



VOL. 11, NO. 4

# Physician's Alcohol NEWSLETTER



DECEMBER 1976

## Smithers Foundation combats Rand Report

The Christopher D. Smithers Foundation, Inc. is making strong efforts to combat the publicity received by the recent Rand Report that the relapse rate is no different for alcoholics using abstinence than for those using "normal drinking." NCA has taken a strong stand against this premise, and its position is that the Rand study has not shown any evidence which mandates a drinking goal for alcohol treatment programs. Leading physicians and research scientists have described the Rand Report and others which have advocated goals other than abstinence as "dangerous and misleading" and lacking in statistical significance.

The Smithers Foundation has just issued the ninth edition of its pamphlet 'Experimentation, the Fallacy of 'Controlled' Drinking where Alcoholism Exists,' with a special insert on the Rand Report. The publication, which was first published in 1969, is available for 80¢, with a quantity discount, from the Foundation at 41 East 57th Street, 21st Floor, New York, N.Y. 10022.

## Rossett reports to Senate on fetal alcohol syndrome

Pregnancy presents an opportunity for identification, treatment, and prevention of health problems in both mother and offspring resulting from heavy alcohol use, Henry L. Rossett, M.D., Associate Professor of Psychiatry at Boston University School of Medicine, told the U.S. Senate Subcommittee on Alcoholism and Narcotics on September 29.

Dr. Rossett reported the most recent findings of the collaborative program to study patterns of alcohol use by prenatal clinic patients at the Boston City Hospital. Of 42 infants born to heavy-drinking women, 69% presented at least one abnormality as compared with 36% of those born to moderate-drinking women and 35% of those born to rare-drinking women. Congenital anomalies,

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## Mice fed alcohol show fetal malformation; other reports from symposium on metabolism

The fetuses of mice fed an alcohol diet showed significantly more malformations, including skeletal, cardiovascular, ophthalmic, abdominal, and urogenital defects, than those of control mice, according to data reported by C. Randall, W.J. Taylor, and D.W. Walker of the University of Florida Department of Neuroscience and Medicine. Their findings, which support the notion that ethanol, either directly or indirectly, is a potent teratogen, were reported to the Second International Symposium on Alcohol and Aldehyde Metabolizing Systems, held at the University of Pennsylvania, October 15-17.

### Other reports

- Investigating the effect of ethanol on cyclic nucleotides in the rat brain, a team from the Boston University School of Medicine, led by L. Volicer, found that GABA and cGMP are reciprocally related and that their changes might mediate some symptoms of ethanol withdrawal.

- D. Frankel et al. of the Toronto Addiction Research Foundation reported that at least part of *p*-CPA's inhibitory effect on "net" tolerance development to ethanol can be accounted for by its accelerating effect on tolerance loss.

- New strains of rats bred for alcohol preference and nonpreference, which are suitable for studying the mechanism underlying natural alcohol preference, were described by L. Lumeng et al. of the Indiana University School of Medicine.

- Because cAMP levels changed temporally with withdrawal behavior in some rat brain areas, A. Shet et al. of the University of Philadelphia conclude that cAMP may participate in the mechanism of physical dependence produced by ethanol.

- Testing the hypothesis that differences in rate and/or capacity of ethanol and acetaldehyde oxidation account for the disparate alcohol preference of inbred rat strains, data reported by T.-L. Li and L. Lumeng of the Indiana University School of Medicine indicate that the marked difference in drinking behavior in these inbred rats is not due to altered ethanol and acetaldehyde metabolism.

- Experiments on rats by C.L. Melchior and R.D. Myers of Purdue University offer the first direct physiological

support of the hypothesis that alkaloid metabolites of the monoamines in the brain are involved in the addictive process.

- S. Tewari and E.P. Noble of the University of California, Irvine, report data showing that rat brain ribosomes are very resistant to dissociation into subunits and that chronic ethanol ingestion produces functional alteration in the properties of both 40S and 60S subunits resulting in the reduction of their biological activities.

- Ethanol did not influence protein degradation in isolated rat liver parenchymal cells but reduced hepatocyte protein synthesis, reported J. Morland and A. Bessesen, University of Tromso, Norway.

