Alcohol has long been known to affect endocrine organs. Early studies of postmortem material and animal investigations showed that alcohol could cause adrenal and testicular atrophy. As the role of the adrenal in glucose metabolism was elucidated, and before direct measures of hormones was possible, it was postulated that alcoholism was an endocrine disease, (adrenocortical insufficiency). While no substantive evidence to justify that hypothesis has evolved to date, the fact remains that endocrine systems are profoundly altered by alcohol. The full extent of this is not known primarily because relatively little effort has been devoted to the question using modern analytic tools such as radioimmunoassay. The following is a summary of the recent work from this and from other laboratories.

1. The Adrenal Cortex

Both clinical and animal studies, conducted prior to 1948 (1) and confirmed in 1961 (2), have shown that chronic alcohol can cause adrenal atrophy. These early studies led to the hypothesis of a
"relative hypoglycemia" which was presumed due to adrenocortical insufficiency (3). Most background work was done before the advent of useful direct measures of urine and plasma corticosteroids.

The adrenal cortex is histologically divided into three zones. Zona glomerulosa is the site of aldosterone biosynthesis. Zona fasciculata is thought to be the primary site of cortisol synthesis. The innermost zone, zona reticularis, is believed to be the site of dehydroepiandrosterone (DHA) synthesis. Because aldosterone and cortisol have separate control mechanisms, these steroids will be discussed separately. Although DHA secretion is primarily in response to adrenocorticotropic (ACTH), we have chosen to discuss it in its functional category as a sex hormone.

2. Aldosterone

Among the best known effects of alcohol are those of diuresis and salt retention. The diuretic action was shown to be caused by an inhibition of vasopressin secretion (4). It has been shown that in spite of an acute diuresis, chronic alcoholic subjects most frequently are over-hydrated rather than dehydrated (5). Since the extra body-water is primarily intravascular, it explains the location of the retained sodium. Early studies (6) inferred that aldosterone might be responsible for sodium retention but the effect of alcohol on aldosterone secretion had not been measured at the time we began our investigations. An earlier review (7) summarized the initial studies in dogs and human alcoholic subjects. We found, briefly, that high blood-ethanol concentrations (300 mg/dl) inhibited aldosterone secretion in the dog. In human alcoholic subjects, low blood levels of ethanol (100-200 mg/dl) stimulated aldosterone secretion while high levels appeared to inhibit aldosterone secretion.

In an attempt to determine the mechanism of the increased aldosterone secretion, we conducted a study in collaboration with Dr. J.H. Mendelson, Harvard Medical School and Dr. Nancy K. Mello, National Institute on Alcohol Abuse and Alcoholism. Simultaneous measures of including serial 24 hour aldosterone excretion as well, plasma aldosterone plasma renin cortisol (6:00 A.M. recumbent and 10:00 A.M. active) were taken during abstinence and during drinking in alcoholic subjects.

Aldosterone excretion was greatest in all three subjects on the first day of drinking. In one subject, whose blood ethanol rose to 300 mg/dl, aldosterone secretion was inhibited after the first two days of drinking but normalized as his blood ethanol level declined to zero. Plasma cortisol increased in two of three subjects but not until the second day of drinking and after aldosterone...