



VOL. 8 NO. 4

Physician's Alcohol NEWSLETTER



DECEMBER 1973

NCA to grant biomedical research funds in 1974-75

The National Council on Alcoholism will make grants totalling \$100,000 to support biomedical research in alcoholism for the year 1974-75. This is the first time a concerted research effort has been undertaken by the 29-year-old voluntary health organization.

The program became possible as a result of an anonymous donation, which has enabled NCA to establish a research and evaluation department.

Dr. Frank A. Seixas, NCA medical director and director of the new research and evaluation department, said that one \$35,000 Research Grant will be awarded together with a limited number of \$8,000 Postdoctoral Fellowship Grants and \$7,000 Supplemental Support Grants.

Dr. Seixas also said: "While emphasis will be on biomedical research in 1974-75, in succeeding years we hope

Smithers Alcoholism Center Opens in New York

The first alcoholism residential rehabilitation facility of its kind ever associated with a major Manhattan teaching hospital is now open.

It is the Smithers Alcoholism Center/Rehabilitation Unit of The Roosevelt Hospital, located at 56 East 93rd Street.

This 40-room, 5-story mansion was built by the late William Goadby Loew in 1932. After Mr. Loew's death in 1955, the house was sold to showman Billy Rose who occupied it until his death in 1966. The Algerian Mission to the United Nations owned the property until it was acquired by The Roosevelt Hospital in April of this year.

LeClair Bissell, M.D., Vice President of AMSA, is Chief of the service.

to broaden the support of research in clinical medicine, psychiatry, psychology, evaluation, sociology, anthropology and epidemiology."

Grants will be made upon the recommendations of a research and evaluation advisory committee.

Detailed information regarding the grants is available by writing to: Research and Evaluation Department, National Council on Alcoholism, Inc., 2 Park Avenue, New York, N.Y. 10016.

At dedication ceremonies prior to the opening of the Center, R. Brinkley Smithers said:

"Treatment and rehabilitation services for alcoholics have been shockingly inadequate in New York. Perhaps the most pressing need has been for a first-rate rehabilitation facility offering the best possible professional attention in restful and gracious surroundings. Such services have heretofore been available to New Yorkers only by traveling to other parts of the country.

"We hope this building will fill that need. At long last, New Yorkers suffering from the disease of alcoholism will receive treatment in a setting with the dignity they—like other sick people—deserve."

To retain its original charm, only minimal structural changes have been made in the building. The Landmarks Preservation Commission notes: "The residence was the last of the large private town houses to be built in the City...few have ever achieved the elegance we find here."

The Smithers Alcoholism Center/Rehabilitation Unit accommodates 44 male and female patients. A staff of 40 provides 24-hour a day services. Minimum stay for patients is 28 days.

A paneled ballroom on the second floor of the five-story building is used as an auditorium/gymnasium. The original dining room serves as the patients' dining room. The bedrooms accommodate from 2 to 6 patients each.

For information concerning Blue Cross coverage and other insurance plans please call Jerome Geisler at (212) 554-6715.



Jack I. Straus, Chairman of the Board, The Roosevelt Hospital; H. Whitfield Carhart, President of the Hospital; R. Brinkley Smithers; LeClair Bissell, M.D., Chief, Smithers Alcoholism Center; Rev. Howard Lowell, Pastor, St. John's of Lattintown Church, Locust Valley, Long Island and Peter B. Terenzio, Executive Vice President of The Roosevelt Hospital at dedication ceremonies of the facility.

EDITORIAL

Smithers Alcoholism Center: A Welcome Addition to the New York Area

The end of this active year in the field of alcoholism is punctuated in the New York area by the opening of the Smithers Alcoholism Center (see story, page 1). We can look forward to this Center playing a strong role as a model not only in according the patient dignity as a human being but also moving his treatment and later participation in AA to a high level of success.

In addition to a dedication to moving the patient away from dependency on alcohol, the Center expects to bring a high level of psychiatric sophistication to the aid of those who require it. It will also monitor its activities to demonstrate what ingredients are required for the most successful treatment in different groups of patients, and it will mount a research program as well.

