THE EFFECT OF PHYSICAL EXERCISE OF VARYING INTENSITIES ON THE BLOOD ETHANOL CURVE

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TABLE OF CONTENTS

LIST OF TABLES

FIGURE

CHAPTER I

INTRODUCTION

Alcohols belong to the chemical family characterized by the substitution of a hydroxyl group for one or more of the hydrogen atoms in a hydrocarbon.[1] Ethyl alcohol or ethanol is easily formed through the fermentation of any of numerous grains.[2] The use of alcohol in beverages probably predates written history since wine could easily have been formed from the accidental fermentation of fruit juices exposed to a hot sun while still in their skin bags or stone vessels.[3] Five-thousand-year-old Egyptian Hieroglyphics mention a type of beer made from some sprouted grain.[4] Biblical reference provides the earliest record of intoxication by portraying a four-thousand-year-old account of Noah inebriated and unconscious in his tent from the consumption of wine made from his vineyard.[5]

Despite this early use of alcohol and knowledge of its intoxicating qualities, serious study involving alcohol did not begin until 1904 when a study of fatal crashes involving "automobile wagons" found a large percentage of drivers had been drinking prior to their accidents.[6] The earliest precise work concerning human alcohol metabolism can be attributed to Haggard and Greenburg who studied the partitioning of ethanol in blood, urine, water and air during the 1930s.[7] In 1933, Widmark derived a mathematical equation which represented the elimination of

ethanol from human blood as a linear constant, independent of the amount ingested or remaining in the body.[8]

During the 1970s, the increased sensitivity of new assay methods more sensitive to minute alcohol concentrations, enabled researchers to discover that blood alcohol (BA) elimination was linear down to approximately 0.2 mg/ml or 0.02 % W/V concentration in the blood; however, below this point the rate of elimination slowed and assumed curvilinear characteristics.[9,10,11,12] Largely as a result of these and other studies, the term "blood alcohol curve" or BAC has been adopted to describe the typical elimination rates of ethanol from blood.[13] As a result of numerous public safety, toxicology and pharmacokinetic studies, methods for estimating the highest occurring or peak BA concentrations and rates of elimination, based upon the amount of ethanol ingested per unit of body weight, were developed.[14,15,16,17]

Numerous studies have been conducted in an attempt to discover those variables which influence the BAC, especially the peak BA concentration and rate of elimination. It was the purpose of this study to examine the effect(s) of physical exercise on the peak BA concentrations and rate of elimination from the blood.

Statement of the Problem

The purpose of this study was to determine if there is a difference between blood alcohol curves during rest and three hours of sustained exercise at 15%, 32.5% and 50% of VO_2 max.

Subproblems

1. Determine if a difference exists among the peak BA concentrations at rest, 15%, 32.5% and 50% of VO_2 max.

2. Determine if a difference exists among the post absorptive BA elimination rates at rest, 15%, 32.5% and 50% of VO_2 max.

Hypotheses

1. There will not be a significant difference among the peak BA concentrations at rest, 15%, 32.5% and 50% of VO_2 max.

2. There will not be a significant difference among the post absorptive BA elimination rates at rest, 15%, 32.5% and 50% of VO_2 max.

Limitations

1. Other than restricting food intake ten hours prior to participation, no attempt was made to control the diet of subjects.

2. Other than requiring total abstinence from alcohol for 48 hours prior to participation, no attempt was made to control the extracurricular activity of subjects.

Delimitations

1. Subjects were limited to male volunteers.

2. The experimental variables were exercise intensities of 15%, 32.5% and 50% of VO_2 max.

3. The blood alcohol curves were plotted from venous blood samples drawn each thirty minutes after alcohol ingestion and encompassing a total period of three hours.

Assumptions

1. It was assumed subjects followed instructions pertaining to fasting and alcohol abstinence.

2. It was assumed subjects VO_2 max., did not change significantly between time of determination and experimentation.

3. It was assumed any error introduced during analytical laboratory analysis of blood was consistent among samples.

Significance of This Study

As a result of studies conducted to date, the effect of physical exercise on human peak BA levels and alcohol elimination is not clear. Some studies fail to show any significant increase in alcohol elimination in response to physical activity,[18,19,20] while others purport to show significantly increased elimination rates.[21,22,23,24] This author's study[25] was the only one found which investigated the effect of physical exercise on the peak BA level. This study indicated that exercise intensities equal to 50% VO_2 max. may reduce peak BA levels if initiated immediately after ethanol ingestion and continued for three hours. If anything can be gleaned from these studies, it may be that exercise itself is not the salient factor but, rather, the intensity at which the exercise occurs.

To date, the exercise intensity parameters, adjusted for individual differences in human work capacity, that may significantly influence the peak BA level and rate of human alcohol elimination, have not been established. Additionally, it is this author's opinion that many studies published in this area employ less than desirable experimental designs and/or permit contamination from excessive, uncontrolled variables.

Also, this study introduced the exercise protocols immediately following alcohol ingestion; therefore, possible changes in peak BA concentrations were discernable. Finally, although it has not been proposed in literature, the possibility of exercise induced reductions in peak BA levels and/or increased rates of elimination, could have beneficial applications for reducing the potentially deleterious effects of alcohol ingestion. One would have to weigh the possible benefits obtainable against the increased risk of exercise in an impaired condition, however.

Definition of Terms

Absorption - The process by which the products of digestion enter the blood stream.

Acetaldehyde - A member of the chemical aldehyde class known as Ethanal, characterized by a carbon-oxygen double bond. Generally considered to be the first metabolic by-product of ethanol oxidation.

Alcohol - A chemical class characterized by the substitution of a hydroxyl group (OH) for one or more of the hydrogen atoms in a hydrocarbon. Throughout this dissertation, the terms alcohol, ethyl alcohol and ethanol will be used synonomously.

Balke Treadmill Stress Test - A test of physical endurance that involves walking on a motorized treadmill at some constant speed with incremental grade increases of 1% at the end of each minute until physical exhaustion or some other limiting factor dictates test termination.

Blood Alcohol - The amount of alcohol present in the blood at a given point in time. Usually expressed in mg% or W/V (see units of measure); hereinafter referred to as BA.

Blood Alcohol Curve - The plotting of individual blood alcohol determinations against time after the ingestion of a given quantity of alcohol; hereinafter referred to as BAC.

Peak Blood Alcohol - The highest concentration of alcohol present in the blood at some point in time after ingestion of a given quantity of alcohol.

Breathalyzer - Any of a number of instruments designed to measure blood alcohol levels through collected breath samples. These machines usually involve the collection and analysis of a single, forceful expiration.

Catalase - An enzyme which some feel may be important in the metabolism of alcohol.

Coenzyme - A substance which permits an enzyme to carry out its catalytic task (see enzyme).

Digestion - The process by which substances are prepared for absorption.

Elimination - The sum total of all bodily functions acting to remove a substance from tissue.

Enzyme - Proteins which act as catalysts to greatly speed up the rate of a chemical reaction.

Gas Chromotography - A method for determining the presence of any number of solutes in a gas by placing the solution in a carrier liquid, gradually heating and transporting the solution along a network and imprinting the detector response on some collecting device for detection and analysis.

Gluconeogenesis - The process by which intermediate metabolic compounds (lactic acid, glycerol and some amino acids) can be utilized to make glucose and glycogen.

Hemodilution - Any process which results in the dilution of blood by increasing the proportion of the liquid volume component.

Heparin - An anticoagulant used to prevent coagulation (clotting) of blood.

Hepatic - A term used when referring to the liver.

Hydrocarbon - Any molecular structure involving only carbon and hydrogen atoms.

In-Vitro - That which occurs outside the human body.

In-Vivo - That which occurs within the human body.

Krebs Cycle - The common, final, oxidative pathway by which intermediate food metabolites are degraded to carbon dioxide and water. It is also called the Citric Acid on Tricarboxylic Acid Cycle.

Liver Alcohol Dehydrogenase - A hepatic enzyme which is reported to be primarily responsible for metabolizing alcohol; hereinafter referred to as LADH.

Microsomal Enzyme Oxidizing System - An additional hepatic enzyme system which some feel may assist in metabolizing alcohol, especially at higher concentrations in the blood; hereinafter referred to as MEOS.

Metabolism - The sum total of all chemical changes occuring in a living organism in the course of its activities.

Nicotinamide Adenine Dinucleotide - A coenzyme required as a co-factor for LADH to metabolize alcohol. It was previously referred to as Coenzyme 1, Cozymase or Diphosphopyridine Nucleotide; hereinafter referred to as NAD.

Nicotinamide Adenine Dinucleotide Hydrogen - The reduced form of NAD. Reduction occurs as a result of metabolizing alcohol to acetaldehyde; hereinafter referred to as NADH.

Oxidation - A process involving a loss of electrons by a substance by combining it with oxygen.

Reduction - A process involving a gain of electrons by a substance by combining it with hydrogen.

Respiratory Quotient - A numerical value equal to or less than one, used to represent which food stuff (carbohydrate, fat or protein) is being oxidized in the production of energy. It is found by dividing the amount of carbon dioxide produced by the amount of oxygen consumed. It will hereinafter be referred to as RQ.

Solute - A substance which is dissolved in a solvent.

Solvent - The medium in which a solute is dissolved.

Spectrophotometer - An instrument for determining the amount of a solute contained in a solvent by introducing a light beam through the solution and measuring the amount of light absorbed due to the presence of the solute.

Substrate - A reactant in an enzyme catalyzed reaction. It is used in this text to refer to the substance with which an enzyme acts.

Units of Measure - the following units of measure will be used throughout this text:

Gram - Metric unit of weight equal to 0.352 ounces; hereinafter referred to as gm.

Kilogram - Metric unit of weight equal to 2.2 pounds or 1,000 gms; hereinafter referred to as kg.

Liter - Metric unit of liquid volume equal to 33.3 ounces or 1,000 ml; hereinafter referred to as l.

Milligram - Metric unit of weight equal to 0.001 gms; hereinafter referred to as mg.

Milligram Percent - The number of mg of a solute present per 100 ml of a solvent; hereinafter referred to as mg%.

Milliliter - Metric unit of liquid volume equal to .001 liter or approximately 1/30th of an ounce; hereinafter referred to as ml.

Meter - Metric unit of length approximately equal of 39.9 inches.

Mole - A chemical weight equivalent represented by the quantity of a substance necessary to equal its molecular weight; hereinafter referred to as m. It is usually expressed in moles of solute per liter (m/l) of solution.

Millimole - A chemical weight equivalent equal to 0.001 m. Hereinafter referred to as mm.

Micromole - A chemical weight equivalent equal to 0.000001 m. Hereinafter referred to as um.

Volume per Volume - The ratio of solute volume to solvent volume when both are liquids. It is usually expressed as a percentage (%); hereinafter referred to as V/V.

Weight per Volume - The ratio of a solute weight to solvent volume when the solute is a solid or has been converted to solid weight units; hereinafter referred to as W/V.

Workload Measures - The following measures of work will be used throughout this text:

Kilometers per Hour - Metric measure of speed approximately equal to .062 miles per hour; herinafter referred to as kph.

Kilogram Meters - The work required to move one kg one meter against normal gravity; hereinafter referred to as kgm.

