for other proteins (Gregoriadis, 1974), and it suggests an interaction of the enzyme with the liposomal lipids. Entrapment of proteins in liposomes that can be tolerated by man can be achieved under sterile conditions (Gregoriadis et al., 1974).

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Precocious Development of Uridine Diphosphate Glucuronyltransferase Activity in Chick-Embryo Liver after Administration of 11β-Hydroxy Steroids with and without Thyroxine

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UDP-Glucuronyltransferase (EC 2.4.1.17) activity is low in or absent from fresh homogenates or microsomal preparations of chick-embryo liver until hatching at 21 days, when it rapidly increases to adult values (Dutton & Ko. 1966). Precocious development of adult activity can occur in embryo liver of 15 days or later, after grafting, 3–4 days earlier, of the cephalic region of the anterior-pituitary gland from a hatching or hatched bird on to the chorioallantoic membrane (Wishart & Dutton, 1974, 1975a). Injection of adrenocorticotrophic, follicle-stimulating or thyrotrophic hormone, known to be secreted by this region of the gland (Brasch & Betz, 1971), had no reproducible effect on the transferase activity (Leakey & Dutton, 1975).

To mimic natural release of hormone from endogenous or grafted tissue we developed a new technique of hormone administration, involving continuous flow down a paper strip from a reservoir on to the chorioallantoic membrane. Rate of flow is controllable. By this means we have demonstrated that adrenocorticotrophic hormone and corticosterone (11β,21-dihydroxy-4-pregnene-3,20-dione) provoke precocious appearance of the transferase on day 17 when applied from day 13 (Leakey & Dutton, 1975).

We summarize here further effects on the enzyme after treatment with corticosteroids of the embryo in ovo and of liver in organ culture.

Corticosterone, cortisol (11β,17,21-trihydroxy-4-pregnene-3,20-dione) and aldosterone (11β,21-dihydroxy-3,20-dioxo-4-pregnene-18-al) all stimulated precocious activity, but 11-deoxycorticosterone, progesterone (4-pregnene-3,20-dione), pregnenolone (3β-hydroxy-5-pregnene-20-one), tetracortisol (3α,17α,21-trihydroxy-5β-pregnene-11,20-dione), testosterone (17β-hydroxy-4-androsten-3-one) and oestriol [1,3,5(10)-estratriene-13,16α,17β-triol] had no effect. Ability to stimulate appeared to require the 11β-hydroxy group; cortisone (17α,21-dihydroxy-4-pregnene-3,11,20-trione) was much less effective than cortisol, requiring 5 times its concentration for stimulation.

Although lower doses occasionally stimulated, the minimal amount of corticosterone or cortisol for reproducible effect was 0.18 μmol per egg administered over the 4 days. Maximal stimulation of transferase was 30-fold, i.e. to some 3–4 times adult activity.

Minimal time of administration required for evident enzyme stimulation 4 days after onset of administration of high doses of corticosteroid was 2–4 h. The minimal time for
transferase to respond depended on steroid dosage. High doses (0.5 μmol/egg per day), which are lethal if applied for 96 h, stimulated activity in 48 h, whereas 0.2 μmol/egg per day (non-lethal) needed 72 h. However, thyroxine (10–15 nmol/day) added to the lower dose of steroid brought activity up in 48 h. Under these conditions thyroxine alone had no effect. As the pituitary graft requires only 48 h for stimulation it may exert its effect through both the adrenocorticotrophic and thyrotrophic hormone.

When applied at 0.05 μmol/egg per day over 4 days (higher doses were lethal), corticosterone had no effect on liver transferase of embryos aged 9 or 10 days at the onset of treatment. Application of this dose from day 11, however, gave the same stimulation as when applied from day 13. As 72 h are needed for stimulation to be apparent, it seems that competence of chick-embryo liver transferase to respond to corticosterone application by this method begins on day 13–14. This is the time of competence after pituitary grafts (Wishart & Dutton, 1975a), and suggests again a linkage between the two effects. Both corticosterone application and grafting if carried out before day 11, provoke liver necrosis. The late onset of competence with these physiological stimulators of the transferase contrasts with the ability of phenobarbital to induce the enzyme within a few hours of incubation from day 0 (Wishart & Dutton, 1975b).

To determine if 11β-hydroxy steroids acted directly on embryo liver, they were added to the medium of organ cultures. Although the transferase is spontaneously developed under these conditions (Ko et al., 1967; Skea & Nemeth, 1969), an increased rate of development is measurable when phenobarbital is added (Burchell et al., 1972). When corticosterone was added at various concentrations, no obvious increase in the rate of the transferase induction was noted in cultures from 15-day embryo liver.

If thyroxine was also present, however, UDP-glucuronyltransferase activity was twofold that of controls after 3 days. Although phenobarbital on injection in ovo at that age raises the enzyme activity 50-fold, its maximum increase of rate of development in cultures then is still only twofold. The doubling observed with corticosterone plus thyroxine may therefore be considered significant. Optimal concentrations of the two hormones in the medium under these conditions were 10–15 μmol and 0.75–1.25 μmol respectively.

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Inhibition of Uridine Uptake by Methylprednisolone in Human Lymphoblastoid Cells

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Glucocorticoids have been shown both in vivo and in vitro to cause the death of sensitive lymphoid cells, and, in combination with other drugs, they are used in the treatment of human lymphoid leukaemias (Simone, 1974). Much work has been directed towards