limited number of experiments does not permit evaluation of the effects of sex, age, physical condition etc., it is clear that the exhaled gases of human subjects are richer in ethylene than the room air inhaled by them. It is known that with fruits, generation of ethylene is an autocatalytic process[1] and the presence of ethylene in room air may act as a stimulant to ethylene production by humans.

For a more quantitative relationship between the ethylene contents of exhaled gases and inhaled air several experiments were conducted with one individual (male, non-smoker). The exhaled gases were collected 4 h after the evening meal, outside the building in the open air, away from possible contamination from such sources such as automobile exhaust. Inhaled air contained ethylene at an average concentration of 3.46 ± 0.02 (standard error) $\cdot 10^{-3}$ parts/million (6 determinations) whereas exhaled air contained ethylene at 6.79 ± 0.13 (6 determinations). The difference between these means was statistically highly significant. These results indicate that the ethylene content of the exhaled gas of the normal adult subject is nearly double that of the air inhaled by him.

The production of ethylene is probably not solely attributable to the gut flora, since we have obtained ethylene from subcellular fractions from rat liver and rat intestinal mucosa (unpublished data from G. RAM CHANDRA AND M. SPENCER).

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Competitive inhibition of corticoid synthesis by estrogens

When estrogens are incubated with rat adrenal tissue they inhibit the synthesis of corticoids[1]. Administration of high levels of estrogens *in vivo* also inhibits production of corticoids[2]. Since glucose-6-phosphate dehydrogenase (EC 1.1.1.49) is inhibited by estrogens, it seemed possible that the regulation of the rate of reduction of NADP is a mechanism in the regulation of adrenal function[3]. Estrogen has an inhibitory effect on other NADP-specific dehydrogenases and at lower levels estrogen stimulates NAD-specific lactate dehydrogenase (EC 1.1.1.27)[4]. However, it has been demonstrated that the generation of $NADPH_2$ by glucose-6-phosphate dehydrogenase is of special significance in corticoid synthesis[5]. The competitive inhibition by estrogens of the rate of reduction of added NADP in adrenal homogenates has now been correlated with the competitive inhibition to corticoid synthesis. In studies of this kind an application of kinetic principles is essential.

Fig. 1 shows an example of the competitive relationship between estrogen and NADP for purified glucose-6-phosphate dehydrogenase. The estrogen inhibition is non-competitive for glucose 6-phosphate. The purification of the enzyme from cow adrenal cortex and the determination of Michaelis constants have been described elsewhere[6]. The same competitive relationship between estrogen and NADP in terms

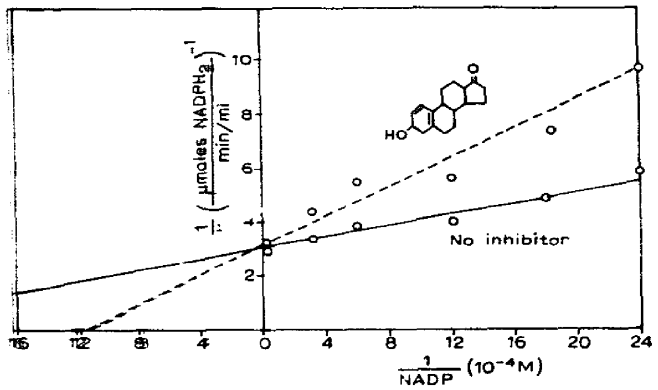

Fig. 1. Competitive inhibition by estrone of the binding of NADP to glucose-6-phosphate dehydrogenase prepared from cow adrenal cortex as demonstrated by a Lineweaver–Burk plot. Each point represents the average of 5 or more determinations. Each reaction mixture in Tris buffer (pH 8.0) contained enzyme, 1 mM glucose 6-phosphate, and varying amounts of NADP. Estrone was added to the inhibitor series at 10 μM. K_m(NADP) = 3.5 μM, K_I = 38 μM.

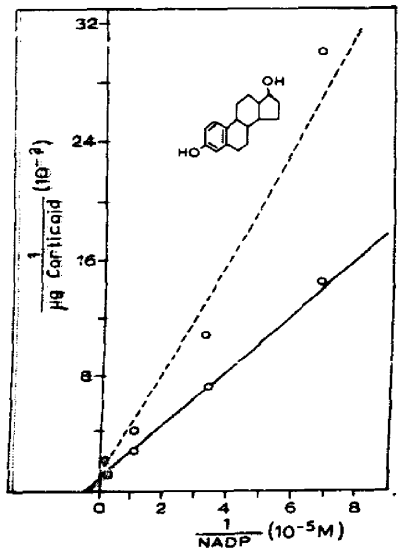

Fig. 2. A Lineweaver–Burk plot of the competitive relationship between 17β-estradiol and NADP in corticoid synthesis. Each beaker contained in 2 ml of final volume of Krebs–Ringer bicarbonate buffer 23 mg of homogenate of rat adrenals, 4 mM glucose 6-phosphate, 22 mM $CaCl_2$ and NADP as shown. Estradiol in ethanol was added to the inhibitor series to give a final concentration of 7.5 μM. There were 4 controls without added NADP, glucose 6-phosphate or estradiol. Incubation was carried out at 37° for 30 min under 95% O_2–5% CO_2. The corticoids formed were extracted with methylene dichloride and measured by the blue tetrazolium reaction. Each point represents the mean of 4 closely agreeing determinations.

of the rate of synthesis of corticoids has been demonstrated with a homogenate preparation from male rat adrenals. The addition of either glucose 6-phosphate or NADP alone to the homogenate stimulated little or no corticoid synthesis. Increasing the amount of both glucose 6-phosphate and NADP increased the rate of synthesis of corticoids from the endogenous precursor steroid, probably cholesterol. A kinetic study of estrogen inhibition was carried out with the homogenate system using excess glucose 6-phosphate and increasing amounts of NADP. An incubation time of 30 min was chosen from time studies to ensure a linear rate of synthesis of corticoids. Corticoids were extracted with methylene dichloride and estimated by the blue tetrazolium method[7]. The results are shown in Fig. 2. The inhibition by estrogen at 7.5 μM was approx. 50% at an NADP concentration of 15 μM and approx. 8% with NADP at 270 μM. Since even the lowest level of added NADP is probably much higher than that found *in vivo*, and the estrogen inhibition is competitive with NADP, much lower levels of estrogen than 7.5 μM could be markedly inhibitory to adrenal synthesis of corticoids *in vivo* if there were not compensation from the pituitary. TROOP AND POSSANZA[8] failed to demonstrate an effect of endogenous estrogen in the female rat adrenal on corticoid synthesis *in vitro* in the presence of glucose 6-phosphate and NADP probably because they added very high levels of NADP. In addition, there was no indication that the rate of synthesis of corticoids was linear at the 2-h incubation time chosen for their studies.

Since there is a requirement for $NADPH_2$ in all the hydroxylation reactions at positions 17, 21 and 11 (ref. 9, 10) and probably also for the 20–22 hydroxylations required before the cleavage of the side chain of cholesterol, production of all corticoids would be lower with sufficient estrogen inhibition of the rate of reduction of NADP. This was found after the administration of high doses of estrogen to the rat[2]. It must be borne in mind that in the intact animal inhibition of the adrenal cortex by low levels of estrogen can be compensated for by an increase in corticotrophin secretion[3]. STUDZINSKI *et al.*[11] have shown also that corticotrophin administration increases the activity of glucose-6-phosphate dehydrogenase in man. This may be the method by which the adrenal compensates for estrogen inhibitions.

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