Operationally, the focus measured in the absence of visual stimulation is referred to as the dark focus. Morgan (*7*) and Schober (*8*) have presented convincing evidence that under such conditions the ciliary body is relaxed and have suggested the term resting state of accommodation. Since we have no direct measurements of the state of relaxation, it seems advisable to avoid confusion by eliminating reference to an inferred state of rest. In the present analysis, the tendency to return to an intermediate focus, determined in the absence of light stimulation, has high predictive value not only for the three anomalous myopias under discussion, but also with respect to the focus (i) assumed while viewing a diffraction pattern for which the sharpness of the image is independent of accommodation and (ii) when the depth of field is enlarged by decreasing pupil size (*11*). It also permits prediction of the maximum of the acuity-distance function for an individual observer (*14*).

With two exceptions, the ideas presented in this report have appeared previously in the literature. First, the marked variability in the intermediate dark focus has not been suggested previously, and provides a basis for explaining difficulties encountered in previous studies. For example, under the assumption that night myopia is the result of factors such as increased spherical aberration with increased pupil size, or chromatic aberrations and the Purkinje shift (*5*), one would not expect to encounter large individual differences, and such variability would be erroneously attributed to experimental error. Similarly, any attempt to ameliorate night or empty field myopia by prescribing a fixed negative correction for all observers (*15*) would be expected to produce inconclusive results. Subjects who have a far dark focus would not be helped by additional negative correction, whereas a small negative correction would not be adequate for subjects with a very near dark focus. Recognition of intersubject variability should permit a quantitative prediction of the magnitude of night myopia as well as the appropriate correction necessary to overcome its deleterious effects under low luminance observation conditions. Second, with respect to the anomalous myopias, our interpretation is unique in providing a unitary explanation for all three phenomena.

There are a number of additional implications of our data. As Morgan (*7*) and Schober (*8*) have pointed out, since the accommodation mechanism has autonomic innervation, the dark focus might represent a tonic balance between the activity of both branches of the autonomic nervous system. Thus, variations in dark focus would reflect the balance between sympathetic and parasympathetic activation. When measurements are made in total darkness, this provides a method for evaluating autonomic activity in the absence of normal light stimulation.

The intermediate dark focus might also have implications for clinical practice since objective examinations are typically made in a darkened room. Under such conditions, to the extent that the subjects return to their intermediate dark focus (*11*), refractive power would be overestimated.

Johnson (*14*) recently demonstrated that, even with high illuminance, accommodation is most accurate and visual acuity is highest when the stimulus is conjugate with the individual subject's dark focus. His data indicate that although variation in distance from the dark focus stimulates accommodation, there is a residual error of underaccommodation for nearer objects and overaccommodation for more distant objects. This accommodative error increases with distance in either direction from the dark focus, and is exaggerated by lowering the illuminance level. This implies that for optimal performance in any demanding visual task, such as photographic or x-ray interpretation, microscopy, visual inspection, driving, and flying, the optical distance of the stimulus should correspond to the dark focus of the individual observer.

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10. These subjects wore their normal corrections, if any, and no attempt was made to evaluate independently the adequacy of the individual prescriptions. Changes in individual prescriptions would not alter the correlations obtained in this study since the same corrections were worn during all phases of the experiment. They could, of course, influence the variability or magnitude of the mean dark focus.
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Prolongation of Gestation by Growth Hormone: A Confounding Factor in the Assessment of Its Prenatal Action

Abstract. *The administration of purified growth hormone to normally nourished pregnant rats prolonged gestation leading to postmaturity of the offspring. The effect explains, in part, the apparent influence of growth hormone on prenatal and early postnatal development and supports the notion that the prenatal action of exogenous growth hormone is restricted to a therapeutic one under conditions of malnutrition.*

Growth hormone (GH) administered to pregnant rats is said to enhance brain development by the time of birth (*1, 2*) or in early life (*2, 3*). Precocious behavioral development (*4*) and improvements in adult learning capability (*3–5*) are further taken to reflect the permanence of these early structural changes in the brain. However, we have been unable to demonstrate any effects of GH treatment on fetuses obtained by cesarean section near term (*6*). A resolution of this conflicting evidence may come from our observation that modern preparations of purified GH prolong the gestation period in the rat, thus raising the possibility that the apparent facilitation of development may be due to errors in estimating true postconception age when dating is made with respect to birth.