Kilogram Meters per Minute - The accomplishment of one kgm of work per minute; hereinafter referred to as kgm/min.

VO_2 max. - A measure depicting the amount of oxygen utilized by an organism in the accomplishment of the maximum level of work attainable for one continuous minute. Usually used in conjunction with the Balke Treadmill or other stress test protocols and is attained through a gradual progression of workloads until the maximum is reached. It is generally considered the single most important measure of cardiovascular work output. It is measured in terms of ml of oxygen consumed per kg of body weight per minute (ml/kg/min).

MET - A workload measure equal to 3.5 ml/kg/min VO_2. One MET is considered equal to the average adult resting metabolic rate.

WATT - A workload measure equal to 6 kgm/min or 10.8 ml/kg/min VO_2.

ENDNOTES

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CHAPTER II

LITERATURE REVIEW

Alcohol Metabolism and Elimination

Orally ingested alcohol does not require digestion and is absorbed into the bloodstream largely through the stomach by simple diffusion.[1,2] The bloodstream carries alcohol to the liver, the organ primarily responsible for alcohol metabolism, where the enzyme LADH and the coenzyme NAD oxidize alcohol to acetaldehyde.[3,4] Still in the liver, acetaldehyde is further reduced to an acetate, most probably acetic acid, by the enzyme aldehyde dehydrogenase.[5] From here, the acetate would enter the Krebs Cycle and be utilized in the production of energy.[6]

In addition to this primary route of metabolism, some alcohol will usually be eliminated unchanged in urine, expired air and perspiration.[7,8,9]

The Effects of Variables on Blood Alcohol Levels

Numerous studies attempting to discover the effects of selected variables on alcohol metabolism and elimination by ascertaining BA levels, have been undertaken. A review of this research follows.

Sex: Several studies indicate women achieve significantly higher BA concentrations than men, even when alcohol doses are adjusted on the

basis of body weight. In a study by Jones and Jones[10] at the University of Oklahoma's Health Sciences Center, two men and two women each consumed the equivalent of 0.33, 0.66 and 1.32 ml of 95% ethanol per kg of body weight. Breathalyzer samples were taken each five minutes after alcohol ingestion until a zero BA level was indicated. Although testing for statistical significance was not accomplished, the following results were noted: (1) the females consistently attained higher peak BA levels at each dose ($\bar{x}$ = 1.4 times as high as men); (2) the females reached peak BA levels faster than men ($\bar{x}$ = 41.6 vs. 62.7 minutes); (3) the females eliminated alcohol from the blood more rapidly than men ($\bar{x}$ = 18.0 vs. 14.0 mg% per hour).

In a subsequent study at the same facility, Jones et al.,[11] reinforced these earlier findings by expanding sample size to include 22 females (11 on oral contraceptives and 11 not) and 11 males. Each subject consumed the equivalent of 0.52 gm of 95% ethanol per kg of body weight and breathalyzer samples were collected every five to ten minutes after ingestion until a zero BA level was reached. Using independent group t-tests, the following results were obtained: (1) peak BA levels and time to peak BA levels were not significantly different between female groups; and (2) when compared with males, both female groups reached higher peak BA levels; ($p < .05$) and (3) females not on contraceptives reached peak BA levels earlier ($p < .05$) and eliminated BA more rapidly ($p < .01$).

In a third study conducted at the same facility, Dubowski[12] had 27 male and 14 female subjects ingest alcohol doses ranging from 0.43 to 1.60 gm of 95% ethanol per kg of body weight. Head Space Gas Chromotography and a breathalyzer were used to determine peak BA levels and

rates of elimination from blood. Although this study was accomplished primarily from a forensic toxicology viewpoint and statistical tests to differentiate males and females were not accomplished, the following findings are revealing: (1) females had higher mean peak BA levels than men for weight adjusted ethanol doses (133.8 vs. 118.6 mg%); (2) females mean time to peak BA level after ingestion was less than that for men (41.9 vs. 56.7 minutes); and (3) females average rate of alcohol elimination from blood was greater than that of men (18.3 vs. 14.8 mg% per hour).

Despite the fact that Jones et al., used independent group t-tests when an ANOVA should been used and Dubowski permitted his subjects to eat a light meal in conjunction with alcohol ingestion, thus introducing another extraneous variable, these studies did provide strong evidence for differences in the rate of alcohol metabolism between men and women. Since alcohol diffuses throughout body compartments in direct proportion to tissue water content[13] and women, on the average, have less water and more fat per kg of body weight than men,[14] body composition could account for these differences attributed to sex.

Age: Qualitative visual observations have led many to believe that advanced age may result in higher peak BA concentrations and slower elimination rates per ingested alcohol dose. Quantitative scientific experiments concerning the effect of aging on alcohol metabolism and elimination have not been extensively studied.

The most comprehensive study in this area to date, was accomplished by Vestal et al.,[15] at the Gerontology Research Center, Baltimore, Maryland. In this study, 50 males aged 21 to 81 ($\bar{x}$ = 53.3) were intravenously administered ethanol equivalent to 0.57 gm per kg body

weight. Repeated blood samples were collected every 15-30 minutes from an indwelling, contralateral, venous catheter for periods encompassing four hours. Gas chromatographic analysis of blood revealed the following: (1) peak BA concentration was positively correlated with age ($r = 0.55$, $p < 0.001$); and (2) rate of ethanol elimination from blood was not affected by age.

Also, this study found the 21-56 year group subjects ($n = 25$) had significantly less body fat than the 57-81 year group ($p < 0.05$). This final finding agrees with statistics which show body fat increases and total body water decreases with advanced age.[16] Again, body composition differences attributable to increased adiposity and not advanced age per se, could well be the salient variable to explain these findings.

Race: Studies attempting to show differences in alcohol metabolism and elimination attributable to race have not, to date, been conclusive. In a study conducted at the University of Oklahoma's Health Sciences Center, Farris and Jones[17] had 17 full blooded American Indians and 17 Caucasians consume the equivalent of 0.52 gm of 95% ethanol per kg of body weight. Approximately 30 breath samples were collected from each subject beginning immediately after ingestion until a zero BA level was reached. Analysis of the samples and application of a t-test provided the following findings: (1) Indians reached higher peak BA levels and reached them more quickly after ingestion ($p < .05$); (2) Indians eliminated alcohol more quickly from blood expressed in percent per hour ($p < .01$) and mg/kg/hr ($p < .05$); and (3) time to zero BA level was less for Indians ($p < .05$).

In a similar study, Reed et al.,[18] of the Zoology Department of the University of Ontario, orally administered alcohol equivalent to 0.8 gm of 95% ethanol per kg of body weight to 37 Caucasian, 20 Chinese and 24 Indian males. Venous blood samples were collected at 60, 90, 120, and 150 minutes after ingestion. Gas chromotographic anaysis of samples coupled with an analysis of variance (ANOVA) of the results, led Reed to conclude that Indian males eliminated alcohol more rapidly than the other groups ($p < .001$), while Chinese eliminated alcohol more rapidly than Caucasians ($p < .01$). These findings were observed using both elimination criteria of mg%/hr and mg/kg/hr.

Among conflicting studies, Fenna et al.,[19] at the Department of Medicine, the University of Alberta, intravenously administered a solution of 10% ethanol to 26 Eskimo, 26 Indian and 17 Caucasian males until BA levels of 125 mg%, as determined by breathalyzer, were reached. Breathalyzer readings taken each 15 minutes after infusion for two hours, coupled with independent group t-tests revealed the following: (1) when compared with Eskimos and Indians, Caucasians eliminated alcohol more rapidly where expressed in mg%/hr and mg/kg/hr; and (2) no difference in elimination rates between Eskimos and Indians could be found.

Zeiner and Paredes,[20] at the University of Oklahoma's Health Sciences Center, orally administered the equivalent of 0.66 ml of 95% ethanol per kg of body weight to 10 Tarahumara Indians and 13 Caucasian males. Breathalyzer samples were collected each 10 minutes after ingestion until subjects reached a BA level of 20 mg% on the descending phase. A t-test disclosed that the Tarahumara reached lower peak BA levels than Caucasians ($p < .01$).

Rounding out the picture Bennion and Li[21] at the National Institute of Arthritis, Metabolism and Digestive Diseases, Phoenix section, administered oral doses of 95% ethanol to 30 American Indians and 30 Caucasians equivalent to 0.75 ml per kg of body weight. After a 90 minute post-ingestion period, seven venous blood samples were collected each half-hour and analyzed by gas chromotography. Using t-tests, this study reported the following: (1) alcohol elimination from the blood, expressed in mg% per minute, showed the Indians to have a faster rate of elimination ($p < .01$); (2) the Indians weighed more ($p < .01$); and (3) alcohol elimination, expressed in mg/kg/hr, failed to show a difference between groups.

In studies involving other racial comparisons, Hannah[22] at the Physiology Department at the University of Hawaii, orally administered the equivalent of 0.59 gm of 95% ethanol per kg of body weight to 30 Chinese, 47 Japanese and 68 European males. Breath samples were collected each 30 minutes during the 90 to 180 minute post-ingestion period and analyzed by gas chromotography to plot rates of ethanol elimination. Using paired t-tests, Hannah could not find any difference in the rates of elimination expressed as mg% per hour; however, when elimination rates were expressed as mg/kg/hr, both Oriental groups eliminated alcohol more rapidly than Europeans ($p < .01$) while no difference was apparent between Japanese and Chinese.

Faced with such an apparent diversity of findings concerning these studies between and among racially different groups, one could easily become perplexed; however, a closer analytical look at methodology and subject selection may be beneficial. In comparing alcohol metabolism between Indians and Caucasians, both Farris and Reed indicate increased

rates of elimination; Fenna finds decreased rates of elimination; and Bennion could find no difference. Fenna's study should be subject to dispute since the 26 Indian subjects were already hospitalized for a variety of illnesses and infections while the remaining subjects were presumably healthy. The Farris study administered ethanol orally while Bennion provided for intravenous introduction. Since intravenous administration circumvents absorption, differences in diffusion rates could effect ethanol metabolic rates by varying enzyme kinetics (saturation rates) among alcohol, LADH and NAD. This could be supported by Farris when he finds Indians reach higher peak BA levels and reach them more quickly than Caucasians of equal weight when both were administered equal oral doses.

Zeiner found the Tarahumara Indians to reach lower peak BA levels than Caucasians when administered equivalent oral ethanol doses; however, the Tarahumara are an extremely active, thin people. If the Tarahumara were significantly leaner than their Caucasian subject counterparts, this could account for this apparent difference.

In comparing Orientals with Caucasians, both Reed and Hannah found increased rates of elimination among the Orientals. Initially, this was supported on the basis that Orientals had a much higher incidence of an atypical LADH supposedly more active in metabolizing alcohol;[23] however, subsequent study has indicated subjects possessing atypical LADH do not metabolize alcohol any more or less rapidly than subjects with typical LADH.[24,25]

Reed[26] sheds additional light on this difficult area by mentioning confounding variables which would tend to accentuate inter-racial differences, such as: (1) alcohol consumption histories of subjects;

(2) use or non-use of certain drugs; (3) body composition differences; (4) sample selection and size; and (5) technical differences. Reed believes if newer studies took these additional variables into consideration, intra-racial differences would be larger than inter-racial ones.