This event calls to our attention the continuing efforts of its donor, Mr. R. Brinkley Smithers, to achieve a better status for alcoholism treatment in this country. His benefactions resulting in the Smithers Building on the Rutgers campus, the continued publication of the *Quarterly Journal on Alcohol Studies*, the support of this newsletter, and of private efforts on alcoholism in this country are well known. Perhaps less well known have been his efforts through the Community Council of New York

Treatment facilities directory available

An *Alcoholism Treatment Facilities Directory* has been published by the Alcohol and Drug Problems Association of North America (ADPA). This Directory provides descriptive information for 2,565 alcoholism treatment facilities in 50 states, the District of Columbia and eight provinces of Canada.

The program description enumerates all treatment facilities available in the agency such as in-patient, out-patient and others. It also includes the treatment modalities provided and, when possible, the principal mode of treatment (individual, group therapy, detoxification, etc.) has been indicated and followed by auxiliary services. Eligibility requirements and fees for services are also listed.

This Directory is available through the Alcohol and Drug Problems Association of North America, 1130 Seventeenth Street, N.W., Washington, D.C. 20036, at \$7.50 per copy plus 50¢ for postage and handling. Discount rates for larger quantities are available on request.

and through the Mayor's Advisory Council of the Health Services Administration, chaired by Col. Harold Riegelman, to stimulate city programs for alcoholism. There are now activities in many hospitals, including Columbus Hospital, The Hospital for Joint Diseases, Beth Israel, Elmhurst, St. Vincent's, Bronx Lebanon, and Einstein, as well as the small program at the Payne-Whitney Division of New York Hospital. Downstate Medical School's long active program was recently selected as one of two sites for training of medical school faculty representatives in developing curriculum programs. Nearby South Oaks, Freeport, Central Islip and Pilgrim State Hospital also serve the metropolitan area.

As "traditional medical models" of treating alcoholism continue to be decried, one must recognize that the emphasis of this phrase is on "traditional" rather than "medical." In fact, traditionally there has been no treatment in health facilities for alcoholism itself, and the development of these new services requires the use of "performance" people rather than those who might have jurisdiction only because of their more general credentials in health. The establishment and encouragement of facilities properly adapted to the treatment of alcoholism within this city's ongoing health facilities is a major step which should be encouraged, as we also find ways to incorporate into the health structure promising free-standing alcoholism treatment activities.

FAS

Wettrick joins NCA

Marian J. Wettrick has been appointed Director of Community Services for the National Council on Alcoholism, according to an announcement by George C. Dimas, NCA Executive Director.

Miss Wettrick has resigned as Executive Director of the National Council on Alcoholism—New York City Affiliate, Inc. to accept the national position.

MEETINGS

MARCH 16, 1974—AMSA-Region IX, Beverly Manor Alcoholism Hospital, Orange, California. Subject will be "After Detox—What?"

APRIL 28-MAY 3—NCA Annual Meeting, Denver, Colorado. For information, write NCA, 2 Park Avenue, New York, N.Y. 10016.

Kemper Group extends alcoholism care coverage

A significant breakthrough in the financing of alcoholism treatment in the United States has been announced by the Kemper Group, one of the nation's largest insurance organizations. Coverage for alcoholism care will be considerably broadened in its group accident and health policies. Approval by insurance regulatory authorities in over 40 states has been obtained.

The new benefit will cover out-patient alcoholism care at hospitals and all care by state-licensed alcoholism treatment facilities. At present, most group accident and health policies restrict alcoholism coverage to in-patient hospital care.

James S. Kemper, Jr. president of Kemper and a member of the National Advisory Council on Alcohol Abuse and Alcoholism, said the unprecedented coverage would be added at no additional charge to group policies.

BOOKS

Skid Row and Its Alternatives: Research and Recommendations from Philadelphia. By Leonard Blumberg, Thomas E. Shipley Jr., and Irving W. Shandler. Philadelphia: Temple University Press, 1973. 307 pp. \$10.

