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^{125}I-Insulin specific binding (IB) to erythrocytes of normal and hypoglycemic infants.

Specific IB to erythrocytes was studied in 15 normal infants aged 1 to 24 months, and in 3 boys aged 2 to 20 months with nesidioblastosis 1/ at time of hyperinsulinism and hypoglycemia 2/ after correction of hypoglycemia by nasogastric feeding, diazoxide and/or partial pancreatectomy. In controls, IB ranged from 2.5 to 12.5 % and was significantly correlated with reticulocytes count : $r = 0.824$, $p < 0.001$. The addition of unlabelled Insulin decreased IB and scatchard analysis demonstrated 2 populations of sites with high (mean : 1.2×10^{-14}M) and low (mean : 32×10^{-14}M) affinity (for $3\ 10^9$ erythrocytes), corresponding affinities being $K = 5.5 \times 10^{9}M^{-1}$ and $1.4 \times 10^{7}M^{-1}$. In patients with nesidioblastosis, IB was elevated for reticulocytes count at the time of hypoglycemia in all cases (9 to 12 %) with an increased number of high affinity sites in 2. After treatment IB was low (2.5 to 4 %), the number of sites remaining identical but K being decreased. These data suggest that an increased receptivity to insulin may play a role in the mechanism of hypoglycemia in infants with hyperinsulinism.

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Reduced insulin binding in a large kindred with severe diabetic retinopathy.

Specific insulin binding to erythrocyte receptors (IRB) has previously been reported to be unaltered in children and adolescents with insulin dependent diabetes mellitus (Ped. 66:385, 1980). However, we report here that five insulin dependent, ketosis-resistant juvenile diabetics from the same kinship have a significant reduction in the percent IRB (normal 8.32±2.71 vs 4.72±0.84 for the diabetic children). Three non-diabetic juveniles in the family have an intermediate value of 5.77±1.08. The youngest child shows normal binding. Scatchard analysis of the high and low affinity insulin binding sites indicates that the reduced IRB is due to a decrease in the number of receptor sites per cell. There is no correlation with circulating plasma insulin values nor with the severity of diabetes. However, the insulin dependent diabetics have an inordinate degree of ocular and vascular complications for the severity of their diabetes. Human lymphocyte antigens A, B, C, and D as well as islet cell antibodies are being determined in all family members to correlate with IRB data. Since diabetes mellitus is a heterogeneous disorder, we postulate that abnormal IRB in these patients may be genetically determined and related etiologically to their severe microangiopathy (retinopathy).

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Glucose turnover and glucose-lactate interrelations in the newborn rat.

A technique of continuous infusion of (6-^{3}H) and (U-^{14}C)glucose and (U-^{14}C) lactate was developed in the 1-day-old suckling rat, allowing the calculation of true and apparent glucose turnover and glucose-lactate interrelations under steady-state conditions. True glucose turnover rate in suckling newborns (16.9 ± 0.4 mg/min/kg) was 50% higher than in fasted adult rats. A 20 ± 3% glucose recycling was found which corresponded approximately to the Cori cycle activity. Although lactate was contributing for 25% to glucose turnover rate, this did not represent a net glucose synthesis since more lactate was formed from glucose (8.6 mg/min/kg) than glucose from lactate (4.1 mg/min/kg). However, recycling from lactate may be physiologically important as it could be the expression of a decrease in glucose oxidation due to an inhibition of pyruvate dehydrogenase by the elevated concentrations of non-esterified fatty acids and ketone bodies found in the plasma of 1-day old suckling rats.This glucose sparing effect could in turn diminish the requirement of aminoacids for glucose synthesis, thus allowing a high rate of protein synthesis.

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Endogenous Opiates Modulate Basal Hepatic Glucose Production.