- The monkey is a valuable model for methanol toxicity in man, said G. Martin-Amat et al., University of Iowa.

- A.B. Makar and T.R. Tephly, University of Iowa, reported the first demonstration of a metabolic acidosis in the rat due to ethanol. The species differences observed between the primate and the rat may be related to folate and its biological disposition.

- Studies conducted in the laboratory of K. Ohnishi and C. S. Lieber, Mt. Sinai Medical School in New York, suggest that a species of cytochrome P-450 specific for ethanol oxidation is induced after chronic ethanol consumption which may explain, in part, the adaptive increase in microsomal ethanol oxidation and the accelerated ethanol metabolism.

- A quantitative analytical method for determining disulfiram and metabolites in plasma and tissue was reported by M.D. Faiman, et al. of the University of Kansas.

## EDITORIAL

### An Indomitable Woman

The award of NCA's Gold Key to pioneering Dr. Ruth Fox was a just reward for an extraordinary woman who has given of herself ceaselessly through a long life to helping people with alcoholism to recover. A graduate of Rush Medical College who was a Rockefeller Fellow in Peking, China, she became director of laboratories at the Neurological Institute at Columbia University's medical school.

Her interest in alcoholism stemmed from a personal confrontation. She studied psychiatry and psychoanalysis, and then began a tireless round of therapeutic, learning, writing, and teaching activities.

She has been vigorously eclectic, seeking out the most advanced professional techniques: LSD, group therapies, hypnosis, biofeedback, and sleep machines. She introduced Antabuse therapy to the United States, and she made psychodrama standard. A host of recovered patients testify to her skill.

She was the consultant who supported Marty Mann's idea of founding NCA, and she started the American Medical Society on Alcoholism. She became NCA's part-time medical director for ten years, then psychiatrist-in-chief to the alcoholism clinic Accept.

At a point in her life when others might rest on their achievements, Dr. Fox continues to contribute her warmth, good sense, and vast experience to the field. She still serves on AMSA's and NCA's Board and Medical Affairs Committee, and she lectures extensively. And she is still in private practice. Characteristically she says, "I can't leave my patients."

FAS

## Physician fellowship program established in Chicago medical center

A fellowship program for physicians who desire further clinical training or research experience in the field of alcoholism has been established at Rush-Presbyterian-St. Luke's Medical Center in Chicago. For information, contact Phillip S. Epstein, M.D., Department of Psychiatry, Alcoholism Treatment Program, Rush-Presbyterian-St. Luke's Medical Center, 1753 West Congress Parkway, Chicago 60612.

## Lieber, Beaubrun receive alcoholism awards in New Orleans

Dr. Charles S. Lieber, President of AMSA, received this year's Jellinek Award during the 27th Annual Meeting of the Alcohol and Drug Problems Association of North America in New Orleans, Louisiana, in September. Dr. Lieber was recognized for his many research accomplishments, one of which establishes that alcohol itself in the presence of a normal diet, could produce cirrhosis. A bronze bust of Dr. Jellinek and a cash award were presented to Dr. Lieber. Dr. Jellinek's book, *The Disease Concept of Alcoholism*, recognized as a classic document throughout the world, was researched and written under a Smithers Foundation grant.

At the same meeting, Dr. Michael Beaubrun of Trinidad was awarded the Edward L. Browning prize for his many contributions to the field. The Browning prize is awarded through a committee of the International Council on Alcohol and the Addictions (ICAA).

## BOOKS

**Behavior Modification for the Treatment of Alcoholism—An Annotated Bibliography.** Compiled by C.E. Weise, et al. Toronto: Addiction Research Foundation of Ontario, 1975. 275 pp. \$8.00.

Abstracts of 347 reports and review articles.

**The Alcoholism Digest Annual, Volume Three, 1974-1975.** Rockville, Md.: Information Planning Associates, Inc., 1976. 480 pp.

A compilation of 12 issues of *The Alcoholism Digest*, which abstracts the literature on alcoholism and alcohol abuse during the described years.

**Alcoholism: Interdisciplinary Approaches to an Enduring Problem.** Edited by Ralph E. Tarter and A. Arthur Sugarman. Reading, Mass.: Addison-Wesley Advanced Book Program, 1976. Cloth: \$27.50; paper: \$13.50. 857 pp.