Consumption Patterns: Qualitative visual observations have led many to believe that individuals with habitual alcohol consumption patterns "handle" alcohol better than the occasional drinker. Scientifically controlled, quantitative studies are limited in this area; however, Ugarte et al.,[27] of the medical faculty of the University of Chile, studied the rate of ethanol metabolism among habitual alcoholics, intermittent alcoholics and social drinkers. The alcoholics average ethanol intake was equal to 350 gm per day for at least four years while the social drinkers averaged less than 50 gm per day. Alcoholics were classified as habitual if average intake rates were maintained daily and intermittent if intake rates were interrupted by periods of abstinence. Intermittent alcoholics were further sub-divided based upon average days of intermittence preceeding testing (one, 11 and 22 days).

Each subject was intravenously administered the equivalent of 1.0 gm per kg body weight of 95% ethanol and venous blood samples were extracted each 30 minutes for 2.5 hours following infusion. Blood samples were analyzed photometrically. Using independent group t-tests, the following results were obtained using mg%/hr as the standard for elimination comparisons: (1) social drinkers eliminated alcohol more slowly than any of the alcoholic groups ($p < .05$); (2) the habitual alcoholics elimination rates were more rapid than any of the

intermittent alcoholics ($p < .05$); and (3) the intermittent alcoholics with the longer periods of abstinence, had slower elimination rates than those with the shorter periods of abstinence ($p < .025$).

Furthermore, a least squares line constructed from intermittent alcoholic elimination data is linear to the 18th day of abstinence with a significant coefficient of correlation between rate of elimination and days of abstinence ($r = -0.64$, $p < .001$). The mechanism(s) responsible for these findings could not be elucidated by enzyme analysis of hepatic biopsies.

In a second study accomplished by Korsten et al.,[28] at the Mt. Sinai School of Medicine in New York, six chronic alcoholics (daily ingestion exceeding 150 gm ethanol for at least 10 years) and five non-alcoholics were intravenously administered ethanol until venous blood levels reached 43 to 54 mm. Sequential blood samples (17-20) were taken from an indwelling venous catheter during an eight to ten hour post infusion period. Gas chromatographic analysis of collected samples coupled with t-tests of results, revealed that peak BA level (mm) and rate of alcohol elimination (mm/min/1) was not significantly different between alcoholics and non-alcoholics.

The apparent discrepancy between the findings of these studies is not easily explained; however, Ugarte's study claimed to show elimination differences between alcoholic groups whose only difference was one day of abstinence prior to testing. This alone makes the study suspect in this author's opinion. Additionally, various stages of hepatic deterioration are bound to exist among chronic alcoholics with concomitant, variable effects for potential alcohol metabolism.

Diurnal Variation: A number of studies purporting to show changes in the rate of alcohol metabolism as a result of possible diurnal differences have been accomplished. In a study by Zeiner[29] at the University of Oklahoma's Health Sciences Center, two independent groups of male social drinkers (eight to nine beers per week) ingested the equivalent of 0.66 ml of 95% ethanol per kg of body weight. Group one ($n = 5$) started at 9:00 AM while group two ($n = 6$) started at 2:00 PM. Both groups had been fasting for at least four hours. Breathalyzer samples were taken every 10 minutes beginning 40 minutes post ingestion and continuing until BA levels reached 20 mg% on the descending phase. Analysis of data by a t-test disclosed the following: (1) group one reached higher peak BA levels ($p < .05$) and took longer to reach 20 mg% level ($p < .02$); and (2) there was no difference in the rate of ethanol disappearance from blood (mg%/hr).

In an earlier study conducted at the Stanford University School of Medicine, Wilson et al.,[30] orally administered 20% ethanol (V/V) to six subjects. Each consumed this amount each hour, for at least 36 hours, at a dosage, determined from previous study, designed to cause a slow rise in BA levels. The BA increases would permit testing for 48 hours without the onset of severe intoxication. Additionally, the subjects took a regular diet at 7:00 AM, 12 noon and 6:00 PM. Finally the 12:00 and 3:00 AM dosages were tripled to permit sleep at night. Micro-diffusion blood or saliva tests were made hourly to construct a BAC for at least 36 hours per subject. The calculation of a mean curve led to the following findings: (1) BA levels increased by 30 mg% between 10:00 PM and 8:00 AM; and (2) BA levels decreased by 30 mg% between 8:00 AM and 2:00 PM.

In a third study accomplished by Madsen and Rossi[31] three men and three women were orally administered the equivalent of 0.6 gm of 95% ethanol per kg of body weight on four separate occasions, each at 11:00 PM. On two occasions subjects were awake and recumbent while they slept during the remaining two. An indwelling venous catheter permitted the collection of 20 serial blood samples drawn during an eight hour post-ingestion period. Head Space Gas Chromotography with application of t-test to the results showed no difference in the rate of alcohol elimination between periods of sleep and wakefulness.

In reviewing these articles, one must be aware of the fact that sample sizes are very small and this is certainly cause for critical scrutiny. Zeiner's study utilized two different groups while a more scientific approach, in this author's opinion, would have utilized a larger single group with two separate, different time of day tests. Finally Zeiner's morning group had been fasting for approximately 12 hours, while the afternoon group for only four.

Wilson's study was so poorly conducted that it has little scientific merit; however, it is included because it is not un-representative of studies in this area. This author's critique of this study includes: (1) one cannot discern the physiological characteristics of the subjects, (e.g., sex, age, weight, drinking history, etc.); (2) one cannot determine the exact amounts of alcohol administered; (3) one cannot determine the number and timing of samples; (4) samples were blood and saliva and one cannot determine if and how these differing tissues were equilibrated; (5) food was introduced during the protocol and could have caused most, if not all, of the reported variation; (6) dosages were tripled on two occasions during the early morning and could have caused

most, if not all of the reported variation; and (7) statistical tests were not accomplished to test for significance.

The study by Madsen and Rossi can only be criticized for the small sample size.

Food: The effect of a food bolus on the rate of alcohol metabolism has been so well established that it has moved from the realm of hypothesis to a scientifically accepted principle. Wallgren and Barry,[32] Goldstein,[33] and Wilkinson[34] all agree that food in the stomach has the following effects on alcohol metabolism: (1) decreased peak BA level; (2) increased time to reach peak BA level; and (3) a smaller area under the BA curve.

These effects can be explained by the tendency of food to delay the absorption of liquids into the bloodstream by decreasing diffusion rates across intestinal membranes and by increasing the time required for liquids to exit the stomach into the small intestine.[35] The total effect, therefore, is to release smaller amounts of ethanol into the bloodstream per unit of time, resulting in more efficient metabolism by the liver.[36]

Since a meal can require up to three hours to be digested and absorbed,[37] virtually all studies of alcohol metabolism stipulate at least a four hour fast prior to inception of experiment.

Exercise. The effects(s) of physical exercise upon alcohol metabolism have not been frequently studied and a clear consensus concerning results has not been evidenced. Nonetheless, several studies claim to find no effect from physical exercise. In one of the earliest of these studies, Carpenter and Lee[38] of the Nutrition

Laboratory of the Carnegie Institute of Boston, orally administered the equivalent of 50 ml of absolute alcohol to a single subject on separate days. During one of the days, the subject rested and on the other rode a bicycle ergometer for two hours at a workload of 415 kgm/min. Blood samples were collected at one, two and four hours after ingestion. This study failed to show any difference in the rate of disappearance of ethanol from blood. Information concerning age and weight of subject, method of BA determination, occurrence of the two hour exercise protocol within the four hour experiment, and comparative rates of ethanol disappearance (mg%/hr) were not provided in the article.

In a second study, Canzanelli et al.,[39] used an 8 kg bitch dog as a subject. The dog had been placed on a 25% fat, 15% protein and 60% carbohydrate diet. The determination of resting, post-absorptive (16-20 hours since last meal) respiratory quotient (RQ) on three different days averaged 0.86. On 10 different occasions spanning one month, 100 ml of 10% ethanol was administered to the dog via stomach tube and similar post absorptive RQs averaged 0.75. A workload equivalent to 5,100 kgm was administered for 15 minutes on three separate days and the post absorptive RQ dropped to 0.81. The same workload combined with the same alcohol dose resulted in a post absorptive exercise RQ of 0.88. Since administration of alcohol caused RQ to drop during rest and increase during exercise, the authors concluded that ethyl alcohol can be used as a source of fuel at rest, but not during exercise.

Finally, both Goldstein[40] and Wallgren and Barry[41] stated that no correlation existed between physical activity levels and ethanol metabolism because physical activity had no effect upon liver function.

Of those studies that claim a positive relationship between physical activity and rate of ethanol metabolism, one of the earliest was completed by Hebbelinck[42] at the Institute of Occupational Health, Helsinki, Finland. In this study, 21 males, aged 19-27 years, were orally given the equivalent of 0.6 ml of 95% ethanol per kg of body weight. During a control day, the subjects rested and had two venous blood samples drawn at 30 and 60 minutes after ingestion. During a separate test day, the following five physical performances were interjected between the 30 and 60 minute blood samples: (1) hand dynamometer compression - six trials; (2) back lift traction - three trials; (3) jump test - three trials; (4) modified Romberg test - 30 seconds; and (5) bicycle ergometry - five minutes at 1,500 kgm/min. Analysis of blood samples by Widmark's micro method and subjection of data to t-test revealed that average increase of BA level was 30.5% lower ($p < .001$) on the test day after exercise.

In one of the most recent studies in this area Schurch et al., [43] at the Institute for Sports Medicine, West Germany, orally administered the equivalent of 0.66 gm of 95% ethanol per kg of body weight to eight male students aged 23-25. This ethanol dose was ingested on three separate occasions or tests. Test one consisted of rest with venous blood samples collected each 30 minutes after ingestion through 4½ hours. Test two employed the same protocol except bicycle ergometry at 50% of VO_2 max. was interposed for 90 minutes between 2 and 3½ hours. Three days elapsed between tests two and three wherein a carbohydrate reduced diet was administered. Test three contained exactly the same protocol as test two. Blood tests were analyzed by gas chromotography. Statistical treatment of data revealed the following: (1) in comparison

with test one, ethanol elimination rates were increased during test two ($p < .001$) and test three ($p < .01$); from 2 to 3½ hours; (2) there was no difference between tests two and three with respect to ethanol elimination rates; and (3) there was no difference in elimination rates among tests prior to two hours or after 3½ hours. This article did not provide sufficient information to enable the reader to determine the exact rates of ethanol elimination or the statistical test(s) employed in analyzing data.

A third study was accomplished by Januszewski and Klimek[44] at the department of Human Physiology, Cracow, Poland. In this study, six men aged 20-22, ingested one ml per kg of body weight equivalent of 95% ethanol on three separate occasions or tests. During each of the tests, bicycle ergometry workloads (100, 150 and 200 watts, respectively) of eight minutes each was interposed between the collection of two capillary blood samples. In each case, the first blood sample was collected 35 minutes after ingestion while the second was collected as soon as possible after the exercise bout (approx. 45 minutes after ingestion). The blood samples were analyzed using Widmark's micro method and the results subjected to t-testing. The results showed the following: (1) decrease in BA level after each exercise protocol was significant ($p < .02$); and (2) no linear correlation between fall in BA level and workload could be made.

