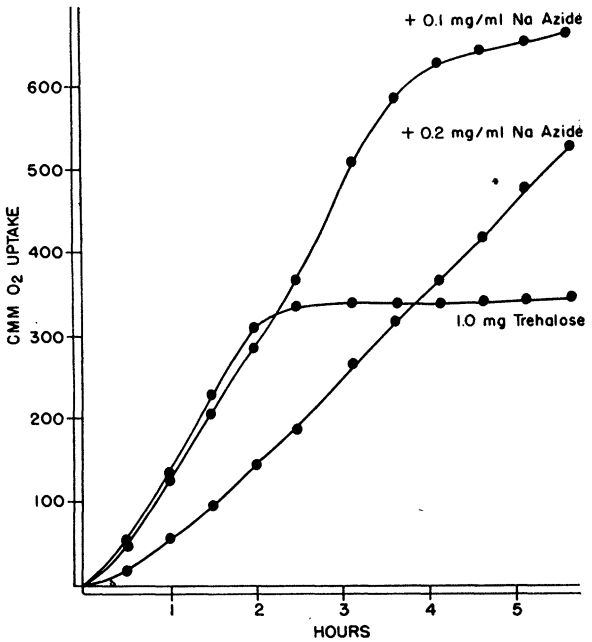

Fig. 2. Effect of two concentrations of azide on the oxidation of trehalose. The respective control respirations have been subtracted.

even the highest concentrations used caused no initial inhibition.

Figure 1 shows the effect of azide and cyanide on the autorespiration and on the oxidation of pyruvate. Pyruvate took up a little less than 2 atoms of oxygen per molecule. The drugs increased this to more than 3. The oxidation of trehalose stopped when 10 to 12 atoms of oxygen per molecule were taken up. This was increased to 18 to 22 by the drugs (Fig. 2). Their effects on the oxidation of the fatty acids such as acetate and caproate were much less striking. The final oxygen uptakes were increased by only a very small amount, and oxidation rates were depressed for several hours. The oxidation of the fatty acids stopped when 50 to 60 percent of the theoretical uptake had been reached. In the absence of added metabolites, both cyanide and azide raised the R.Q. from 0.82 to 0.91, which indicates that the endogenous carbohydrate metabolism is also preferentially affected.

The azide and cyanide effect on autorespiration was not altered after the cells were exposed for 3 min in a sonic vibrator at 9000 cy/sec. The rate of formation of the adaptive enzyme for benzoic acid was decreased 50 percent by this treatment. Exposure for 10 min eliminated the effect of the drugs, although pyruvate was still oxidized at about 25 percent of the normal rate. Neither 1.0 mg/ml of versene nor 0.05 mg/ml of 8-hydroxyquinoline affected the action of the drugs. Ferrous sulfate ($FeSO_4$) in a concentration of 0.5 mg/ml did not inhibit the effect of azide and cyanide on the autorespiration. Cupric sulfate ($CuSO_4$) inhibited respiration and this was not reversed by the drugs. Cyanate had very little effect and azide was neither reduced to ammonia nor oxidized to nitrite.

Summary. Azide and cyanide affect the autorespiration of these organisms in the same way as they do the oxidation of added metabolites. The effect of these drugs on the autorespiration occurs in the presence of the added metabolites.

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21 May 1954.

Site of Conversion of Desoxycorticosterone Acetate to Progestin

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The progestational action of parenterally administered desoxycorticosterone acetate (DCA) has been known for some time. Within recent years, however, it has been demonstrated that DCA has no progestational activity when applied locally to the endometrium of the rabbit (*1*) or mouse (*2*). From a consideration of the chemical configuration, Pfiffner (*3*) has suggested that desoxycorticosterone is probably converted to progesterone in the body and that one step in its metabolic degradation may be by the removal of the primary hydroxyl group. Zarrow, Hisaw, and Bryans (*4*) have presented evidence concerning the conversion of DCA to progesterone *in vivo,* but no information has been advanced regarding the site of this conversion in the organism.

In an attempt to gain information concerning the organs that are involved in such conversion, we have determined the progestin concentrations in the serum of castrated, adrenalectomized, and nephrectomized rats after an intramuscular injection of DCA. All determinations for circulating progestational activity were made by the method of Hooker and Forbes (*5*). Since chemical evidence for the identity of the substance measured by this test is lacking, the term *progestin* will be used for the hormonal activity measured in these experiments. In keeping with previous studies, however, the activity of the progestin has been standardized against progesterone (*6*).