A collection of essays that attempts to "bring together the known data about alcoholism." While the editors may not have totally succeeded in "achieving a synthesis," the collection will prompt thought-provoking insight.

**Counseling Manual for DWI Counterattack Programs.** By James L. Malfetti, and Darlene J. Winter. New York: Teachers College, Columbia University, 1976. 457 pp. Available from: AAA Foundation for Traffic Safety, 8111 Gatehouse Road, Falls Church, VA 22042.

## MEETINGS

JANUARY 24-28, 1977—7th International Conference on Alcohol, Drug and Traffic Safety, Melbourne, Australia. Information on conference and reduced rate group flights from Dr. Bernard H. Fox, 4241 N. 25th St. Arlington, Va. 22207.

JANUARY 26-28, 1977—"Alcoholism: The Search for the Sources," a conference organized by the North Carolina Alcoholism Research Authority, as part of North Carolina's Alcoholism Awareness Week. Governors Inn, Research Triangle Park, N.C. For information, write John A. Ewing, M.D., Director, Center for Alcohol Studies, University of North Carolina, Chapel Hill, N.C. 27514.

FEBRUARY 25-MARCH 5, 1977—Medical Seminar and deluxe cruise, sponsored by University of North Carolina Center for Alcohol Studies, in cooperation with NCA and Caribbean Institute. Lecturers (Category I AMA Continuing Education Credit), visits to alcoholism facilities on five Caribbean islands. For more information, write John A. Ewing, M.D., Professor of Psychiatry, Center for Alcohol Studies, University of North Carolina Chapel Hill, N.C. 27514.

APRIL 29-MAY 4—NCA National Alcoholism Forum, San Diego, California. For information, write NCA, 733 Third Ave., New York, N.Y. 10017.

MAY 5-9—National Drug Abuse Conference 1977, "A Multicultural View of Drug Abuse." Hyatt Regency Hotel, San Francisco. For information write to David E. Smith, M.D., NDAC-1977, Haight Ashbury Training and Education Project, 409 Clayton Street, San Francisco, CA 94117.

AUGUST 21-26—International Medical Symposium on Alcohol and Drug Dependence, Tokyo and Kyoto, Japan. For information, write ICAA, case postale 140, 1001 Lausanne, Switzerland.

AUGUST 28-SEPTEMBER 1—NATO International Conference on "Behavioral Approaches to Alcoholism," to be held at the Solstrand Fjord Hotel near Bergen, Norway. Deadline for Call for Papers: February 1. For further information, contact Dr. Peter Nathan, Department of Psychology, Rutgers University, New Brunswick, N.J. 08903.

# RESEARCH AND REVIEW

## Ethanol induces testicular atrophy in chronic alcoholics

An animal model system for the hypogonadism and feminization observed in chronic alcoholic men has been reported by David H. Van Thiel, M.D. et al. of the University of Pittsburgh School of Medicine. The data from studies of rats indicate that the caloric deprivation associated with chronic ethanol ingestion is not responsible for gonadal injury and atrophy of the sex steroid-sensitive tissues in alcohol-fed animals. The authors suggest that ethanol is a primary testicular toxin. (*Gastroenterology* 69: 326-332, 1975).

## Family histories of patients with manic depression and alcoholism

The presence of both alcoholism and manic-depressive disease in a patient's family history should put the clinician on special alert for risk of suicide, according to James R. Morrison, M.D. of the Department of Psychiatry, University of California, San Diego. He conducted an investigation of family histories of bipolar affective disorder patients with and without an additional diagnosis of alcoholism and found that bipolar affective disorder and alcoholism may be transmitted independently of one another. He suggests that it may be possible to identify prior to the onset of heavy drinking those bipolar patients who are at great risk for the development of alcoholism. (*Journal of Nervous and Mental Disease*, Vol. 160, No. 3, 1975, pp. 227-29)