In the final study to be mentioned, Kulling[45] at the Exercise Physiology Laboratory of Oklahoma State University, orally administered the equivalent of 0.9 gm of 95% ethanol per kg of body weight to two male subjects. The alcohol was administered on two separate tests, four days apart. During test one, the subjects rested and during test two,

subjects walked a treadmill at 3.5 miles per hour at a grade sufficient to introduce a 50% VO_2 max. workload. Both tests lasted a total of four hours during which venous blood samples were collected each 30 minutes after ingestion. Blood samples were analyzed enzymatically by spectrophotometer. The results were as follows: (1) mean peak BA levels at rest and during exercise were 130.0 and 103.2 mg%, respectively and (2) average elimination rates during rest and exercise were 13.5 and 11.3 mg%/hr respectively.

With respect to analyzing the relative merits of these studies, this author will analyze each in turn. A number of criticisms have already been directed at the article by Carpenter and Lee, primarily because sufficient information concerning the subject, methodology and data were not evident. Using information provided, the exercise protocol consisted of bicycle ergometry at 415 kgm/min. Since one kgm equals 1.8 ml VO_2,[46] the total energy expenditure per minute would equal 747 ml/min VO_2. Assuming the subject was an average 155 pound man (70 kg), this represents an energy expenditure of 10.7 ml/kg/min VO_2. According to Fox and Matthews,[47] this represents a mild workload. As previously mentioned at the beginning of this chapter, alcohol could be eliminated from the blood in several ways: (1) as a fuel substrate in the provision of energy; and (2) as unchanged alcohol via breath, urine and perspiration. In either case, one would envision fairly strenuous workloads as being necessary to statistically show any difference in BA levels. The workload in this study was probably not sufficiently intense to meet this criterion.

In the second study by Canzanelli et al., RQs collected from a dog preceding and during exercise, purported to show the use of alcohol as

a fuel during rest, but not exercise. This study indicated that RQ dropped from 0.86 to 0.75 during ethanol infusion at rest, but it increased from 0.81 to 0.88 during exercise. Since it can be shown that the RQ of ethyl alcohol, assuming oxidation as the sole fuel source, is equal to 0.67, the RQ reduction during rest would seem to indicate utilization of ethanol as a fuel. Likewise, the increase in RQ during exercise would tend to indicate lack of alcohol metabolism as fuel; however, as exercise intensity increases, RQ becomes an unreliable test for food substrate utilization since carbon dioxide is disproportionately increased in response to cellular metabolism.[48] This causes RQ to rise artificially. Even though this study compared exercise RQ before and after alcohol administration, the findings must be labeled suspect.

Hebbelinck's study appears to be well conceived and administered except one cannot tell from the article the exact workload equivalents of the exercises performed or how much time they consumed between the 30 and 60 minute blood tests.

Janusewski and Klimek showed significant decreases in BA levels with pre and post tests in conjunction with three differing physical workloads. In this author's opinion, this study suffers from a severe methodological mistake; namely, the statistical comparison should have been between normal, resting decreases in BA levels and those observed with the administered exercise protocols over time. Instead, this study compares only pre and post exercise. Reports of resting alcohol metabolism from literature, range from 12.1 to 26.0 mg%/hr.[49] Adjusted for a 10 minute time frame equal to the exercise protocols of this study, these equate to 2.0 and 4.3 mg%/10 min. The mean fall observed in this study (19.5 mg%/10 min) would indeed appear to be significant. Even if

significance were shown, this author would tend to question the extrapolation of these findings since such a small time period (10 minutes) was examined in relation to the total BAC. The minimum and maximum workloads used in this study correspond to 15.4 and 30.8 ml/mg/min VO_2, assuming average subject weight of 70 kg. If, as Ellestad[50] states, average male VO_2 max. equals 42 ml/kg/min, these workloads represent 36.7 and 73.3% of VO_2 max. The latter would certainly be of sufficient intensity to increase rate of alcohol disappearance if activity is a factor.

With respect to the findings of Schurch et al., this author can only repeat that data did not provide sufficient information to enable a determination of the exact rates of ethanol elimination or statistical tests employed. Additionally, it made no attempt to determine the effect upon peak BA concentration.

Kulling's study is interesting since it shows a great decrease in peak BA level in response to exercise at 50% of VO_2 max. with little change in the rate of elimination from blood in mg%/hr. The number of subjects was far too few to permit meaningful statistical analysis.

Summary

Plausible explanations to account for mechanisms by which alcohol is removed from blood are basically two fold: (1) use as a fuel substrate (acetic acid) in the Krebs Cycle to support cellular metabolism; and (2) elimination through expired breath, urine and perspiration in an unchanged state.

Studies attempting to compare sex and age with alcohol metabolism are fairly consistent in showing females and the aged reaching higher

peak BA levels and reaching them more quickly than their male and more youthful counterparts, even with weight adjusted doses. Since a lean person has more body water per kg of body weight than a less lean person, body compositional differences may account for most, if not all, of these observed differences.

Racial studies include so many uncontrolled variables and produce such a wide range of conflicting findings, that generalizations of results is virtually impossible.

Studies comparing individuals with high comsumption rates (alcoholics) and low consumption rates (non-alcoholics) are mixed with respect to findings. Difficulties exist here since chronic alcoholics almost always possess some degree of liver function impairment. If alcoholics do metabolize alcohol more rapidly, it is almost certainly not the result of increased amounts or increased activity of LADH.

Studies attempting to show diurnal variation include so many uncontrolled variables and provide such small sample size as to make generalization of results impossible.

The effect of a food bolus in the stomach will decrease peak BA levels; increase the time required to reach peak BA levels; and result in a smaller area under the BAC. These findings are so well established as to be accepted as scientific principle.

The effect of exercise upon alcohol elimination receives mixed reviews with respect to scientific findings. The key here, however, appears to be the intensity at which the workload occurs and the measures employed to define elimination rates from the blood. Those with heavier workloads over extended time periods tend to show increased

elimination rates measured as mg%/hr. Very little work with respect to exercise effects upon peak BA levels are evidenced in literature.

ENDNOTES

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CHAPTER III

METHODS AND PROCEDURES

Selection of Subjects

The subjects in this study were male volunteers from the school of Health Physical Education and Leisure Services at Oklahoma State University and from the Stillwater, Oklahoma, community. As a result, seven male students and one male businessman aged 22 to 39 ($\bar{x}$ = 27.9) were selected to constitute the eight volunteer subjects. The repeated measures, technical difficulty and expense associated with testing precluded a larger sample size. The following characteristics were verbally ascertained about each subject: (1) subject was in good health and free from disease, injury and infection; (2) subject was not taking any drug(s), prescription or otherwise, during nor within 12 weeks preceding testing; and (3) subject had not donated blood within 12 weeks preceding testing.

Personal Data Collected

Prior to testing, each subject was required to read and sign an informed consent form which detailed the procedures, possible risks and discomforts associated with testing. A copy of this form is found on page 79 in the appendix. Each subject was questioned to collect data concerning age and drinking history while the variables of height, weight

and VO_2 max., were determined prior to testing. The results are depicted on page 82 in the appendix.

Experimental Design

The experimental design utilized for this study employed a multiple group methodology with the injection of three different but closely related, experimental variables or treatments administered in a Latin squares arrangement. Approximately one week prior to testing each subject reported to the Exercise Physiology Laboratory at Oklahoma State University in tennis shoes, shorts and sweat shirt for the purpose of determining VO_2 max. This determination was accomplished by administering a Balke Treadmill Stress Test utilizing a motorized treadmill. (Quinton model 72-24, Quinton Instruments, Inc., Seattle, Washington.)

The treadmill was calibrated at 3.4 miles per hour and the grade was increased from zero to two percent at the end of the first minute and an additional percent at the end of each additional minute. Each subject's heart rate and EKG were continuously monitored and blood pressure was determined at five minute intervals throughout testing. The test continued until each subject reached a voluntary maximum workload and predicted VO_2 max., in ml/kg/min was determined from the corresponding treadmill elevation and speed using conversion equations.[1] The final treadmill elevation was checked using a square and level.

After determination of VO_2 max., each subject returned to the Exercise Physiology Laboratory on four additional occasions, with approximately one week between each visit. During each of these four visits each subject arrived after having fasted for ten hours. At the beginning of each of these four sessions, each subject had a 20 gauge by

1¼ inch indwelling venous catheter with a heparin lock flush cap unit (Angiocath by Dessert Medical Inc., model no. 2878, Sandy, Utah) inserted into a forearm vein and affixed to the forearm using surgical tape. The venipuncture site was disinfected using a betadine, non-alcoholic antiseptic solution. One ml-10 USP units of heparin flush (Wyeth Laboratories, Inc., no. 0008-0523-01, Philadelphia, PA) was immediately injected into the cap unit to prevent coagulation of blood at the venous catheter site.

Each subject then consumed, within a 20 to 30 minute period, the equivalent of 0.8 gm of pure ethanol per kg of body weight by drinking a 10% mixture of 95% ethanol in cranberry juice. The 0.8 gm/kg dose was selected since this is the minimum dose to insure the attainment of the legal intoxication level in blood of 100 mg%.[2] The legal intoxication level was selected because it would insure a sufficient blood concentration to enable comparative study of ethanol elimination rates over several hours yet not present a danger of toxicity in the subjects. The 10% mixture was chosen for the following reasons: (1) Five of the eight subjects drank only rarely and it was felt the large amount of non-alcoholic dilutant would minimize the possibility of nausea. This was important since vomiting prior to complete absorption can influence blood alcohol levels.[3] (2) The large amount of non-alcoholic dilutant tended to minimize the possibility of dehydration during the exercise protocols. (3) Finally, a study investigating the effect of dose dilution and rate of ingestion found that neither exerts a significant influence on peak BA levels or the times in which they are reached.[4] A table depicting the amount of 95% ethanol and dilutant

cranberry juice consumed by each subject during each of the four experiments is contained on page 83 of the appendix.

Blood samples were withdrawn from the venous catheter each half hour after alcohol consumption, for a period encompassing three hours, for the purpose of constructing a BA curve. Each blood sample collection procedure proceeded as follows: (1) The catheter hub was disinfected using the non-alcoholic betadine solution. (2) Two ml of blood was collected using a three ml disposable plastic syringe with disposable 21 gauge, 1½ inch needle. This sample was discarded since it would be diluted with heparin previously injected to prevent coagulation of blood at the venipuncture site. (3) A five ml blood sample to be used for testing was withdrawn using a Vacutainer hub with 20 gauge, 1½ inch disposable needle and a seven ml gray top Vacutainer tube containing 14 mg of potassium oxalate and 17.5 mg of sodium floride. (Beckton Dickinson Co., Rutherford, N.J., tube no. 6470.) (4) One ml-10 USP units of heparin was injected through the catheter cap to prevent blood coagulation until the next sample was withdrawn.