This comprehensive appraisal of Skid Row rehabilitation reports on over a decade of work at Philadelphia's Diagnostic and Rehabilitation Center. The authors candidly appraise the methods used, which include group therapy, housing relocation, and a residential "Half-way House." An intensive casework program was found very promising. The authors directed the Center's operations.

Recovery from Alcoholism: A Social Treatment Model. By Robert G. O'Brian, M.D. and Henry L. Lennard, Ph.D. Springfield, Ill.: Charles C. Thomas, 1973. 93 pp. \$6.95.

The authors propose that alcoholism is sustained or arrested by social arrangements and human associations, and describe and analyze a successful alcoholism treatment program in San Joaquin, California, that has been set up on this premise.

Alcohol Detoxification Programs: Treatment Instead of Jail. By Harvey H. Siegel. Springfield, Ill.: Charles C. Thomas, 1973. 94 pp.

Guidelines, directions, and resources for the development of detoxification centers, with illustrations of those already in operation and their experiences.

AMA conference discusses medical complications of alcohol abuse

Alcoholism is an illness of major concern and importance to surgical specialists, Marshall J. Orloff, M.D., Chairman of the Department of Surgery at the University of California, San Diego, told a conference on "Medical Complications of Alcohol Abuse." The meetings, presented by the AMA and co-sponsored by NCA, NIAAA, and the VA, were held in Washington, October 11-12.

The problems of alcoholism are regularly and frequently encountered in the practice of surgery, he said. Alcoholics who require surgical treatment present a number of general problems, including difficulties in diagnosing disease, inability to cooperate with therapy, postoperative delirium tremens, frequent pulmonary infection, delayed wound healing, liver dysfunction, and difficulties with anesthesia. Alcoholism causes several specific surgical diseases, including cirrhosis, traumatic injuries, burns, pancreatitis, gastric bleeding, rupture of the esophagus, several types of cancer, and a variety of lesions of the extremities.

Alcoholic cirrhosis and portal hypertension produce several surgical complications, the most important of which is bleeding esophageal varices. Varix hemorrhage is frequently lethal, and emergency treatment is of paramount importance. The emergency portacaval shunt has proved to be the most effective therapeutic measure.

Surgical treatment of the complications of cirrhosis does not affect the underlying alcoholism or liver disease. A program of rehabilitation that includes effective therapy of alcoholism would

improve the percentage of patients who can resume productive lives without resort to alcohol.

Alcohol and hematopoiesis

Thomas W. Sheehy, M.D. of the University of Alabama, described the major effects of alcohol on hematopoiesis. These are related to protein calorie malnutrition; folate, pyridoxine and iron deficiency; liver disease; lipemia; and interference with folate, iron, and pyridoxine metabolism. Thrombocytopenia occurs in $\frac{1}{4}$ to $\frac{1}{3}$ of acutely ill alcoholics. It is related to folate deficiency, marrow suppression, decreased platelet survival, and a combination of these factors. Alcoholic thrombocytopenia adds another lethal hazard to the life of the accident-prone alcoholic, which may be compounded by liver disease, or plasma clotting factors, or the ingestion of drugs such as aspirin that also impair hemostasis.

Common muscle diseases

Muscle disease is another common finding in chronic alcoholics, said Gerald T. Perkoff, M.D. of Washington University in St. Louis. The muscle disease may be subclinical, manifested only by biochemical abnormalities, or it may be acute or chronic. Acute alcoholic myopathy presents with muscle cramps, diffuse muscle weakness, or severe swelling, pain, tenderness, and necrosis from acute alcoholic myopathy. Patients may develop chronic alcoholic myopathy either by progression from acute alcoholic myopathy or de novo. The treatment of

all forms of alcoholic myopathy consists of withdrawal of alcohol. Abstinence is associated with improvement in all instances and recovery in most, said Dr. Perkoff.