Long-Evans virgin rats (Blue Spruce Farms, Altamont, New York) were housed in a thermostatically controlled (20° to 22.5°C) room maintained on a 12-hour light-dark cycle (LD, 12 : 12) with light onset at 0800 hours. Purina laboratory chow, containing at least 23 percent protein, and water were available at all times. After 2 weeks of acclimatization, animals were mated, and insemination was verified by vaginal lavage daily (between 0900 and 1000 hours). Presence of sperm defined day 0 of pregnancy, and only females in the body-weight range 200 to 215 g on day 0 were used. On day 7 of gestation, subjects

were randomly assigned to one of two groups. Nine subjects received daily subcutaneous injections of 3 international units of bovine growth hormone (NIH-GH-B17) contained in 0.2 ml of physiological saline in the *p*H range 8.0 to 9.0. Injections were given from day 7 through day 20; limitations in the quantity of hormone available restricted the size of this group. Control subjects (21) received the same volume of the vehicle in the same *p*H range. In view of the effect of GH on body weight of the pregnant rat (*6–8*) a further 27 uninjected control mothers, with body weights on day 0 ranging from 194 to 284 g, were studied to investigate possible effects of maternal body weight in the absence of any experimentally induced changes. On day 18 of gestation, subjects were transferred to specially adapted cages, which provided a continuous record of the entries and exits of the mother from a nest box located at one end of the cage. Although these cages were used to study maternal behavior in the postnatal period, they also served to substantiate estimates of the time of parturition; mothers invariably gave birth in the nest box, and the event record usually indicated a period of inactivity prior to parturition. Under normal conditions with this strain, we have found that parturition occurs during the light period, and it was possible, with two exceptions, to observe it directly. In the case of the two GH births that occurred during the dark period, the time of birth was estimated from the event record, confirmed by the state of cleanliness of the litter, presence or absence of placentas in the nest, and milk in the stomach.

The distribution of birth times (Fig. 1) is in agreement with previous reports (*9, 10*) that parturition is photoperiodic in the rat. No significant differences were found between the injected and uninjected control groups ($P > .1$, *t*-test), and the results were pooled. Of the control mothers, 45 gave birth during the light period of day 21 and 3 during the light period of day 22; of the GH mothers, 1 delivered in the light period of day 21, and 8 just before or in the light period of day 22. The mean difference in length of gestation period between GH and control mothers was highly significant ($P < .00001$, *t*-test). The administration of GH during pregnancy therefore prolonged the normal gestation period.

It is possible that the gestation period was prolonged because of a GH-induced reduction in litter size, since prenatal treatment with GH is reported to increase prenatal mortality (*11*), and an inverse relationship normally obtains between litter size and the length of gestation period (*10, 12, 13*). In our study, however, no significant differences in litter size were found between the GH group (mean ± S.D.: 10.56 ± 2.19) and the control groups (11.67 ± 2.01); nor were any differences found in our previous study in which mothers were delivered by cesarean section.

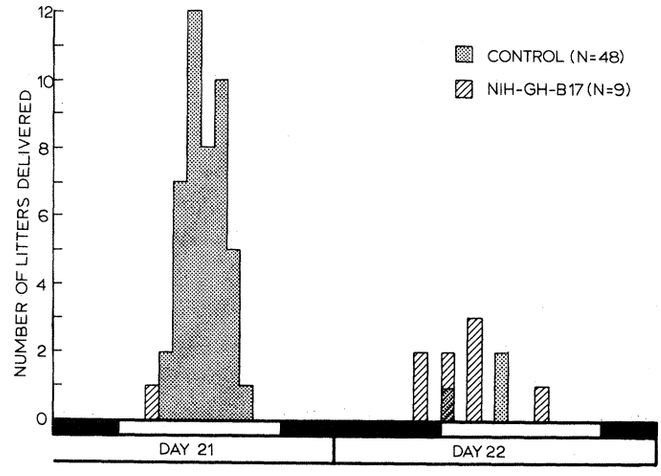

Fig. 1. Distribution of birth times for control and GH-treated mothers. The light periods (0800 to 2000 hours) are shown by open bars on abscissa.