This alcohol ingestion and blood collection procedure was followed during each of the four protocols each subject completed in the exercise physiology laboratory. The only difference among the four visits was the amount of activity the subject was required to maintain during the three hours after alcohol ingestion. During one visit, each subject rested while activity levels corresponding to 15, 32.5 and 50% of VO_2 max., were maintained during the remaining three visits. The activity levels were administered among subjects in a counterbalanced order in a Latin squares design where subjects were considered as rows, order as columns and exercise intensities were the treatments. Two Latin squares were

constructed and run to provide eight measurements at each treatment level. Furthermore, as is the case in any Latin squares design, each treatment level must occur only once in each column and row of each square.[5] The counterbalanced results of this specified arrangement as depicted by Cochran and Cox,[6] are presented in Table I, page 42. The following example will be presented to assist the reader in interpreting Table I: Subject four of square one, rested during the three hours following his ingestion of alcohol during his first visit to the laboratory. The remaining three visits, approximately one week apart, found subject four walking the treadmill at exercise intensities corresponding to 50%, 15% and 32.5% of his VO_2 max., respectively, for the three hours following alcohol ingestion. The activity level was provided by the previously described Quinton motorized treadmill at grade and speed combinations corresponding to the appropriate VO_2 percentages of each subject as calculated from workload conversion formulae.[7] The exact speed and treadmill angle corresponding to each subject's workload is depicted on page 84 in the appendix. A treadmill speed of 3.4 miles per hour was chosen whenever possible as this represents an average walking pace, easily sustainable for prolonged periods.

The exercise administered was continuous for three hours following ingestion of alcohol, except a five minute break was necessitated each half hour for the collection of blood samples, urinary excretion and the drinking of water. Each subject was required to drink 2.5 ml of water per kg of body weight, each half hour after alcohol ingestion during each of the four visits to the laboratory, irrespective of activity level. The water was necessary to prevent dehydration at the higher activity levels and to insure continuity of experimental conditions at

TABLE I

LATIN SQUARES ARRANGEMENT OF SUBJECTS, ORDER AND TREATMENTS

	Order				
Subject	1	2	3	4	
1	15	32.5	R	50	
2	50	R	32.5	15	
3	32.5	15	50	R	Square I
4	R	50	15	32.5	

	Order				
Subject	1	2	3	4	
5	R	32.5	50	15	
6	50	15	R	32.5	
7	15	50	32.5	R	Square II
8	32.5	R	15	50	

Key: R = Rest

15 = 15%

32.5 = 32.5%

50 = 50%

VO_2 max.

lower activity levels. The record of water consumption per subject is presented on page 83 of the appendix. The 2.5 ml per kg figure was arrived at by averaging subjects voluntary liquid consumption during an earlier, similar test procedure.[8]

Clinical Laboratory Procedures

Each blood sample was centrifuged at 5,000 revolutions per minute for five minutes in a table top clinical centrifuge. (International Equipment Co. model # 428-17108, Needham, MA) This was accomplished immediately after the last blood sample was collected and total expired time between collection of first and final samples was 2½ hours. The supernatant plasma was aspirated using a disposable transfer pipete and pinch bulb and analyzed using a method first proposed by Horecker and Kornberg[9] and modified by the Sigma Chemical Company.[10] The Sigma procedure catalyzed the conversion of ethanol to acetaldehyde (ethanal) by introducing the plasma into specifically prepared vials containing LADH and NAD. The formation of acetaldehyde (ethanal) was favored because the plasma was diluted five fold using a glycine buffer which raised the pH to approximately nine. The increase in absorbance at 340 nanometers which occurred when NAD was converted to NADH was used to measure the amount of ethanol present.

When compared with a non-alcoholic blank and a calibration curve previously constructed using ethanol standards of 40, 80, 120 and 160 mg%, the absorbancy reading from each sample was immediately converted into a BA concentration expressed in mg%. The ethanol standards were supplied by the Sigma Chemical Co., P. O. Box 14508, St. Louis, Missouri.

The ethanol calibration curve developed and used for the Sigma procedure is reproduced on page 85 of the appendix.

The instrument used for measuring absorbancy was a Spectrophotometer (Spectronic 20, model no. 33.31.72, 340-960 nanometer light path, Bausch and Lomb, Inc., 1400 N. Goodman St., Rochester, New York). The sample was introduced into the Spectrophotometer by means of a 12 X 100 millimeter round cuvette (Fisher Scientific Co., no., F7-144-15, 4301 Alpha Road, Dallas, Texas).

All cuvettes and test tubes were kept tightly stoppered or covered with paraffin block strips as much as possible to prevent evaporation or contamination. Additionally, each set of absorbancy readings included a re-check of instrumentation and procedures by including two of the four ethanol standards with other plasma samples. Finally, approximately 1/3 of all samples (usually the highest and lowest of each subject trial) were double checked. Using this procedure, a coefficient of correlation (r) of 0.998 was obtained by the Sigma Chemical Company when comparing 47 samples of plasma, serum and blood with a gas chromatographic method.[11] The BA concentration results will be presented in Chapter IV of this dissertation.

Analysis of Data

The data thus collected were analyzed to determine possible differences between BA curves, specifically differences between peak BA levels and rates of alcohol elimination from the blood. This was accomplished using a Latin squares Analysis of Variance (ANOVA) format where subjects were considered as rows, order as columns and exercise intensities (rest and 15%, 32.5% and 50% of VO_2 max.) as the treat-

ments at column and row intersections. Two Latin squares were constructed and statistically combined thus permitting eight measurements of each treatment level. This design also permitted each subject to serve as his own control.

The primary reason for the use of a Latin squares design was to incorporate order, as well as subjects and treatments, as a variable for analysis. The author felt this necessary since the possibility of a non-cognitive learning effect associated with each subject's multiple participation, was highly likely. Some of the plausible learning effects and their possible influence follow: (1) The process of subjecting non-drinkers to four, weekly intoxicating alcohol doses could conceivably increase their hepatic enzyme system efficiency. This could manifest itself in lower peak BA levels and/or increased rates of alcohol elimination from the blood toward the latter part of their participation schedule. (2) The process of subjecting non-drinkers to intoxicating alcohol doses on four successive weeks could conceivably cause an increase in motor skill coordination while in an intoxicated state. This means it could become progressively easier to walk a motorized treadmill toward the end of their weekly participation schedule. This could mean a reduction of required effort and a possible increase in peak BA levels and/or decrease in the rate of alcohol elimination from the blood. (3) The practice of collecting approximately 50 ml of blood during each of the four weekly visits to the lab, could result in hemodilution toward the end of the participation schedule. Hemodilution would decrease blood viscosity and increase blood flow rate or velocity past any given point in the circulatory system. Increased blood velocity through the liver could result in less contact time between alcohol and

enzyme systems with a possible increase in peak BA levels and/or a reduction in the rate of alcohol elimination from the blood. Therefore, the three "learning" factors discussed could have compound, multiple effects on the BA curve.

Having established the Latin squares, the following data were used: (1) The highest observed peak BA level per subject per treatment, irrespective of the time period in which it occurred. (2) A calculated BA level at time zero (C_0) obtained by constructing a least squares regression line using the highest observed value and all values following in time. This line was then extrapolated until it intersected the Y ordinate (time zero) as mentioned by Wilkinson.[12] The value at the Y intersection represented C_0. This value could prove beneficial since continuous blood sampling was not feasible and one can never be sure observed peak levels represented actual peak levels. If the observed levels are not representative of actual peak levels, C_0 may assist in this determination. (3) The rate of alcohol elimination from blood was determined using a method employed by Makoid.[13] The procedure used the same regression line calculated for C_0 and the resultant slope converted to depict elimination rate in mg% per hour (mg%/hour).

Subjects, order and treatments were tested for significance at the 0.05 level, although the area of primary interest was obviously treatments. Order was tested to confirm or deny possible extraneous variation attributable to the "learning" effect and adjudge justification for the Latin squares design. Additionally, treatments were partitioned into linear, quadratic and cubic components for purposes of evaluating significance.

ENDNOTES

[1]Lea and Febiger, Guidelines for Graded Exercise Testing and Exercise Prescription (Philadephia, PA, 1980), pp. 138-141.

[2]Kurt M. Dubowski, "Human Pharmacokinetics of Ethanol: Peak Blood Concentration and Elimination in Male and Female Subjects," Alcohol Technical Reports, Vol. 5, No. 4 (April, 1976), p. 55.

[3]H. Joachim et al., "Studies on the Effect of Vomiting on the Blood Alcohol Curve by Means of Continuous Blood Alcohol Determinations," Blutalkohol, Vol. 11, No. 1 (Jan., 1974), pp. 88-89.

[4]Brian O'Neill, "Variability in Blood Alcohol Concentrations," Journal of Studies on Alcohol, Vol. 44, No. 2 (Mar., 1983), pp. 222-230.

[5]K.A. Brownlee, Statistical Theory and Methodology in Science and Engineering (New York, NY, 1960), p. 513.

[6]Cochran and Cox, Experimental Designs (New York, NY, 1957), p. 146.

[7]Lea and Febiger, pp. 138-141.

[8]Frank Kulling, "The Effect of Physical Exercise at 50% VO_2 max. on the Blood Ethanol Curves of Two Men," (Unpublished paper presented to Dr. Aix B. Harrison, School of HPELS, Oklahoma State University, 1983), pp. 1-16.

[9]B.L. Horecker and Arthur Kornberg, "The Extinction of Coefficients of the Reduced Band of Pyridine Nucleotides," Journal of Biological Chemistry, Vol. 175, No. 1 (Aug.-Sept., 1948), pp. 385-390.

[10]Sigma Chemical Co., "The Quantitative Ultraviolet Enzymatic Determination of Ethyl Alcohol in Blood Serum on Plasma," Sigma Technical Bulletin, No. 332-UV (Apr., 1982), pp. 1-22.

[11]Ibid., p. 12.

[12]Paul K. Wilkinson, "Pharmacokinetics of Ethanol: A Review," Alcoholism: Clinical and Experimental Research, Vol. 4, No. 1 (Jan., 1980), p. 7.

[13]Michael E. Makoid et al., "Elimination of Alcohol from Human Blood," Journal of Pharmaceutical Sciences, Vol. 65, No. 1 (Jan., 1976), p. 152.

CHAPTER IV

ANALYSIS OF DATA AND DISCUSSION OF RESULTS

The purpose of this study was to determine if there was a difference between male BA curves during rest and three hours of sustained exercise at 15%, 32.5% and 50% VO_2 max. Since the peak BA value and rate of elimination or disappearance from blood are two of the more important components of the BA curve, possible differences in these areas constituted the focus of this analysis. As previously mentioned, this experimental design was constructed using a Latin squares format where subjects were considered as rows, order as columns and intensities of exercise as treatments. Two Latin squares were constructed and run to provide eight measurements at each treatment level.

Results of Blood Alcohol Analysis

The results of the blood alcohol analysis by subject and treatment for each collection period and for each of the two Latin squares are depicted in Tables II and III on pages 49 and 50, respectively. Even though the treatments were administered by subjects in the counterbalanced order as indicated in Table I, they are depicted in progressive order, from lowest to highest, in Tables II and III for benefit of the reader.

