INTRODUCTION

There is now a large literature to support the view that thyroid hormones have little role in fetal growth and development (1-5). Athyroid human newborns have few if any signs of their chemical hypothyroidism, and length, weight and head circumference at birth are normal for gestation age. Moreover, IQ and neurological function parameters are normal in the vast majority of hypothyroid newborns detected by chemical screening and treated in the early neonatal period (6,7). Selected intrauterine effects of thyroid hormone deficiency have been recognized. Serum TSH concentrations are regularly elevated at birth in hypothyroid infants indicating active negative feedback control of pituitary TSH secretion by thyroid hormone in utero (2-5,8). Also, newborn thermogenesis may be mildly impaired, and the fall in body temperature in the athyroid human infant may be more marked than in a normal, euthyroid neonate (2-4). Thermogenesis in the newborn is largely a function of brown adipose tissue (BAT), and recent evidence in the sheep suggests that norepinephrine-stimulated oxygen consumption in newborn BAT is obtunded by hypothyroidism (9,10).

The above manifestations of the neonatal hypothyroid state are mild and subtle, however, and the classic signs and symptoms of cretinism develop in infants with congenital hypothyroidism during the early months of extrauterine life. These signs and symptoms include the deficiencies in thermogenesis and metabolism characteristic of the hypothyroid state in adults. In addition there are profound effects of thyroid hormone deficiency on growth and development. These include deficient statural growth and growth of lean body mass, delayed epiphyseal maturation, deficiencies of brain growth and development, and delayed development/maturation of a variety of organs and tissues (1,11).

ONTogenesis OF THYROID HORMOnE ACTIONS IN RODENTS

A number of investigators have studied the timing of appearance of thyroid hormone effects in developing rodents. These altricial species (in particular the rat and mouse) are born relatively immature with an undeveloped hypothalamic-pituitary-thyroid system as well as poikilothermia. They have a pattern of thyroid system development analogous to that of humans except that the late ontogenic events occur after birth (12). The ontogenesis of nuclear triiodothyronine (T3) receptors in brain and liver as these relate to serum TSH and serum thyroid hormone levels are demonstrated in figure 1 (12-16).
The ontogenesis of a variety of thyroid actions have been characterized in these altricial species. These include tissue thermogenesis; hepatic enzyme activities; beta adrenergic receptor binding in the heart, lung and brain; body weight gain; carcass and muscle growth; skeletal maturation; skin maturation including eye opening and tooth eruption; brain maturation; pituitary and serum growth hormone concentrations; submandibular gland nerve growth factor (NGF) and epidermal growth factor (EGF) concentrations; EGF levels in skin, eye, kidney and urine; and EGF receptor binding in skin and liver (17-41).

**Figure 1.** Maturation of thyroid receptors, serum TSH and thyroid hormone secretion in the developing rodent. Fractional thyroid system maturation is shown with the age to allow comparisons among species (see figures 3, 5). Data are derived from references 12-16.

Some of these effects represent thyroid hormone actions on specific gene products probably mediated via thyroid hormone receptor control of gene transcription. These include effects on hepatic enzymes, pituitary growth hormone synthesis, EGF and NGF synthesis in submandibular glands and EGF synthesis in kidneys; and EGF receptor binding in skin and liver (42-45). Other thyroid hormone actions represent complex events the mechanism(s) of which are not yet clear. Such actions include thyroid hormone stimulation of growth, skeletal maturation and brain development. Recent reviews of the role(s) of thyroid hormones in these events are available (1,17-20).