## Schedule-induced physical dependence on ethanol

John L. Falk and Herman H. Samson of the Department of Psychology,

Rutgers University, report that they have been able to produce unequivocal physical dependence on ethanol in rats by oral self-administration of an aqueous ethanol solution. One advantage to the schedule-induction method is that the temporal distribution of the polydipsic episodes can be controlled by manipulating schedule parameters while still allowing continuous access to the ethanol solution. They suggest that blood ethanol concentration must be maintained above some critical level for prolonged periods each day for an unequivocal state of physical dependence to develop. They hope eventually to produce an animal model of alcoholism. (*Pharmacological Reviews*, Vol. 27, No. 4, 1976, pp. 449-64)

## Potassium chloride reduces blood alcohol level in rats

Simultaneous intragastric administration of large doses of KCl with ethanol significantly reduces blood alcohol levels and diminishes manifestations of alcohol intoxication in rats, according to studies by Helmut M. Redetzki, William L. Dees, and John H. Maddox of the Department of Pharmacology and Therapeutics, Louisiana State University School of Medicine in Shreveport.

It was shown with parenteral administration of alcohol that the effect is not related to an acceleration of alcohol metabolism. Analysis of alcohol concentrations of gastric and intestinal content as well as *in situ* studies with animals whose stomachs were ligated at the pylorus revealed that KCl interferes with the absorption of alcohol through inhibition of gastric absorption and gastric emptying. The finding that equimolar concentrations of NaCl were unable to duplicate the described effects charac-

terizes them as specific actions of the potassium ion. (*Life Sciences*, Vol. 15, pp. 2145-56).

## Outpatient alcoholics give valid self-reports

Thirty-nine male alcoholics in a voluntary outpatient treatment program gave valid self-reports about both alcohol and nonalcohol-related questions, based on an assessment of official records and documents. The study, conducted by Linda C. Sobell, M.A. and Mark B. Sobell, Ph.D., involved individual interviews on two separate occasions. Critical test questions were identical for both interviews and were embedded among different filler items. Self-reports of life history data provided by this group of outpatient alcoholics under specific interview procedures were highly reliable and valid. The authors suggest that further research efforts start by establishing the reliability of answers to nonverifiable questions and then to consider better ways of measuring and validating these kinds of subjective data. (*Journal of Nervous and Mental Disease*, Vol. 161, No. 1, 1975, pp. 32-42).

## Lithium kinetics in chronic alcoholics

A preliminary clinical study of lithium serum kinetics in chronic alcoholics, compared to a control group of depressive patients with normal liver function, showed that the mean circadian curves of serum lithium concentration were significantly higher in the alcoholic group.

This result, according to A.C. Altamura, G. Invernizzi and A. Vitali of the University of Milan, reflects an alteration of water and electrolyte balance, maintained by mineralocorticoid hormones that are catabolized more slowly in the liver of alcohol addicts than in the normal liver.

The authors point out the practical clinical importance of understanding the several factors that may influence the intestinal absorption and renal clearance of the lithium ion and hence its plasma concentrations. (*J. Pharmacol. Clin.* 1975, II, 2, 115-120).

● Based on the available kinetic data, J.P. Klinman et al. of the Institute for Cancer Research, Philadelphia, conclude that aldehyde reduction occurs either by a two-step radical mechanism, or by a hybrid mechanism involving a pre-equilibrium displacement of water from zinc by substrate.

● The quantity of alcohol consumption per drinking occasion is inversely related to cognitive test performance in samples other than chronic alcoholics, reported E.S. Parker and E.P. Noble, University of California, Irvine.

## Physician's Alcohol Newsletter

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## Research progress in alcohol, drug dependence

Evidence that a relationship between alcohol dependence and opiate dependence exists in mice was reported by Kenneth Blum, Joseph D. Eubanks, and Jack E. Wallace of the University of Texas Health Science Center, San Antonio, to the Committee on Problems of Drug Dependence of the National Academy of Sciences, May 19-21, 1975, at a meeting reporting research progress. The narcotic antagonist Naloxone blocked withdrawal convulsions in ethanol-dependent mice and has a similar effect on TIQ alkaloids. The authors speculate that there is a possible commonality between the biochemical and behavioral actions of opiates and alcohol.