It will be recalled that the ethanol dose of 0.8 gm/kg of body weight was designed to enable subjects to reach the legal intoxication

TABLE II

ALCOHOL VALUES (MG%) RESULTING FROM
ANALYSIS OF BLOOD SAMPLES
(LATIN SQUARE I)

Subject	Treatment	Time in Hours						Peak
	% VO_2 max.	0.5	1.0	1.5	2.0	2.5	3.0	Value
1	R	105.0	95.0	87.5	85.0	72.5	67.5	105.0
	15	100.0	95.0	87.5	82.5	72.5	57.5	100.0
	32.5	95.0	90.0	87.5	70.0	65.0	55.0	95.0
	50	85.0	77.5	70.0	60.0	50.0	40.0	85.0
2	R	135.0	117.5	95.0	87.5	82.5	80.0	135.0
	15	117.0	110.0	110.0	95.0	85.0	75.0	117.0
	32.5	117.5	110.0	95.0	82.5	82.0	67.5	117.5
	50	122.5	117.5	110.0	95.0	87.5	75.0	122.5
3	R	65.0	85.0	90.0	90.0	75.0	67.5	90.0
	15	95.0	107.5	100.0	87.5	87.5	80.0	107.5
	32.5	65.0	80.0	91.2	91.2	82.5	72.5	91.2
	50	62.5	70.0	70.5	67.5	65.0	57.5	70.5
4	R	110.0	115.0	95.0	85.0	80.0	72.5	115.0
	15	85.0	105.5	90.0	80.0	72.0	65.5	105.5
	32.5	105.0	87.5	85.0	85.0	75.0	67.5	105.0
	50	87.5	102.0	87.5	80.0	67.5	65.0	102.0

TABLE III

ALCOHOL VALUES (MG%) RESULTING FROM
ANALYSIS OF BLOOD SAMPLES
(LATIN SQUARE II)

Subject	Treatment	Time in Hours						Peak
	% VO_2 max.	0.5	1.0	1.5	2.0	2.5	3.0	Value
5	R	87.5	92.5	85.0	77.5	72.5	65.0	92.5
	15	85.0	90.0	80.0	70.0	67.5	60.0	90.0
	32.5	90.0	85.0	77.5	70.0	65.0	55.0	90.0
	50	110.0	95.0	82.5	65.0	57.5	50.0	110.0
6	R	90.0	110.0	100.0	87.5	85.0	70.0	110.0
	15	90.0	110.0	85.0	82.5	75.0	65.0	110.0
	32.5	67.5	85.0	80.0	70.0	62.5	52.5	85.0
	50	100.0	90.0	85.0	80.0	70.0	62.5	100.0
7	R	97.5	110.0	97.5	90.0	77.5	67.5	110.0
	15	72.5	105.0	100.0	95.0	85.0	80.0	105.0
	32.5	90.0	120.0	105.0	95.0	90.0	80.0	120.0
	50	82.5	117.0	110.0	100.0	95.0	75.0	117.0
8	R	120.0	110.0	97.5	87.5	80.0	77.5	120.0
	15	117.5	112.5	107.5	100.0	87.5	80.0	117.5
	32.5	110.0	107.5	97.5	90.0	77.5	70.0	110.0
	50	102.5	100.0	95.0	85.0	80.0	70.0	102.5

level of 100 mg%. The mean of the resting peak BA values of the eight subjects was 109.7 mg%; therefore, this criterion was reached. Additionally, one can see from an examination of Tables II and III that peak BA values, at rest, occurred at the 30 minute period three times, the 60 minute period four times and the 90 minute period once. The mean time to peak BA concentration at rest was 52.5 minutes, a time which agrees with the 51 minute figure found by O'Neill[1] in a study of 32 subjects which ingested the equivalent of 0.92 gm/kg of ethanol within 30 minutes.

The data contained in the two Latin squares of Tables II and III were used for the remainder of the analyses in this chapter. Specifically, the following areas were examined for possible differences: (1) the highest observed peak BA levels; (2) the peak BA levels as calculated at time zero; and (3) the rate of alcohol elimination from blood as an absolute (mg%/hour).

Latin Squares ANOVA of Highest Observed Blood Alcohol Level

The highest observed BA level, as the name implies, was the highest recorded concentration irrespective of the collection period in which it occurred. For the Latin squares analysis, the data were arranged in the order as specified in Table I. From an examination of Tables II and III, it can be seen that the highest observed peak BA level occurred 16 times at the 30 minute period, 13 times at the 60 minute period and three times at the 90 minute period.

The means of the highest observed peak BA levels, by treatments and Latin squares, are depicted in Table IV on page 52. All figures were rounded to two decimal places. The Latin squares ANOVA by the Statisti-

TABLE IV

MEANS OF THE HIGHEST OBSERVED PEAK BLOOD ALCOHOL LEVELS BY SQUARE AND TREATMENT

Treatment	Blood Alcohol Level (MG%)		
% VO_2 max.	Square I	Square II	Both Squares
Rest	111.25	108.12	109.69
15.0%	107.50	105.62	106.56
32.5%	102.18	101.25	101.71
50.0%	95.00	107.38	101.19

cal Analysis System for the highest observed peak BA levels is presented in Table V, on page 54. An examination of Table V reveals a highly significant source of intersubject (Subj in SQ) variation. This was expected due to differences in body composition, drinking histories and possible differences in the rate of liver enzyme activity. Also there was a significant variation due to order, as was anticipated in Chapter III. To better analyze this source of variation, Table VI on page 55 depicts the means of the highest observed peak BA level by order and Latin squares.

An analysis of Table VI revealed that with respect to order, subjects realized their highest observed peak BA values somewhere in the middle of their four participative visits to the laboratory while the first and last visits produced the lowest peak values. Furthermore, the last of the four involvements produced the lowest peak value. Although this author cannot know for certain the exact causes of this variation, some speculation based upon previously explained reasons for including order as a variable are required. Since each blood sample collected required approximately seven ml of blood, each subject would lose approximately 50 ml of blood during each visit to the lab. Even though the liquid portion of the blood withdrawn would certainly be replaced by subsequent visits one week apart, cellular elements almost certainly would not be. This could result in a slight hemodilution with decrease in blood viscosity and increase in blood flow rate or velocity past any given point. Assuming this to be the case for hepatic blood flow, less alcohol would contact the coenzyme NAD and more alcohol would be unchanged, circulating in the bloodstream. Additionally, each subject could be expected to gain proficiency in walking the treadmill in an

TABLE V

LATIN SQUARES ANOVA FOR THE HIGHEST OBSERVED PEAK BLOOD ALCOHOL LEVELS

Source	DF	SS	MS	F	P > F
SQ	1	20.80	20.80	--	
Subj in SQ	6	3407.04	567.84	14.83	0.00*
Order	3	583.92	194.64	5.08	0.02*
SQ by Order	3	482.57	160.86	--	
TRT	3	396.61	132.20	3.45	0.05*
(a) Linear	(1)	(365.45)	(365.45)	9.55	0.01*
(b) Quadratic	(1)	(20.24)	(20.24)	0.53	0.48
(c) Cubic	(1)	(10.92)	(10.92)	0.28	0.60
SQ by TRT	3	313.75	104.58	--	
Error	12	459.30	38.28		
Total	31	5663.99			

Key: SQ = Square

Subj = Subject

TRT = Treatment

* = Significance at 0.05 Level

TABLE VI

MEANS OF THE HIGHEST OBSERVED PEAK
BLOOD ALCOHOL LEVELS BY
ORDER AND SQUARE

Order	Blood Alcohol Level (MG%)		
	Square I	Square II	Both Squares
1	107.18	101.88	104.53
2	109.88	109.25	109.56
3	99.62	114.38	107.00
4	99.25	96.88	98.06

intoxicated state; therefore, less energy would be expended during subsequent walking protocols. These reasons could explain the increase observed past the first order, however it does not explain the decrease again during the fourth order. This could be explained by an increase in hepatic enzyme efficiency as a result of non-drinkers being subjected to intoxicating drinking bouts on four successive weeks. Such an increase in enzyme efficiency would probably involve some mechanism whereby NADH was more rapidly re-converted back to the active coenzyme NAD.[2]

Having identified order as a significant source of variation which would otherwise confound any inherent variability due to treatments, order variability can be removed from the order term as accomplished in the statistical Latin squares procedure depicted in Table V. Doing so showed treatments to be significant at the 0.05 level if results are rounded off to two decimal places. If results were carried to four decimal places, the $P > F$ value became 0.0509 and was not significant. The above argument becomes academic, however, when the three degrees of freedom associated with treatments are partitioned into linear, quadratic and cubic components, with one degree of freedom each, in a procedure as specified by Brownlee.[3]

Using this linear analysis and the results depicted in Table V, it can be seen that some 365 of the 397 sums of squares were due to a linear relationship, virtually ruling out any quadratic or cubic tendencies. Therefore, the means of the highest observed peak BA levels by treatment (Table IV) had a highly significant ($p < .01$) linear relationship with a non-zero slope. Using this information and Table IV, it can be said that if blood samples are collected each 30 minutes after ingesting an intoxicating alcohol dose, the highest observed peak BA level signi-

ficantly declined in conjunction with each increase in exercise intensity ranging from 15% to 50% of VO_2 max., if exercise is begun immediately after alcohol ingestion and continued until the peak value is observed.

As a result of consulting with colleagues, this author feels that some may view the utilization of a Latin squares design as nothing more than an attempt to reduce the error term, thereby increasing the F value and the probability of significance. To these critics, this author would say that the possible sources of variation were stipulated before statistical analysis; therefore, if these additional sources did not contain significant amounts of variation, nothing would have been gained since degrees of freedom had been lost. As an example, the degrees of freedom permitted by the present design for treatments and error were three and 12 respectively. Using a simple repeated measure ANOVA without considering order as a variable, the same degrees of freedom would be three and 21 respectively. The Latin squares design is beneficial, with respect to proving significance, only if the additional considered sources of variation offset the loss of degrees of freedom.

Latin Squares ANOVA of Blood Alcohol Levels at Time Zero

The BA level at time zero represents the theoretical concentration which would occur in the blood if the entire ethanol dose could immediately be present in the bloodstream.[4] It was constructed by calculating a least squares line from the post-absorptive or downward sloping blood concentrations observed and extrapolating the line until it intersected the Y ordinate representing time.[5] Obviously, such a value could not be

physically obtained since instantaneous infusion or absorption is impossible; however, this does not mean the value is without merit. Blood alcohol concentration at time zero (C_0) may be beneficial in making peak BA comparisons because continuous sampling is not feasible and one can never be sure an observed level actually represents the maximum or peak concentration.

The means of the calculated C_0 levels by treatments and Latin squares, is depicted in Table VII on page 59. Each of the 32 C_0 levels was calculated as previously explained. The Latin squares ANOVA by the Statistical Analysis System for the C_0 BA levels is depicted in Table VIII on page 60. From Table VIII, it can be seen that, again, there was significant intersubject variation; however, there was not a significant order effect. This was not totally unexpected since the C_0 value is the extrapolation of a line fitted about multiple observation points and multiple observations over time will be less likely to be influenced by extraneous variables.

Again, when three degrees of freedom associated with treatments are divided into linear, quadratic and cubic components, a high degree of significance ($p < 0.02$) is associated with the linear component. The conclusion would be exactly the same as that reached for the highest observed peak BA level; namely, that C_0 significantly declined in response to each increase in exercise intensity ranging from 15% to 50% of VO_2 max., if begun immediately after ingestion of an intoxicating alcohol dose and continued for three hours.