It is also possible that the prolongation of gestation was related to increases in maternal body weight, induced by the GH treatment. By day 21 the mean weight of the GH group of mothers was 50 g more than that of the injected control group, and the difference was highly significant ($P < .00001$, *t*-test). However, in the uninjected group of 26 mothers, in which the range of body weight was wide, no significant correlation was found between maternal body weight and the length of gestation period ($r = .20$; $P < .1$).

The mechanism by which GH prolongs the gestation period is not clear. It is known that ovarian function is maintained by the placenta in the second half of pregnancy in the rat (*14*) and, in view of the immunological similarity between placental luteotropin and GH (*15*), it is possible that exogenous GH may mimic the luteotropic action of the placental hormone, thereby delaying progesterone withdrawal, which is necessary for the onset of parturition (*16*).

Although prolonged gestation was noted in earlier studies in which impure preparations of GH were used (*1, 7, 17*), the effect has not been reported in more recent work in which highly purified preparations have been employed (*2–5, 18*), presumably because the exact time of parturition was not recorded. Even though the prolongation in our study amounts to less than a day, failure to take account of this difference would affect the interpretation of structural measures made on the newborn, leading to spurious differences in body and brain weight and in total brain protein (*13*). As the rate of net increase in total brain DNA is much reduced in the perinatal period (*6*), an error of 1 day in the estimation of neonatal age may not result in large differences in this measure; however, under different conditions, or with other preparations of GH (*19*), the prolongation may be more severe than that described here. Prolongation of gestation also accounts for the apparent precocity of GH offspring in the early postnatal period (*13*).

A recent study by Sara *et al.* (*20*) deserves special comment as the findings may not be explained by prolonged gestation, and are in conflict with our earlier results (*6*) in which no effects of GH treatment could be demonstrated in the 21-day fetus. Daily injections of GH over the last 2 weeks of gestation were reported to increase cerebral weight and thymidine uptake into cerebral DNA in the 21-day fetus, and uptake of thymidine into placental DNA. However, it appears that the sample number was based on the total number of fetuses and, as the individuals in a litter are not independent (*21*), and presumably more than one animal from some litters was used, the significance levels of the differences in group means may be open to question. Nevertheless, the direction of these effects suggest that GH may have exerted some facilitative influence. A second possible difficulty derives from the fact that the parents in this study (and possibly preceding generations) appear to have been raised on a diet deficient in protein (< 10 percent). Although the diet was subsequently corrected so that mothers were adequately nourished during the course of the study, other work (*22*) suggests that their prior malnutrition would have adversely affected the subsequent experimental generation, and the very low body weights of their 21-day fetuses support this view. The results of other studies indicate that any facilitative action that GH may have is restricted to situations where malnutrition is known to occur (*23*) or where birth weight is otherwise depressed (*24*). The apparently selective action of GH under these conditions may be explained, perhaps, by the high rate of brain growth relative to body growth in the prenatal stage of development.

The possible therapeutic action of GH on the first filial generation of previously undernourished rats may explain, in part, the findings of an earlier study from the same laboratory in which differences in the adult behavior of GH offspring were observed (*3*), but would not account for the apparent improvements in adult behavior found in other studies in which there were no adverse nutritional circumstances (*4, 5*). However, it has been demonstrated that the maternal behavior of GH mothers differs from that of control mothers throughout the first 2 weeks postpartum (*13*); and, given the importance of early experience in the determination of adult behavior, these different patterns of maternal behavior may account for the permanent changes that have been observed in the offspring born to and reared by GH mothers.