The serum progestin levels of intact male (*7*) or castrated female rats in our colony have been shown to vary between 0 and 1 μg/ml. It may be seen from the data in Table 1, that following the administration of 5 mg of DCA to castrated animals, a maximum level of serum progestin was observed within 4 hr and a return to preinjection levels within 24 hr. Bilateral adrenalectomy or nephrectomy followed by 5 mg of

DCA resulted in maximum serum progestin levels of 2 to 3 μg/ml. These concentrations are not significantly different from the values seen in the castrated control rats and definitely indicate that conversion of DCA to progestin occurred in adrenalectomized or nephrectomized rats. In animals deprived of both the adrenals and the kidneys, however, no detectable circulating progestin was found.

The experiments of Engelhart (*8*), who found that progestational changes could be induced in the uteri of young, unmated rabbits by subcutaneous injections of adrenocortical extracts, were probably the first suggestion concerning the possible elaboration of progestins by the adrenal gland of the mammal. Callow and Parkes (*9*) prepared extracts from the adrenals that caused full progestational changes in the rabbit's uterus, while Beall and Reichstein (*10*) were the first actually to isolate progesterone from the adrenal gland. The detection of circulating, progesterone-like activity in the male has been shown in the intact bird (*11*) and the intact or castrated mammal (*7*). In the case of the rat, increases in serum progestin have been reported within 6 hr following adrenal stimulation (*12*), and the titers of serum progestin present in the intact animal have been shown to disappear following adrenalectomy (*7*). Further evidence for the elaboration of progestin by the adrenal gland may be seen in the results of Lyons *et al.* (*13*) who produced deciduomata in the hypophysectomized, oophorectomized rat treated with ACTH. These facts purport an adrenal source of progestins in the male, but it is not known whether the hormone is secreted specifically by the adrenal gland or whether it results through conversion from other adrenal steroids, such as desoxycorticosterone.

Summary. The conversion of DCA to progestin *in vivo,* which has been shown in the case of the monkey (*4*) and now the rat, indicates one possible mechanism by which progestin may occur in the male. In addition, these studies also show that, at least in the rodent, the adrenals and the kidneys are the sites of this conversion.

Investigations on the conversion of DCA to progestin in other species, as well as studies on the release of progestin by tissue slices incubated with or without DCA, are currently in progress.

Table 1. Mean progestin levels in the serum of the rat following administration of 5 mg desoxycorticosterone acetate (DCA).

Hours after treatment with DCA	Serum progestin (μg/ml) in the rat			
	Castrated	Castrated and adrenalectomized	Castrated and nephrectomized	Castrated, adrenalectomized, and nephrectomized
2	2.00	1.00	1.50	0.00
4	3.33	3.00	2.00	.00
6	2.00	2.00	2.00	.00
12	1.00	1.00	1.00	.00
24	0.33	0.67	0.33	.00

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15 April 1954.

Light-Scattering Studies on Hyaluronic Acid

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Hyaluronic acid is an important constituent of many body tissues and occurs in synovial fluid, vitreous humor, and umbilical cord. This acidic polysaccharide is also present in some connective tissue and, as such, may take part in the physiological functions of connective tissue—that is, transport, storage, repair, and resistance to infection (*1*). In addition, it appears that there are physicochemical changes of the hyaluronic acid of joint fluids in rheumatoid arthritis (*2*). It is felt that a study of the size and shape of the molecule may contribute to an understanding of the role of this substance in its various physical functions. In the present work we are concerned with the results of light-scattering determinations. Other physicochemical studies are in progress.

Ogston and Stanier (*3*) have studied raw ox-synovial fluid and its ultrafiltrate containing hyaluronic acid. The material in the ultrafiltrates contains approximately 30 percent protein with the hyaluronic acid. By means of flow birefringence and viscosity studies, Ogston and Stainer concluded that the particles are highly hydrated spheres and that under the influence of a shear gradient the particles are deformed.

Light scattering affords a means whereby the size and shape of the particles in solution are determined without subjecting the particles to any external stress and where the theoretical interpretation of the experimental data is explicit.