TABLE VII

MEANS OF THE CALCULATED C_0 BLOOD ALCOHOL LEVELS BY TREATMENT AND SQUARE

Treatment	Calculated C_0 Levels (MG%)		
% VO_2 max.	Square I	Square II	Both Squares
Rest	128.19	122.79	125.49
15.0%	120.24	118.21	119.22
32.5%	117.22	114.71	115.96
50.0%	108.20	119.29	113.74

TABLE VIII

LATIN SQUARES ANOVA FOR THE C_0 CALCULATED BLOOD ALCOHOL LEVELS

Source	DF	SS	MS	F	P > F
SQ	1	0.66	0.66	--	
Subj in SQ	6	2725.41	454.24	5.29	0.01*
Order	3	232.53	77.51	0.90	0.53
SQ by Order	3	955.46	318.49	--	
TRT	3	625.92	208.64	2.43	0.11
(a) Linear	(1)	(581.71)	(581.71)	6.78	0.02*
(b) Quadratic	(1)	(41.41)	(41.41)	0.48	0.50
(c) Cubic	(1)	(3.80)	(3.80)	0.04	0.84
SQ by TRT	3	324.51	108.17	--	
Error	12	1030.24	85.85		
Total	31	5894.73			

Key: SQ = Square

Subj = Subject

TRT = Treatment

* = Significance at 0.05 Level

Latin Squares ANOVA of Rate of Alcohol Elimination from Blood

The rate at which alcohol is eliminated from the blood is one of the most important characteristics of the BA curve. It will be recalled from Chapter II that numerous studies purported to show differences in this rate of elimination resulting from race, sex and exercise. A common way of determining the rate of elimination is to construct a least squares line using the observations corresponding to and following the peak BA concentrations and calculating the resultant rate in mg% per hour.[6] The means of the elimination rates by treatments and Latin squares, is presented in Table IX, page 62. The resting elimination rate of 18.84 mg%/hour, agreed well with the 12.06 to 22.2 mg%/hour findings of other researchers.[7]

The Latin squares ANOVA by the Statistical Analysis System for the alcohol elimination rates from blood in mg%/hour is portrayed in Table X, page 63. A cursory examination of this table revealed a lack of statistical significance among source measures. Even the intersubject variation was minimal. This indicated that alcohol elimination rates from blood among the subjects was remarkably consistent and unchanging irrespective of changes in exercise intensity. Additionally, order apparently had no affect in bringing about elimination rate changes.

This finding may be somewhat surprising to some since the end product of alcohol metabolism, acetic acid, could conceivably be utilized in the production of energy to meet active cellular demands imposed by exercise. One would expect this to be especially the case when subjects were fasting and competing food substrates were at their lowest levels in circulating blood. Certainly the highest exercise

TABLE IX

MEANS OF THE ALCOHOL ELIMINATION RATES
FROM BLOOD BY TREATMENT AND SQUARE

Treatment	Alcohol Elimination Rates from Blood (MG%/hr)		
% VO_2 max.	Square I	Square II	Both Squares
Rest	19.84	17.84	18.84
15.0%	16.63	15.73	16.18
32.5%	17.02	16.59	16.80
50.0%	16.20	18.02	17.11

TABLE X

LATIN SQUARES ANOVA FOR THE ALCOHOL ELIMINATION RATES FROM BLOOD

Source	DF	SS	MS	F	P > F
SQ	1	1.14	1.14	--	
Subj in SQ	6	47.76	7.96	0.48	0.76
Order	3	7.78	2.59	0.16	0.92
SQ by Order	3	67.39	22.46	--	
TRT	3	31.07	10.36	0.62	0.62
(a) Linear	(1)	(7.33)	(7.33)	0.44	0.52
(b) Quadratic	(1)	(17.29)	(17.29)	1.04	0.33
(c) Cubic	(1)	(6.45)	(6.45)	0.39	0.54
SQ by TRT	3	15.46	5.15	--	
Error	12	199.34	16.61		
Total	31	369.94			

Key: SQ = Square

Subj = Subject

TRT = Treatment

intensity (50% VO_2 max.) used in this study was sufficient to demand increased oxidation of available, suitable food substrate to fuel the additional metabolic demand imposed. One can only conclude from these results that ethanol was not a significant energy source available for muscle work.

Summary

The eight male volunteer subjects participating in this study reported to the Oklahoma State University Exercise Physiology Laboratory on four separate occasions, approximately one week apart. No more than two subjects were present during any given testing session. Subjects reported in a 10 hour fasting condition and were required to consume within 30 minutes a 10% ethanol-cranberry juice mixture equal to 0.8 gm of pure ethanol per kg of body weight. Immediately upon completion of alcohol ingestion, subjects were required to complete treatments consisting of rest and exercise corresponding to 15%, 32.5% and 50% of VO_2 max. for a period of three hours with five minute breaks each 30 minutes. Subjects completed a specific, different treatment during each of the four visits. The order of treatment administration was counter-balanced according to a Latin squares design. Exercise treatments were administered using a motorized treadmill and varying combination of speed and grade inclination. Rest was restricted to the laboratory where subjects usually remained seated.

Blood samples were collected from an indwelling venous catheter each 30 minutes. When all six blood samples had been collected from a subject during a visit, samples were centrifuged and the supernatant plasma analyzed for alcohol concentration. The method of analysis

consisted of photometrically measuring the increase in light absorbancy at 340 nanometers wavelength, caused by the reduction of NAD to NADH. Results were derived by plotting readings against a calibration curve constructed from commercially prepared ethanol standards.

The resultant figures were analyzed using a Latin squares design where subjects were rows, order was columns and treatments the levels of exercise at row and column intersections. Two squares of four subjects each were run and combined using the Statistical Analysis System. The design permitted each subject to serve as his own control. The data were analyzed to investigate possible differences between: (1) Highest observed peak BA levels (mg%); (2) calculated peak BA levels extrapolated backwards to time zero; and (3) rates of alcohol elimination from the blood (mg%/hour).

The Latin squares ANOVA results revealed the following: (1) There was a significant difference between highest observed peak BA concentrations associated with treatment levels ($p = .05$). (2) When total treatment effect was partitioned into linear, quadratic and cubic components, the linear component of the highest observed peak BA level was highly significant ($p < .01$) indicating a significant, non-zero slope representing the least squares line constructed from treatment means. (3) The order effect associated with highest observed peak BA level was significant ($p < .02$) indicating considerable variation due to a non-cognitive "learning" effect. (4) There was a significant amount of intersubject variability ($p < .001$) associated with the highest observed peak BA levels. (5) When total treatment effect for the calculated peak BA level at time zero (C_0) was partitioned into linear, quadratic and cubic components, the linear component was significant

($p < .02$). (6) There was a significant amount of intersubject variability ($p < .01$) associated with calculated peak BA level at time zero (C_0). (7) The rate of elimination of alcohol from blood was remarkably consistent and failed to show any significant differences due to intersubject, order or treatment variability.

The above data can be interpreted as follows: (1) Exercise initiated immediately after the consumption of a minimally intoxicating dose of alcohol and continued at least until the peak value is observed, will result in a significant linear reduction of the observed peak level at each intensity ranging from 15% through 50% of VO_2 max. (2) Non-cognitive "learning" effects associated with each subject serving as his own control and repeating the experiment on four successive, weekly occasions will cause the introduction of significant variation not directly related to the treatments. Speculation concerning the "learning" effects might include increased motor proficiency in an intoxicated condition, accumulative reduction in blood viscosity due to repeated blood samplings over four weeks and increased efficiency of the hepatic enzyme system resulting from repeated exposure to intoxicating alcohol dosages among non-drinkers. (3) Exercise initiated immediately after the consumption of a minimally intoxicating dose of alcohol and continued for three hours, will result in a significant linear reduction of the calculated C_0 BA level at each intensity ranging from 15% through 50% of VO_2 max. (4) The rate of alcohol elimination from blood was consistent among subjects, order and treatments with no significant differences evidenced.

In the final analysis, all testing and findings can be summarized as follows: (1) Exercise as specified and administered will cause signi-

ficant reductions in peak blood alcohol levels, whether observed or linearly extrapolated from observations, and will do so progressively at each intensity ranging from 15% through 50% of VO_2 max. (2) One can expect non-cognitive "learning" effects to contribute significant extraneous variation which if not accounted for, will tend to reduce or eliminate the significance previously discussed. (3) There was significant intersubject variability associated with observing peak BA levels as collected each 30 minutes, even with weight equilibrated dosages. (4) There was not a significant difference in alcohol elimination rates with respect to the tested subjects, order or exercise intensities.

Therefore, changes in the BA curve as the result of exercise will be manifested as a result of decreased peak BA values with no change in the rate of elimination from blood. Additionally, it can be extrapolated that the above findings will result in a decreased area under the BA curve and a reduced time to a zero BA level as a result of exercise injection ranging from 15% to 50% of VO_2 max. The author feels this is caused by reduced blood flow to the gut as microcirculatory components of active muscle tissue vasodilate in response to exercise. Therefore, the reduced blood flow slows the rate of alcohol absorption into the bloodstream and increases the efficiency of the liver by reducing enzyme over saturation.

From a practical point of view, an individual desiring to minimize his or her BA level after imbibing in alcoholic beverages, would be advised to remain as active as possible during and for at least 90 minutes after drinking. It is unlikely that an individual would remain active at intensities equalling 50% of VO_2 max., especially indoors. However, even minimal activity such as continuous walking would achieve

the following: (1) Reduce the peak BA level. (2) Reduce the post-absorptive BA level at any given point in time. (3) Reduce the time required to totally eliminate alcohol from the blood. The more continuously active the individual, the more pronounced the effects just mentioned. Since this study only used fasting subjects, the same cannot be said with certainty for subjects having a food bolus in the stomach.

FOOTNOTES

[1]Brian O'Neill et al., "Variability in Blood Alcohol Concentrations: Implications for Estimating Individual Results," Journal of Studies on Alcohol, Vol. 44, No. 2 (Mar., 1983), pp. 222-230.

[2]Henrik Wallgren and Herbert Barry III, Actions of Alcohol: Biochemical, Physiological and Psychological Aspects (New York, NY, 1970), p. 83.

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[4]Kurt M. Dubowski, "Human Pharmacokinetics of Alcohol: Peak Blood Concentrations and Elimination in Male and Female Subjects," Alcohol Technical Reports, Vol. 5, No. 4 (April, 1976), p. 56.

[5]Paul K. Wilkinson, "Pharmacokinetics of Ethanol: A Review," Alcoholism: Clinical and Experimental Research, Vol. 4, No. 1 (Jan., 1980), p. 7.

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CHAPTER V

CONCLUSIONS AND RECOMMENDATIONS

Conclusions

The purpose of this study was to determine the effect of physical exercise at varying intensities on the blood ethanol curve. The results of the Latin squares, repeated measures ANOVA permit statement of the following conclusions:

1. The null hypothesis stating there would not be a significant difference among the peak BA concentrations at rest, 15%, 32.5% and 50% of VO_2 max., was rejected.

2. The null hypothesis stating there would not be a significant difference among the post absorptive BA elimination rates at rest, 15%, 32.5% and 50% of VO_2 max., was accepted.

3. The introduction of exercise ranging from 15% through 50% of VO_2 max. immediately after alcohol ingestion and continued until an observed peak value is reached, resulted in significant, progressive reductions of the observed peak levels at a specific reference time at each of the exercise intensities.

