar to A.A. are recommended.

Premature abandonment of therapy is to be avoided. Regular visits to the physician for his advice and support are important. The desire on the part of the patient to stop medication should be discouraged until the physician feels that a good social readjustment has been made.

The patient himself remains the decisive factor; drugs are not enough.

The follow up is still too short to ascertain how long the results will last, or if there will be any side effects from the protracted use of antabuse.

If this drug were to get into the hands of pranksters or other irresponsible persons, very serious consequences might result.

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