Alfred A. Smith, Charles Engelsher, and Marsha Crofford of New York Medical College reported data from studies with mice that showed that respiratory depression induced by ethanol is modulated by a serotonergic mechanism, whereas the antinoceptive action of levorphanol is significantly attenuated by treatment of the mice with compounds that deplete catecholamines. Moreover, respiratory depression induced by opioids or other narcotics, such as barbiturates, paraldehyde or chloral hydrate remains unaffected by such treatment.

A survey of drugs and sexual activity in the Haight-Ashbury, conducted by George Gay, M.D. et al. showed that alcohol was included in the group of drugs considered to decrease sexual activity. Two mechanisms were important: that of diminishing basic desire, and that (particularly in the male) of decreasing potency.

In a national study of patterns of nonopiate/polydrug abuse, John A. Benvenuto, Jr., M.D., John Lau, and Robert Cohen reported that the polydrug abuse problem is one-fifth as large as the alcohol abuse problem.

## Fetal alcohol syndrome

(Continued from page 1)

particularly major malformations which limit development or require extensive treatment, were significantly more frequent among infants born to the heavy-drinking women.

Women who after counseling were able to abstain or markedly reduce alcohol consumption during the third trimester showed much lower rates of infant anomalies.

Dr. Rossett called for further research on the effects of alcohol on the fetus and for therapeutic programs for pregnant women.

## APA meetings in Miami Beach focus on alcoholism and education programs

Alcoholism was the focus of several panels and workshops at the 129th Annual Meeting of the American Psychiatric Association in Miami Beach May 10-14.

A panel on "Alcohol Education in the Medical Community" was moderated by Stephen H. Bender, M.D. of the Bronx. Among the panelists were Harvey Bluestone, M.D., George S. Glass, M.D., Jerrold S. Maxmen, M.D., and Frank A. Seixas, M.D.

A session on alcoholism, chaired by John A. Ewing, M.D., included presentations on treatment outcome of court-committed alcoholics, by J.B. Bastani, M.D. and William H. Keller, Ph.D., Lincoln, Nebraska; loss of control in alcoholics, by Arnold M. Ludwig, M.D., Lexington, Ky. and others; disulfiram toxicity and CS<sub>2</sub> poisoning, by John M. Rainey, Jr., M.D. of Detroit; controlled study of disulfiram effects, by Martin H. Keeler, M.D., Charleston, S.C. and others:

## Browne-Mayers reviews alcohol and intelligence

Alcohol affects human intelligence from birth to death, Albert N. Browne-Mayers, M.D., Associate Medical Director of NCA, told the Eastern Psychiatric Research Association's conference and testimonial in honor of Dr. David Wechsler, held Oct. 21-22, in New York. Dr. Browne-Mayers paid tribute to Dr. Wechsler's pioneering studies of experimental intoxication, begun some 35 years ago. Browne-Mayers reviewed the many variables that need to be considered in determining the effect of alcohol on intelligence—the agent, alcohol, itself; congeners; term of intake; state of health and nutrition, among others.

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and alcohol and central serotonin metabolism in man, by James C. Ballenge, Bethesda, Md. and others.

Ari Kiev, M.D. of New York presented a paper on alcohol, drug abuse, and attempted suicide in a session on suicide, depression, and social stress.

Among the other panels devoted to alcoholism were one on controlled drinking as a treatment for alcoholism, moderated by James L. Stinnett, M.D. of Philadelphia, and combining approaches to alcohol programs moderated by Robert A. Israely, M.D. of New York; the physician's wife as alcoholic, moderated by George S. Glass, M.D. of Houston; drugs and alcohol abuse in clinical practice, moderated by Marc Galanter, M.D. of the Bronx.

Charles S. Lieber, M.D. of the Bronx was the director of a course in somatic correlates of alcoholism in psychiatry, presented by AMSA and approved for continuing education credit by the AMA.

## AMSA official journal to start publication

ALCOHOLISM—*Clinical and Experimental Research*, a quarterly journal to be published by Grune & Stratton, will be issued quarterly starting in January 1977. The editor will be Dr. Frank A. Seixas; Dr. Charles S. Lieber will be chairman of the Editorial Board and Dr. Ernest P. Noble is Chairman of the Editorial Advisory Board. It will be the official journal of the American Medical Society on Alcoholism and the Research Society on Alcoholism, now in formation.

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