Alcoholic heart disease

Alcoholic cardiomyopathy cuts across all social and economic classes and levels of nutrition, said Rolf M. Gunnar, M.D., of the Stritch School of Medicine in Maywood, Ill. The etiology of alcoholic heart disease appears to be the direct effects of alcohol on the myocardium. In a study of 57 patients at Cook County Hospital, only four of the 39 patients who continued to drink heavily improved, while 11 of the 18 patients who abstained improved.

The skin is a unique indicator of alcoholism and a barometer of the systemic complications of the disease, said Alex W. Young, M.D. of St. Luke's Hospital Center in New York. Before the problem is recognized by the patient, the early flush of the potential alcoholic becomes evident. These skin markers develop from patterns of alcoholic behavior which appear as inadvertent injury to the skin, peculiar reaction to drugs, exposure to disease, and physical and emotional sequelae of detoxification. At a later stage the skin mirrors hepatic, gastrointestinal, and peripheral nerve damage. Throughout the various stages, specific skin disorders appear.

Although explanation for many of the features of the skin syndrome are incomplete, their appearance is helpful in diagnosing alcoholism.

Alcohol consumption per se can cause the reversible lesion, alcoholic fatty liver; and alcoholic hepatitis can also be produced experimentally without dietary inadequacy, according to Lawrence Feinman, M.D. of Mt. Sinai School of Medicine. Accumulation of hepatic fibrous tissues explained in part by an alcohol-induced stimulation of collagen synthesis, has been noted in rats and primates.

Also on the program Donald L. Damsstra, M.D., reviewed current approaches to treatment; James L. Luke, M.D., discussed the causes of death in alcoholics; and Sheldon M. Wolff, M.D., discussed the management of infection.

Summer School scholarship

Applications from physicians and medical students are now being accepted for the A. E. Bennett Scholarship to the Rutgers Summer Institute of Alcohol Studies, which will be held June 23-July 12, 1974. Write AMSA, 2 Park Avenue, Suite 1720, New York 10016, N.Y.

Physician's Alcohol Newsletter

is published quarterly by the American Medical Society on Alcoholism, Inc., a component of the National Council on Alcoholism. Publication has been made possible by a grant from the Christopher D. Smithers Foundation.

For membership information, contact AMSA at address below.

Copyright 1973 by American Medical Society on Alcoholism, Inc.
Two Park Avenue—Suite 1720
New York, N.Y. 10016

All rights reserved.

Editorial Board

Editor-in-Chief:

FRANK A. SEIXAS, M.D., Internist,
New York City

Managing Editor: CAROL LEVINE

Associate Editors:

CHARLES E. BECKER, M.D., internist,
San Francisco, Calif.

LUTHER CLOUD, M.D., internist,
New York City

JOHN EWING, M.D., psychiatrist,
Chapel Hill, N.C.

RUTH FOX, M.D., psychiatrist,
New York City

DONALD G. MACKAY, M.D.,
Montreal, Quebec

ALFONSO PAREDES, M.D., psychiatrist,
Oklahoma City

MMPI reveals characteristics of pre-alcoholics; other reports from ADPA annual meetings in Minnesota

Rebellious, impulsive, gregarious young men are more likely to become alcoholics later in life than their more conventional peers, according to a study described to the 24th Annual Meetings of the Alcohol and Drug Problems Association of North America held in Bloomington, Minnesota, September 23-28. Rodney G. Loper of the Student Counseling Bureau of the University of Minnesota reported on a study comparing the scores on the Minnesota Multiphasic Personality Inventory (MMPI) of 32 college freshmen who later were hospitalized for alcoholism in Minnesota treatment centers with a control group of male classmates.

The pre-alcoholics were 19 or 20 when tested and in their mid-30's when hospitalized. The results of the comparison suggests that the pre-alcoholic freshmen were apt to be more socially aggressive, more expansive, and not bound by custom.

Loper said that the 560-question MMPI showed that the young men destined for alcoholism were generally lively, socially active, and typically more "interesting" people than the controls. They exhibited more social cynicism and romanticism, and admitted to having had more minor escapades in which they rebelled against authority.