The endogenous opiates have effects on many hormone systems including insulin and glucagon, but their influence on glucose turnover is unknown. We examined the effect of naloxone, an opiate blocker, on glucose production (Ra) and glucose utilization (Rd) in conscious trained dogs (n=5). A primed constant infusion of 3-^{3}H glucose was continued throughout the study. When steady state was reached, naloxone was infused as a bolus of 1.2 mg followed by 10 µg/min for 90 min. Glucose did not change, but within 5 min of naloxone both Ra and Rd fell by 50%: Ra from 3.8 ± 0.6 to 1.8 ± 0.3 mg/kg/min ($p<0.05$), and Rd from 3.9 ± 0.7 to 2.0 ± 0.4 mg/kg/min ($p<0.01$). Glucose clearance also fell by 50%. Ra and Rd then recovered by 15 minutes, reaching basal levels at 60 min. Insulin did not change, but glucagon rose in a biphasic manner,showing an acute spike followed by a sustained rise ($p<0.05$). Cortisol rose three-fold ($p< 0.01$)at 15 min. Conclusions: 1) Endogenous opiate blockade leads to an immediate, but transient, decrease in glucose production and utilization without affecting insulin, and despite a rise in glucagon. This suggests that the endogenous opiates directly affect basal hepatic glucose production. 2) Independent of the effect on Ra and Rd, naloxone (bolus-infusion) biphasically increases glucagon. 3) The recovery of glucose production, despite on-going naloxone, may be related to auto-regulatory mechanisms or to the rises in glucagon and cortisol.

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The baboon as a model for puberty: growth, testis size, plasma testosterone, and somatomedin-C.

Physical and hormonal changes of human puberty have been described extensively, yet a nonhuman primate model for pubertal events is lacking. This study is a cross-section analysis of pubertal growth, testis size, and plasma concentration of testosterone (T) and somatomedin-C (SM-C) in the male baboon (*Papio* sp.). Baboons (n = 84) with known dates of birth (3 - 272 weeks of age) and 10 adults (> 10 years) were examined by the same investigators for body weight (BWt), crown-rump length (CRL), and testis size. A plasma sample was drawn for determination of T by RIA. A separate group of 26 male baboons, ages 3 weeks to adult, were studied cross-sectionally for SM-C. As in the human, testis size increased only slightly before puberty. By 3 to 3.5 years, there was a marked increase in testis size coincident with or slightly preceding increases in BWt, CRL, and plasma T. Testis size continued to increase slightly after 5 years to adult size. By 3 to 4 years, there was a significant increase in SM-C which declined in adults (0 - 3 yr, M ± SE = 1.00 ± 0.14, n = 12; 3 - 4 yr, 8.46 ± 0.57, n = 10; >6 yr, 3.90 ± 0.21, n = 4). Regression analyses of BWt, CRL, and testis size vs. age revealed significant changes in slope beginning at about 3 years. In conclusion, these data define the age of puberty and describe pubertal changes in somatic growth and testicular development in the baboon and suggest that this species may be an appropriate nonhuman primate model for human pubertal growth and development. (SM-C tracer supplied by J. Van Wyk.)

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Micro-/macro-pulsatile gonadotropin secretion in male subhuman primate during sexual development.

Systematic longitudinal and cross-sectional studies to characterize changes in 24 h secretory patterns of LH/FSH have not been done. We report pulsatile LH/FSH and GnRH stimulation in monkeys: 5-10 mo., 14-24 mo. and adult >5 yr. Some monkeys were castrated at birth and later to determine when testicular negative feedback was restored. Monkeys (N=22) were fitted with a vest and mobile tether permitting chronic cannulation; blood was drawn at 15 min intervals over 24 h without anesthesia. Pulsatile LH/FSH occurred as: 1) micro-pulses with amplitudes <2X; 2) macro-pulses with increases >2X. LH/FSH and testosterone (T) were measured by RIA. Throughout, FSH secretion occurred as a steady state undulating pattern with infrequent macro-pulses in both prepubertal and adult monkeys; in adults, there was ↑ frequency of FSH micro-pulses. In contrast, occasional LH macro-pulses occurred in prepubertal animals and LH micro-pulses at all ages. GnRH stimulation showed ↑ T response at 24 mo. LH/FSH secretion associated with normal sexual development was highly individual; uniformly the amplitude and frequency of LH/FSH pulses varied. Among eunuchs markedly dichotomous patterns were apparent. Those who advanced into "puberty" had ↑ LH/FSH; LH micro- and macro-pulses (up to 5X) and ↑ FSH were seen throughout. These data indicate that changes in frequency and amplitude of LH/FSH pulsatile secretion correlate with testicular maturation.