selected from animal data because of the limitations on using human data, mainly the difficulty of identifying sensitive endpoints with noninvasive techniques With optimal data—chronic duration, human subjects, sensitive endpoints—there will be much less uncertainty in the estimates Mathematical approaches focus either on refinements to the existing approach or modeling of the dose-response relationship Refinements under study include statistical estimation of the expected value and variability of the NOAEL, and modeling the probability distribution of the standard scaling factors Other approaches under investigation include dose-incidence and dose-severity models The selection of biologically valid dose-response models is complicated by the multiplicity of endpoints, the varying degrees of severity and the shift of toxic endpoint with dose The presentation will discuss mathematical and biologic considerations in developing models for animal data and extrapolating to humans, limitations of existing models, and utilizing human data in the models

SYMPOSIUM
Severity Issues in Substance Use Disorders
Sunday August 30, 1987 • 1 00 p m –2 50 p m
Marriott Marquis Hotel • Julliard/Imperial Room
Chair *Dace Svikis,* Johns Hopkins University

SEVERITY INDICATORS AS PREDICTORS OF NATURAL HISTORY IN TREATED ALCOHOLICS Thomas E Babor, Ph D University of Connecticut Health Center

This paper begins with a review of treatment evaluation studies with alcoholic patients The literature reveals a remarkable lack of consistency across studies in the significance of various severity indicators in predicting treatment response and natural history of alcoholism The methodological limitations of this research are discussed in terms of sampling bias, statistical artifact and failure to measure relevant variables Data from a prospective, longitudinal study of 321 alcoholics are used to illustrate the relative contributions of different types of variables to the prediction of course over a three-year period Included in an extensive battery of predictor variables are measures of familial alcoholism, psychopathology, life stress, cognitive function, psychiatric diagnoses, lifetime alcohol consumption, recent alcohol and drug use, severity of dependence, blood chemistry abnormalities, and history of institutional treatment for alcohol problems The results indicate that a variety of biological, behavioral and psychosocial indicators contribute to prediction of various outcome measures three years later Although a number of severity indicators predict outcome status, no one domain predominates The methodological and theoretical implications of these findings for alcoholism treatment research are discussed

PSYCHOPATHOLOGY AS A MEASURE OF SEVERITY Thomas McLellan, Ph D VA Medical Center, Philadelphia

This paper discusses the concept of severity and presents the available data relating drug use severity to treatment outcome in one or more forms of treatments and among different classes of drug abusers The case is presented that much of the relationship that has been demonstrated between this variable and outcome depends upon the specific definition of severity, and its relation to the particular outcome criteria measures Part of the difficulty involved in evaluating the relationship between the severity of the drug use disorder and treatment outcome is that there have been several reasonable yet different definitions of severity each involving different degrees of emphasis upon factors such as number and types of drugs used, physical dependence (i e , tolerance-withdrawal), social problems resulting from drug use, loss of control over the use, etc

INHERITANCE OF SEVERITY OF ALCOHOLISM Roy W Pickens, Ph D and Dace S Svikis National Institute on Drug Abuse and Johns Hopkins University

Previously we have shown that genetic factors are involved in the etiology of alcoholism and drug dependence Monozygotic (MZ) twins were found to be about 1 4 times more likely to be concordant for DSM-III diagnosis of Alcohol Abuse/Dependence than were dizygotic (DZ) twins In the present paper we examine the role of genetic factors as determinants of severity of alcoholism The present data were drawn from a twin study of alcoholism currently being conducted at the University of Minnesota Patients entering alcoholism treatment programs are screened to determine twin status Questionnaire and structured personal interview data are being collected on probands and cotwins to determine history of personal and family alcohol use and psychopathological symptomatology Zygosity is being determined by questionnaire items concerning pair similarity (95% accuracy), supplemented when necessary by results from blood group analyses The present report is based on preliminary analyses of questionnaire data from 132 same-sex twin pairs, where at least one member of each pair met DSM-III criteria for Alcohol Abuse/Dependence There was no significant difference in mean age and sex ratio for the 59 MZ and 73 DZ pairs In determining alcoholism severity in probands and cotwins, several measures were used The primary measure was number of pathological use indicators reported by each subject Pathological use indicators were 12 items taken from the DSM-III criteria that included loss of control over alcohol use, drinking of nonbeverage alcohol, etc Other severity measures included reported frequency and quantity of use and admission of previous "heavy" use While MZ and DZ probands reported a similar number of pathological use symptoms (mean 7 6 and 7 5, respectively), concordance rates for greater than 9 symptoms was 40 0 for MZ and 6 2 for DZ, approximately a six-fold difference Concordance rates for quantity of use (drinking at least a pint of alcohol on each drinking occasion) was 14 3 for MZ and 4 8 for DZ, approximately a three-fold difference Concordance rates for admission of previous "heavy" use was 56 0 for MZ and 24 3 for DZ, approximately a two-fold difference Only for frequency of drinking (drinking at least daily) were concordance rates comparable for MZ and DZ twins (41 2 and 44 2, respectively) These results suggest a role for genetic factors in determination of severity of alcoholism, as well as in determination of the transmission of the clinical disorder

DRUG SELF-ADMINISTRATION AS AN INDICATOR OF SEVERITY POTENTIAL Martin Iguchi, Ph D and Roland Griffiths, Ph D Johns Hopkins University, Francis Scott Key Medical Center

While considerable attention has focused upon organis-