Other reports from the conference follow:

Effects of ethanol on brain polyribosome stability

Polyribosomes, a functional entity of the cellular complex which produces new proteins, are required to exist in an aggregated state to maintain active normal protein synthesis. Brain protein synthesis has been associated with normal learning and memory processes. Thus, brain dysfunctions of learning and memory associated with alcoholism could be due to alterations by ethanol directly or indirectly upon these cellular complexes.

John H. Copenhagen, Ph.D. of the Nebraska Psychiatric Institute reported that his team was able to demonstrate a disaggregated free polyribosome complex in 14-day-old rat brain following the *in vivo* administration of 5-hydroxytryptophan. Evidence of the disaggregation was obtained by measuring increases in the monosome and disome fractions and decreases in the polysomes (polyribosomes equal to or larger than trisomes) of isolated brain free polyribosomes. Disaggregation was potentiated by the prior

administration of a monamine oxidase inhibitor, suggesting that the formation of 5-hydroxytryptamine (serotonin) produced the instability in the polyribosome complex. The acute administration of ethanol to neonatal rats also resulted in a decrease in polyribosome stability shortly after ethanol was administered and continued to increase over a 5- to 6-hour period before returning to normal. Fetal brain polyribosome integrity was similarly disrupted after ethanol was given to a maternal animal.

Poverty blacks prime treatment target

Alcoholism among American blacks today cuts across economic and social lines, and alcoholics exhibit a great diversity in behavior patterns, said Fred T. Davis, Jr., NCA/NIAAA Field Consultant. However, the primary need for alcoholism services is among poverty alcoholics, who do not respond to conventional modalities of therapy which are based on the needs of middle-class clients and patients. He stressed the need for developing additional ways of meeting the needs of poverty blacks in both rural and urban communities. Because blacks can and do see themselves in a positive light and not always as a patient, parole, or petitioner for welfare aid, it is important to regard the personalities of black alcoholics in terms of strengths, not just weaknesses, he said.

Transactional analysis in alcoholism treatment

In a preliminary study of 28 patients treated in a residential program at the Fort Logan Mental Health Center in Denver, transactional analysis (T-A) resulted in a significant improvement in several areas such as attained sobriety, employment, monthly income, living situation, and interpersonal relationships. However, significant differences were not found between the T-A treated group and an earlier treated residential group. Donald Fairchild, Kenneth Wanberg, and Sandra Williams conclude that a longer residential treatment experience rather than the utilization of any particular treatment method such as T-A is the key factor in the improvement shown compared to nonresidential controls. However, they feel that the younger, more intellectually open, shorter-term patient can be effectively treated by T-A, which involves alcoholic "life-scripts" and "game-playing."

Joint diseases, anesthetic effects of alcohol on agenda of AMSA annual meeting

Aside from the inevitable fracture sustained during alcoholic inebriation, femoral head necrosis is the major skeletal lesion complicating alcoholism, John J. Dowling, Jr., M.D., Chief of the Department of Orthopedic Surgery at Lankenau Hospital in Philadelphia, told the Annual Meeting of AMSA held in Valley Forge, Pa., September 28-30.

The clinical situation is not necessarily that of an established alcoholic who presents with complaints referable to the hip. Rather more often, the joint complaints lead backwards to a history of alcoholism, sometimes admitted by the patient, but often only confirmed by family members.

Nontraumatic femoral head necrosis occurs mainly in men, at an average age of mid-40's. Characteristically there is a gradual onset of pain in the hip, groin, thigh, knee, or in a combination of these areas. However, the onset may be quite sudden. It is distinct from degenerative joint disease, though it leads later to more destructive and secondary degenerative changes. It exhibits a high incidence of bilaterality and an inexorable progress if untreated.

Robert Johnstone, M.D., Research Associate in Anesthesiology at the Hospital of the University of Pennsylvania, reported on studies that show that even very high blood concentrations of ethyl alcohol in alcoholics caused only moderate respiratory depression. In a study using six healthy males, dosages of alcohol sufficient to produce moderate to severe intoxication failed to produce signs of respiratory depression at rest. Only a more sensitive technique (ventilatory response to CO₂) revealed respiratory depression, and even this was less than that observed following small doses of meperidine. Compared to various drugs possessing sedative and analgesic properties, ethanol is relatively free of respiratory effects. Nonetheless, Dr. Johnstone said, these data should not be interpreted to suggest that low doses of ethanol will be equally free of depressant effects when combined with ataractic, hypnotic, or analgesic drugs. Treatment of severely intoxicated patients must include their metabolic and neurologic problems, which may be more threatening than respiratory, he said.

