

## Somatomedin-C and Thymidine Activity in Appropriate and Small-for-Gestational-Age Human Newborns

During the past ten years, several reports on serum growth factors in newborns and premature infants have been published. In this report, two well-defined groups of term newborns are compared, using two different procedures. Ten infants had appropriate birth weights for gestational age (AGA);  $\bar{x} = 3,492 \pm \text{SEM } 1,388$ . Eleven infants were small for gestational age (SGA) with a mean birth weight of  $2,610 \pm 46$  g. Blood from the infants was obtained directly from neonatal vessels, rather than from the umbilical cord. Thymidine activity (TA) was determined by measuring the effect of the serum on thymidine incorporation into human lymphocytes activated by phytohemagglutinin. Somatomedin-C (Sm-C) was measured by radioimmunoassay (RIA) after separation from carrier protein. In addition, transferrin was determined using Mancini's technique of radial immunodiffusion.

The mean  $\pm$  SEM results obtained in the two groups are shown in the table.

Measurements	AGA	SGA	P
TA (U/ml)	1.51 $\pm$ 0.08	1.04 $\pm$ 0.11	<0.001
Sm-C (U/ml)	0.52 $\pm$ 0.03	0.32 $\pm$ 0.03	<0.001
Transferrin (g/l)	1.69 $\pm$ 0.15	1.61 $\pm$ 0.13	Not significant

The TA values in the SGA newborns correspond to normal adult values (1.0 U/ml), whereas those of the AGA infants are 50% higher (1.5 U/ml). The Sm-C levels, by contrast, are markedly lower (0.52 and 0.32 U/ml) in both groups of infants than in normal adults (1.0 U/ml). The transferrin levels were similar in both groups and significantly below the mean adult level.

Thiériot-Prévost G, Doffos F, Forrestier F: *Acta Endocrinol* 1985;110: 32-35.

**Editor's comment**—The results presented here agree with previously reported results, obtained by radioimmunologic as well as biologic methods. The advantage of this study, however, is its simultaneous application of both assays, thus permitting their immediate comparison. TA values were positively correlated with the Sm-C levels in the AGA newborns ( $r=0.72$ ,  $P<0.05$ ) but not in the SGA group.

The significant difference of the TA values v the Sm-C-RIA values suggests that Sm-C plays a major role in the growth factors determined as thymidine activity, but is certainly not the only substance generating growth-promoting activity, as reflected by thymidine uptake. The importance of other factors, including the embryonic somatomedin described by Sara et al (1981), remains to be elucidated.

Obviously, there exists a relationship between impaired fetal growth and diminished Sm production and thymidine activity. Nevertheless, no individual correlation between the Sm levels and the birth weight was observed. The data on transferrin confirm previous investigations and demonstrate again that transferrin apparently does not play a direct role in fetal growth.

The entire subject of fetal growth and fetal growth factors remains a challenging field for investigation. Our understanding of the phenomena involved remains exceedingly limited.

## Effects of Intravenous, Subcutaneous, and Intranasal Administration of GH-Releasing Hormone-40 on Serum GH Concentrations in Normal Men

The effects of intravenous (IV), subcutaneous (SC), and intranasal growth-hormone-releasing hormone 40 (GHRH-40) on growth-hormone (GH) secretion were measured in normal adult volunteers. To better define the dose-response relationship between GHRH-40 and secreted GH, the circulating levels of immunoreactive GHRH-40 were quantitated. Normal men received either vehicle solution or GHRH-40

IV (0.003 to 0.1  $\mu\text{g}/\text{kg}$ ), SC (1 to 10  $\mu\text{g}/\text{kg}$ ), or intranasally (3 to 100  $\mu\text{g}/\text{kg}$ ). The table gives the results obtained during the two-hour period after IV administration or the three-hour period after SC or intranasal administration of GHRH-40.

In addition, significant dose-response relationships were documented between the maximal increments above basal in serum GH and GHRH-40 administered by all routes.

The mean peak plasma level of GHRH achieved after IV administration of 10  $\mu\text{g}/\text{kg}$  GHRH-40 was approximately 60 and 500 times greater than the mean levels achieved after the same dose SC

and intranasally, respectively.

Evans WS, Vance ML, Kaiser DL, et al: *JCEM* 1984;61:846-850.

**Editor's comment**—If chronic GHRH therapy is to become a reasonable alternative to GH therapy, one must be able to give appropriate quantities by SC or intranasal routes. The present preparation is active SC when given as 1 to 3  $\mu\text{g}/\text{kg}$  SC every three hours by micropump (see Thorne et al, *N Engl J Med* 1985;312:4). The present data indicate that the intranasal route is not yet practical. If the intranasal route is to be used, what is clearly needed are more lipid-soluble analogs (a peptide composed of the first 29 amino acids of GHRH is biologically active) or the fabrication of a lipophilic delivery system that allows the peptide to cross biological membranes. The dose-response relationships confirm that levels of GHRH of 40 to 60  $\text{pg}/\text{ml}$  are necessary to evoke GH secretion.

Route of administration	Dose ( $\mu\text{g}/\text{kg}$ )	Maximal GH increment over basal (ng/ml)
Intravenous	0.1	15.5
Subcutaneous	3.3	26.2
	10	63.6
Intranasal	30	18.5
	100	21.7