4. The introduction of exercise ranging from 15% through 50% of VO_2 max. immediately after alcohol ingestion and continued for three hours, resulted in significant, progressive reductions of C_0 at each of the exercise intensities.

5. In the subjects of this study, the introduction of exercise ranging from 15% through 50% of VO_2 max. immediately after alcohol ingestion and continued for at least 90 minutes, will result in a reduced time to zero BA level and reductions in the area under the BA curve associated at each of the exercise intensities.

Recommendations

The experience gained by this author would lead to the following recommendations concerning this and possible future studies:

1. Observations directed to discovering the peak BA level should emphasize an increase in blood sampling between zero and 90 minutes post ingestion. This study included only three blood samples (30, 60 and 90 minutes) during this time frame. Since continuous blood sampling is not physiologically feasible, an alternative might be to incorporate Breathalyzer tests each 10 minutes and establish a correlation equation between Breathalyzer and blood tests to permit incorporation of results collected via two different methods and two different sample mediums.

2. Observations directed to discovering the rate of alcohol elimination from blood could proceed more uniformly if ethanol were infused intravenously until a given, similar level were reached during each experiment and then measuring elimination rates from this same peak. The peak level could be ascertained from Breathalyzer readings; however, ethanol infusion would require the services of a licensed anaesthesiologist.

3. It was obvious from the large intersubject variation inherent in the measures tested, that weight equilibrated alcohol doses (mg/kg) do not insure uniformity of blood alcohol concentration. Incorporation

of body composition measures (percent body fat) could help reduce this variation in two possible ways: (1) dosages could be based on lean body weight instead of total body weight, or (2) measures derived from total body weight dosages could be mathematically adjusted after the fact.

4. The large order or "learning" variation could possibly have been reduced by increasing the time between administration of treatments. Another possibility would be to include only subjects who are "moderate" drinkers and therefore, less susceptible to the possible accumulative effects of repeated testing. Obviously, some combination of increased time and "experienced" drinkers would also be worthy of investigation.

5. This study was accomplished by testing subjects in a ten hour fasting state. It would be interesting to determine if similar results could be obtained with subjects containing a food bolus in the stomach.

6. Much literature makes mention of differences in peak BA levels and rates of elimination between races, the sexes, and the young and the aged. A study or studies incorporating equilibrated lean body weight ethanol dosages would be beneficial in resolving the nature of such possible differences.

7. Although it was not the intended purpose of this work, some doubt concerning the use of alcohol as an energy source for muscle work has been raised. Carbon labeled ethanol studies (in vivo) incorporating muscle biopsies might be beneficial in resolving this issue. Such studies should be done in both fasting and fed states.

8. Although it was not a stated purpose of this work, an investigation of the effect of exercise on the temporal occurrence of the peak

BA concentration would be worthwhile. Again, more frequent sampling between the zero and 90 minute post-ingestion period would be required.

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APPENDIX

INFORMED CONSENT FORM

SUBJECTS NAME: _____ DATE: _____

I hereby authorize Frank A. Kulling and/or such assistants as may be selected by him to perform the following procedures and investigation:

(1) A labortory physical fitness evaluation including electrocardiogram and a treadmill stress test to predict maximum oxygen intake capacity (VO_2 max.).

(2) Administration of an alcoholic beverage in amounts designed to attain the legal intoxication level (0.01% W/V). This will be accomplished on four separate occasions, approximately one week apart.

(3) Collection of approximately 7 ml of blood from a fixed venous catheter, each 30 minutes for a period not to exceed three hours, for the purpose of determining blood alcohol levels in the construction of a blood alcohol curve. This will be accomplished on four separate occasions, approximately one week apart in conjunction with activity levels corresponding to rest and 15%, 32.5% and 50% of VO_2 max. as determined in step (1) above. Exercise sessions will begin immediately after alcohol ingestion and continue throughout the three hour period with 5 minute breaks each half hour.

I understand the procedures and investigation involve the following possible risks and discomfort:

(1) The treadmill stress test will be physically demanding and will continue to physical exhaustion unless other symptoms dictate early termination.

(2) Insertion of the venous catheter may cause some pain. The exact amount, if any, will be dependent upon individual pain threshold levels.

(3) Consumption of the alcoholic beverage will cause some degree of temporary impairment with respect to coordination and reaction times. The exact level and duration will vary widely among individuals as will possible side effects.

Every attempt will be made to insure return to an acceptable level of coordination and reaction before release from the lab. This may necessitate staying more than the three hours required for experimentation. When released from the lab, even though coordination and reactions may be "normal", the subject is advised to refrain from engaging in potentially dangerous or risky activities such as driving, operating machinery, etc., for an additional 12 hours.

All test/experiment records are subject to publication in the form of research findings; however, such data will be identified by number and not name.

I also agree not to hold Frank A. Kulling nor any of his assistants nor Oklahoma State University and its officers and employees liable for any sickness(es), accident(s), or injury (injuries) that may occur to me or others as a result of these procedures and this experiment. I have

read and understand to my satisfaction, all three pages of this informed consent form and voluntarily accept the risks and responsibilities stated herein.

SIGNED: _____ WITNESSED: _____

TABLE XII

SUBJECT DATA

Subject	Age	Weight (KG)	Height (CM)	VO_2 max. (ML/KG/MIN)	Alcohol Consumption* (Drinks per week)
1	23	57.7	179	50.3	< 3
2	39	82.3	177	43.7	5
3	26	79.5	178	47.0	< 3
4	22	83.6	184	47.0	< 3
5	27	78.2	181	66.6	< 3
6	23	73.6	179	51.9	< 3
7	30	84.5	174	40.4	< 3
8	33	81.8	178	53.6	12

*Drink refers to bottle of beer, glass of wine, shot of whiskey, high-ball, etc.

TABLE XIII

ALCOHOL AND LIQUID CONSUMPTION DATA

Subject	Weight (KG)	95% Ethanol (ML)	Cranberry Juice (ML)	Water Each 30 Minutes (ML)
1	57.7	61.1	549.9	144
2	82.3	87.2	784.8	206
3	79.5	84.3	758.7	199
4	83.6	88.6	797.4	209
5	78.2	82.9	746.1	196
6	73.6	78.0	702.0	184
7	84.5	89.6	806.0	211
8	81.8	86.7	780.3	204

TABLE XIV

SUBJECT WORKLOAD DATA

	Percent of VO_2 max.							
	15.0		32.5		50.0		100.0	
	Treadmill Attitude							
Subject	Grade	Speed	Grade	Speed	Grade	Speed	Grade	Speed
1	0	1.5	2.2	3.4	7.7	3.4	23	3.4
2	0	1.1	1.0	3.4	5.6	3.4	19	3.4
3	0	1.3	1.6	3.4	6.7	3.4	21	3.4
4	0	1.3	1.6	3.4	6.7	3.4	21	3.4
5	0	2.4	5.5	3.4	12.6	3.4	33	3.4
6	0	1.6	2.6	3.4	8.2	3.4	24	3.4
7	0	1.0	0.3	3.4	4.6	3.4	17	3.4
8	0	1.7	2.9	3.4	8.7	3.4	25	3.4

Key: Speed in Miles per Hour (MPH)

Grade in Percent (%)

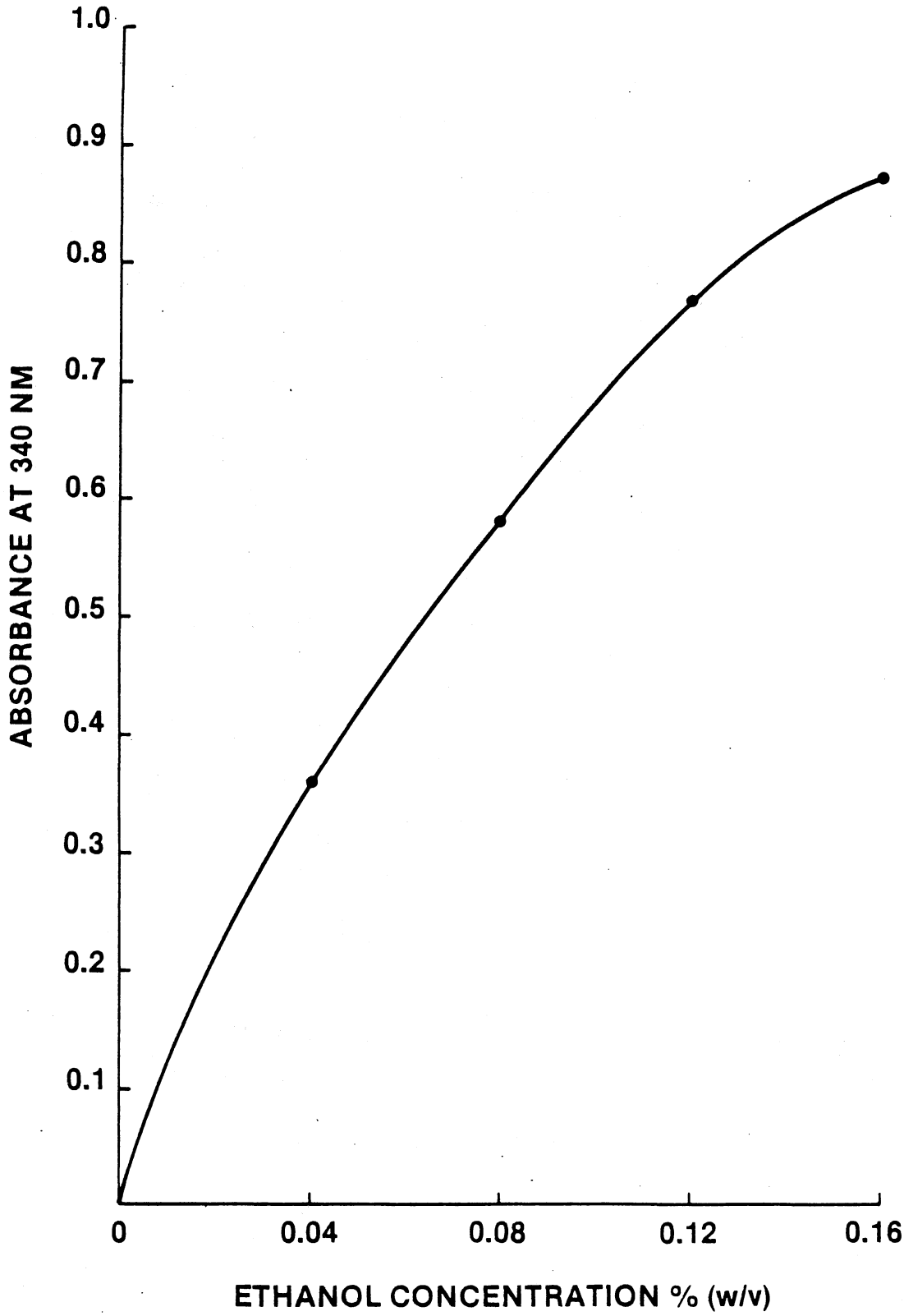

Figure 1. Ethanol Calibration Curve (SIGMA 332-UV)

VITA[v]

Frank Allen Kulling

Candidate for the Degree of

Doctor of Education

Thesis: THE EFFECT OF PHYSICAL EXERCISE OF VARYING INTENSITIES ON THE BLOOD ETHANOL CURVE

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