Among the other speakers on the program were G. Douglas Talbott, M.D.; Charles S. Lieber, M.D.; H. James Day, M.D.; LeClair Bissell, M.D.; Stanley E. Gitlow, M.D.; David H. Knott, M.D., Ph.D.; Donald J. Ottenberg, M.D.; Maxwell N. Weisman, M.D.; Carl Seigel, M.D.; Sidney E. Bender, M.D.; and Chester A. Swinyard, M.D.

Crises in British alcoholism stressed at international meeting in London

An unprecedented statement recognizing the alarming problem of alcoholism and promising governmental action towards its amelioration by the Secretary of State for Social Service, Sir Keith Joseph, marked the beginning of the First International Medical Conference on Alcoholism held in September at the Royal College of Physicians, sponsored by the British Medical Council on Alcoholism.

In a conference during which ample opportunity was given for airing of views surrounding the disease nature of alcoholism, one of the most telling papers was that of Professor W. K. Van Dijk of the Psychiatric Clinic in Groningen, Holland, who outlined criticisms of the medical model of alcoholism and fitted them into a concept of pathology and health into which the medical model becomes a logical one in alcoholism. "The medical model is a multidimensional construct" he said, "which takes into account psychological and social as well as physical aspects of the afflicted person. For this reason, the medical model should not be replaced by other constructs, but it should reckon with them and incorporate them wherever this is possible and useful."

Dr. Rodney Wilkins of the University of Manchester, in another paper, described a study in which a questionnaire about drinking habits was administered to high-risk patients of general practitioners. By assessing this questionnaire, the incidence of the diagnosis of alcoholism was increased by 9 times over what it had been previously.

In two epidemiological papers, Jan de Lint of the Addiction Research Foundation, Toronto, Canada, and Per Sunby of the University of Oslo, Norway, assessed the size of the alcoholism problem. De Lint's paper demonstrated the increased amount of physical and psychosocial problems with a higher intake of alcohol, whereas Sunby's paper associated alcoholism with physical pathology and death. Dr. A. D. C. S. Cameron, Director of Health Services for the London Borough of Hammersmith, pointed to forthcoming changes in the British health system which were likely to have negative effects in alcoholism treatment. Dr. Herbert Barry of the University of Pittsburgh presented data to support the role of dependency conflict in producing alcoholism.

In a remarkably comprehensive paper and literature review with 126 references, Dr. John Ewing, of the Center for Alcohol Studies in Chapel Hill, N.C., assessed the question of comparison between the type of alcoholism and prog-

nostic factors. In reviewing types, he discovered a great heterogeneity of classifications among the authors.

Dr. Jack H. Mendelson of Boston City Hospital focused on the lethal consequences of alcohol abuse, the two most common being highway fatalities and hepatic disease. He cited several studies which are attempting to determine the effects of heavy drinking on risk-taking behavior and aggression, and he presented data concerning the interrelationship between aggression and androgen function.

Alcoholism is generally considered to be caused by a combination of several factors, said Dr. Clive S. Mellor of Memorial University of Newfoundland. However, so far little consideration has been given to the mode of combining—whether, for instance, alcoholism is the endpoint of a historical causal chain or due to a number of small additive causes.

Considering the problem of "loss of control," Dr. Max Glatt of University College Hospital in London said that it is not a definite pharmacological borderline but a rather diffused interdisciplinary borderland. Moderate drinking in an alcoholic seems to depend on the maintenance of a fortunate constellation of factors, which is unlikely to last forever in most people.