The administration of GH, then, produces at least two definite effects in the rat: (i) prolonged gestation leading to postmaturity of the offspring and (ii) alterations in the maternal behavior of the GH mother. It is possible that prenatal treatment with GH may produce other changes in the adequately nourished rat which have not been detected this far. Also, GH preparations derived from different sources or species may exert differing qualitative and quantitative (*19*) influences possibly because of contamination by other pituitary hormones. However, in view of our failure to demonstrate any obvious influence of GH on prenatal development of body or brain (*6*), and the data reported here (*6*), it is doubtful that structural or functional differences in the offspring of normally nourished rats can be ascribed to changes produced prenatally by GH.

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Bottlenosed Dolphin: Double-Slit Pupil Yields Equivalent Aerial and Underwater Diurnal Acuity

Abstract. *In bright daylight, and at best viewing distances, the bottlenosed dolphin resolves visual gratings approximately equally well in air and in water. Aerial resolution improves with increased viewing distance, while underwater resolution improves with decreased viewing distance. The double-slit pupil overcomes the gross myopia in air measured by ophthalmoscope and produces the indicated effects of viewing distance.*

We present here the first behavioral evidence that daylight visual resolution acuity of the bottlenosed dolphin, *Tursiops truncatus*, is approximately equally good in air and water. Although informal observations of captive bottlenosed dolphins suggest good aerial acuity, measurements of the eye by ophthalmoscope reveal a gross aerial myopia of 16 to 20 diopters (*1, 2*). This large refractive error in air derives from the considerable power of the cornea added to that of the large, spherical lens. In water, where the cornea is ineffective as an optical device (its refractive index is approximately that of water), measurements by ophthalmoscope indicate emmetropia (*1*) to moderate hypermetropia (*2*). Functionally, these measurements predict con-

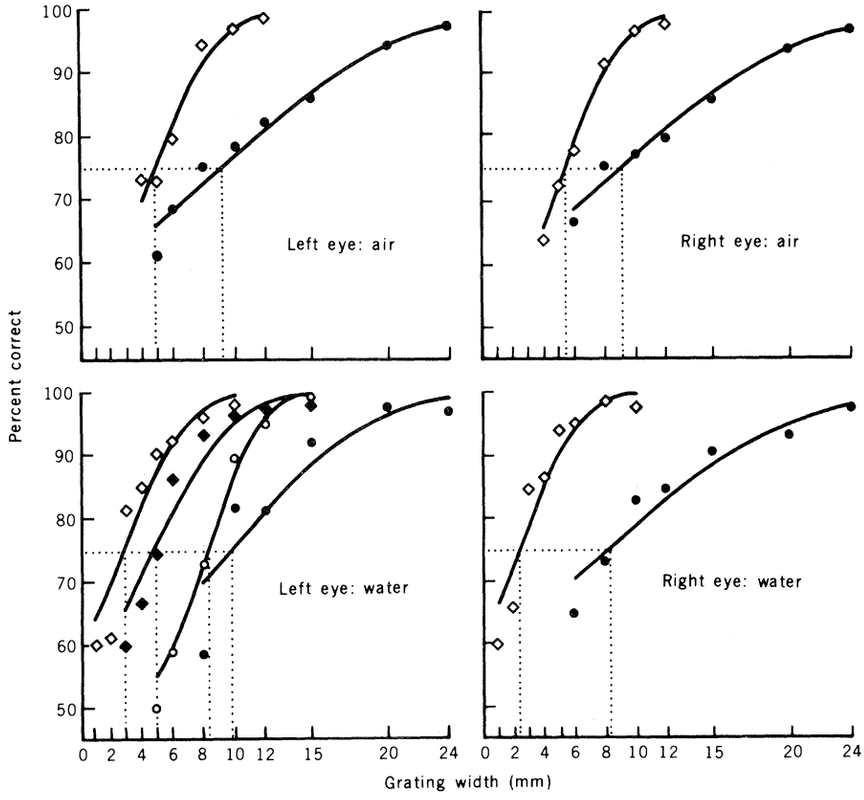

Fig. 1. Percentage of correct responses with each comparison target as a function of left or right monocular viewing, air or water medium, and viewing distance (◇ = 1 m; ◆ = 1.5 m; ○ = 2 m; ● = 2.5 m). Resolution thresholds for the criterion 75 percent correct are shown.