Biochemical pharmacology of ethanol subject of symposium

At a special symposium sponsored by the Division of Biological Chemistry of the American Chemical Society, research reports covering recent work in the biochemical pharmacology of ethanol were presented. The symposium was held in Chicago on August 30.

Edward Majchrowicz of NIAAA's Laboratory of Alcohol Research, who organized the conference, presented the latest results of his work on the ethanol-induced accumulation of methanol in alcoholic subjects (see PAN, Vol 5, No. 1). A study of 42 alcoholics showed that methanol and its toxic metabolites, formaldehyde and formic acid, may be related to withdrawal signs and symptoms.

Regina Pietruszko of the Center of Alcohol Studies of Rutgers University described some properties of alcohol dehydrogenases from mammalian livers. Mammalian liver alcohol dehydrogenase (ADH) catalyzes reversible interconversion of a large variety of aliphatic and

aromatic alcohols and the corresponding aldehydes and ketones utilizing NAD(H) as coenzyme. The substrates include saturated and unsaturated primary alcohols, secondary alcohols, glycols, and 3 beta-hydroxy-steroids. Liver ADH readily combines with NADH to form complexes with low dissociation constants. ADH from horse liver is a heterogeneous enzyme consisting of two kinds of subunits (E and S). Horse liver ADH isoenzymes composed of E or S subunits differ markedly in solubility; enzymes containing S subunits are very soluble and therefore not readily crystallizable.

Indirect evidence indicates that ADH activity in the brain is equal to approximately 1/4000 of that in the liver, said Boris Tabakoff of the Chicago Medical School. Such evidence is based on a concomitant reduction of lactaldehyde to propanediol in the presence of ethanol and NAD⁺ and the inhibition of this activity by pyrazole. In rat brain tissue the conversion of short chain aliphatic aldehydes to alcohols does not seem to be inhibited by pyrazole. Recent research results indicate a significant increase in 5-HIAA in mouse brain, both after acute and chronic administration of alcohol.

Studies by several investigators have confirmed that the microsomal fraction of mammalian liver oxidizes ethanol to acetaldehyde, said Mary K. Roach of the Texas Research Institute of Mental Sciences. The enzymes involved have not been identified unequivocally, but the reaction's requirement for NADPH₂ and oxygen indicates participation of some component of the mixed function oxidase system. Whatever the mechanism of microsomal ethanol oxidation, the activity of this system in vitro is enhanced both by chronic alcohol intake and by the administration of such microsomal inducing agents as phenobarbital. However, studies by several research groups have failed to demonstrate the activity of the microsomal ethanol oxidizing system in vivo.

Ronald G. Thurman of the Johnson Research Foundation in Philadelphia described the pathways proposed for the metabolism of ethanol in the liver and a variety of redox techniques to evaluate these pathways. He found that up to 50% of control rates of ethanol utilization occurs with a combination of MeP and glycolate without the deleterious effects of an elevated PN redox state, a finding that may have clinical implications. In addition, the altered redox state of PN that results from the activity of the ADH pathway has extreme consequences upon the metabolic functions of liver. One of the most important consequences of ethanol, he concluded, is its influence upon metabolic pathways mediated via a shift in the redox state.

RESEARCH and REVIEW

Hypothermic effects of ethanol and benzyl alcohol

The acute administration of ethanol, like other CNS-depressing drugs, lowers body temperature in mice. Many of the biological effects attributed to ethanol itself, such as the depression of amino acid incorporation into brain protein, may be secondary to hypothermia, reports Gerhard Freund of the VA Hospital and University of Florida at Gainesville.

In a series of experiments with mice, he found that the degree of hypothermia was dose-dependent and ranged from 1.5° C after 1.9 g/kg to 4.5° C after 5.7 g/kg body weight. This effect was independent of the route of administration (oral, intraperitoneal), the temperature of the administered solutions, and the tonicity (0.9% sodium chloride).

Hypothermia was prevented by elevating environmental temperatures. The elevated body temperature of mice kept at 37° C may be secondary to an inability to dissipate the heat created by basal metabolism when the thermoregulatory center is impaired by alcohol.

Benzyl alcohol, which is widely used as a preservative in parenteral solutions, also has a behaviorally sedating and hypothermic effect. (*Life Sciences*, Vol. 13, 1973, pp. 345-49).

Genetic disorder linked to cirrhosis

Alcohol addicts with a primary type IV hyperlipoproteinemia show a striking elevation of triglycerides in the serum during long periods of alcohol consumption as compared with controls, without an accompanying significant increase in free fatty acids in the serum. These data, presented by Jack H. Mendelson of the Department of Psychiatry, Harvard Medical School and Nancy K. Mello of the Laboratory of Alcohol Research, NIAAA, suggest that this genetically related lipid abnormality may be a significant factor in the pathogenesis of alcohol hyperlipemia and the alcohol-induced fatty liver.

The presence of this disorder in the general population is quite common. (*Science*, Vol. 180, June 29, 1973, pp. 1372-74).

Circadian rhythms vary effect of alcohol

Alcohol administered to a group of 40 paid volunteer male medical students impaired their cognitive performance more in the afternoon than in the evening, Ben Morgan Jones of the University of Oklahoma Health Sciences Center reports. The rate of alcohol metabolism, as measured by elimination rates, was also faster in the afternoon than in the evening. These results may be related to other circadian rhythms such as body

temperature or endogenous testosterone levels or may be related to state-dependent effects.

The performance of a placebo group was consistent with reports of cognitive performance varying throughout the day. Alcohol may reverse the normal circadian variation of cognitive performance, since alcohol subjects performed more poorly in the afternoon and placebo subjects demonstrated the opposite trend.

There was no relation between cognitive performance and elimination rate. It may be that cognitive performance following alcohol was better in the evening, not because of differences in alcohol elimination rates, but because most subjects were accustomed to drinking in the evening and had "learned" to compensate for the deleterious effects of alcohol. (*Alcohol Technical Reports*, Vol. 1, No. 1, October 1973, pp. 4-11.)

Drug maintenance and coercion improve outpatient attendance and results

Coercion is an important motivator in alcohol treatment, more important in fact than the type of treatment, according to Dr. Chaim M. Rosenberg, Director, Division of Alcoholism, Boston City Hospital. In a study of outpatients at the clinic, he found that mandatory attendance required of persons convicted of drunken driving resulted in substantially higher attendance patterns and steadier improvement than the rest of the clinic population.

Although the drop-out rate during the early stage was high, the patients who received maintenance tranquilizers or disulfiram were more likely to continue in treatment than those who received no medication. In addition, the patients who received tranquilizers became less anxious and depressed, while those on disulfiram had the highest degree of sobriety.

The findings of the study indicate the value of drug maintenance using tranquilizers for those patients who reject d. sulfiram. Although chlordiazepoxide was used in this study, it is likely that comparable results would be achieved with related drugs. In contrast, there seems to be no value in using substances such as vitamins in the hope of obtaining placebo effects.

In the mixed patient populations seen in outpatient alcoholism clinics psychological treatments alone are often inadequate in dealing with the immediate difficulties. Similarly, the routine prescription of drugs has not been shown to be effective. What is important is *how* the drugs are given. During the early stages of treatment frequent and supervised administration of drugs can play a role in stabilizing many patients.

Dr. Rosenberg's report was presented at the 35th meeting of the Committee on Problems of Drug Dependence of the National Academy of Sciences, National Academy of Engineering, and National Research Council, held in Chapel Hill, N.C., May 21-23, 1973.

Alcohol use in Arab countries

The Panarab Organization for Social Defense has begun to study the extent of alcohol use in those Arab countries in which alcohol is not simply forbidden for religious reasons.

A report on "Alcohol and Dependence in the Arab Countries" has been issued by the International Arab Bureau for the Prevention of Crime, with an English summary. The difficulty in obtaining accurate statistics and the diversity of record-keeping practices throughout the Arab world are impeding research. (*ICAA News*, Vol. 1, No. 3, August 1973, p. 5.)

PHYSICIAN'S ALCOHOL NEWSLETTER
Two Park Avenue
New York, New York 10016