References and Notes

1. W. P. Jacobs and I. B. Morrow, *Am. J. Botany* 44, 823 (1957).

2. This work was supported by a grant from the National Science Foundation and by the Eugene Higgins Trust Fund.

17 March 1958

Changes in Tryptophan Peroxidase Activity in Developing Liver

Some enzymes found in adult mammalian liver are absent from fetal liver. These enzymes are present in low activity at the end of gestation, and they increase rapidly to adult levels in a matter of hours or days after birth. This developmental pattern was first demonstrated for glucose-6-phosphatase (*1*); more recently it has been shown for phenylalanine hydroxylase, tyrosine-oxidizing enzymes, and uridine diphosphoglucuronic acid transferase (*2*). The questions arise: What mechanisms control the appearance of these enzymes late in gestation? What factors control the dramatic increase in activity which occurs after birth? One suggested mechanism is that of substrate induction. Knox reported that injection of L-tryptophan into normal adult rats or into adrenalectomized animals caused a transient increase in activity of liver tryptophan peroxidase (*3*). Knox presented evidence that the effect depended upon substrate induction.

To assess the possible role of substrate induction in the development of enzymes, we studied liver tryptophan peroxidase in the guinea pig, measuring levels of activity and the effect of L-tryptophan injection in fetal and postnatal stages up to the adult (*4*). This survey of tryptophan peroxidase revealed that, as with glucose-6-phosphatase, two distinct changes occur during development: an initial appearance of activity late in gestation and a rapid increase to adult levels after birth (Fig. 1). We found that injection of L-tryptophan into the fetus or into the mother before term had no effect on fetal liver tryptophan peroxidase activity. Injection of L-tryptophan in combination with ACTH or ACE also had no effect. Injection of a term fetus, *in utero* or after delivery by section, resulted in a small increase in fetal liver activity. A newborn guinea pig, after injection, showed a similar small increase. Twenty-four hours after birth, when liver tryptophan peroxidase activity had attained adult levels, the increase in activity following injection was as great as in the adult (Fig. 1).

As Knox has shown, the controlling mechanism increasing tryptophan peroxidase activity in adult liver after L-tryptophan injection is substrate induction (*3*). The relative refractoriness of fetal liver to L-tryptophan suggests that substrate induction is not the rate-limiting mechanism controlling the changes in enzyme activity observed during development.

In brief, the observations discussed above were made in the following manner. Assay of tryptophan peroxidase activity was carried out in 12.5-percent homogenates, as described by Knox (*5*). All assays were done on single livers. Conversion of L-tryptophan to kynurenine was measured. This is a two-step reaction; the first step is catalyzed by tryptophan peroxidase, the second, by formylase. Formylase is not rate-limiting in the over-all reaction in adult or fetal guinea-pig liver homogenates, for formylkynurenine, the product of the first step, does not accumulate. Also kynurenine is not metabolized in such homogenates, so the over-all conversion of L-tryptophan to kynurenine is a measure of tryptophan peroxidase activity.

To study the effect of L-tryptophan on liver tryptophan peroxidase activity, an animal was given 1 mmole of L-tryptophan intraperitoneally for each 200 g of weight. After 5 hours the animal was sacrificed by cervical dislocation, and the liver was assayed. Subcutaneous injection of L-tryptophan in the adult was as effective as intraperitoneal injection in raising tryptophan peroxidase activity. Injection of saline was without effect.

L-Tryptophan was injected into fetuses *in utero* in amounts proportional to the estimated weight. The mother was anesthetized with diethyl ether, a paramedian abdominal incision was made, and the fetus was injected intraperitoneally through the uterine wall. After 5 hours the mother was sacrificed, the fetuses were delivered by hysterotomy, and the livers were assayed. Anesthesia and laparotomy alone did not increase maternal liver tryptophan peroxidase activity. Intraperitoneal injection of L-tryptophan into the pregnant animal or into the fetus increased maternal liver tryptophan peroxidase activity about fivefold without affecting fetal liver activity. In all cases the injected fetuses seemed to be normal at the time of sacrifice.

It should be emphasized that the deficit of tryptophan peroxidase activity observed in fetal liver is due to absence of the active enzyme and not to a deficiency of a heat-stable cofactor or to the presence of an inhibitor in the homogenate. This conclusion was reached because the addition of fetal liver homogenate to adult liver homogenate had no effect on the activity found in the latter. Also, addition of a heated extract of adult liver failed to stimulate activity in fetal liver homogenates.

Some enzymes which have no activity in fetal liver until the end of gestation have been found to have little or no activity in certain hereditary diseases (*6*). It has been suggested (*1*) that such a disease can be viewed as a persistence of the fetal condition into postnatal life. One might predict that an inherited deficit will be discovered for each enzyme with a developmental pattern like tryptophan peroxidase. However, an inherited deficit of an enzyme necessary for fetal metabolism would probably elude discovery

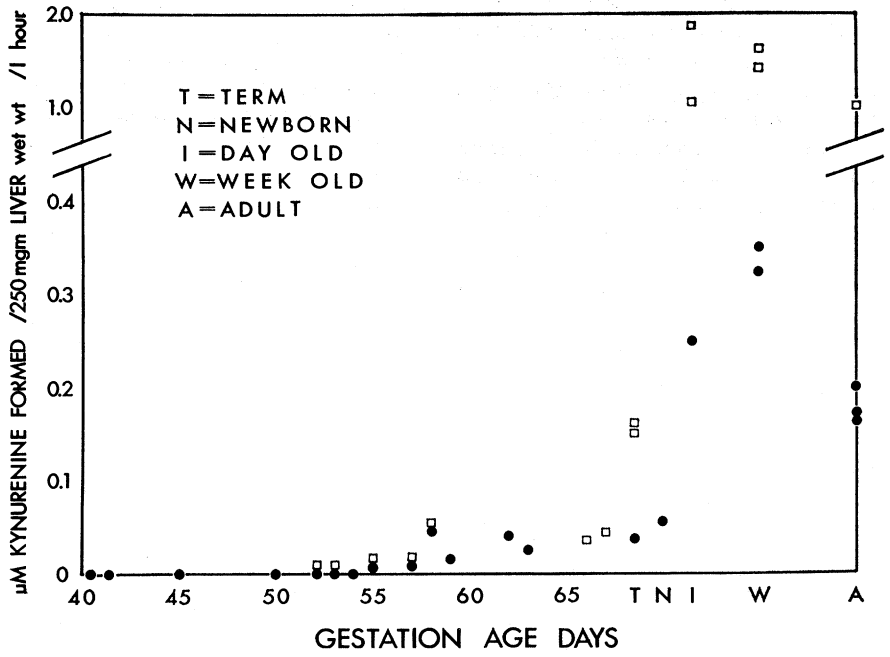

Fig. 1. (Solid circles) Tryptophan peroxidase activity; (squares) tryptophan peroxidase activity 5 hours after injection of 1 mmole of L-tryptophan per 200 g of weight.

because of the likelihood of intra-uterine death. Though, as yet, no inherited disease characterized by a deficit in tryptophan peroxidase activity has been described, a case reported by Baron is suggestive (*7*).

ANDREW M. NEMETH
VIVIANNE T. NACHMIAS*
Department of Anatomy,
University of Pennsylvania,
Philadelphia

References and Notes

1. A. M. Nemeth, *J. Biol. Chem.* **208**, 773 (1954).
2. F. T. Kenny, G. H. Reem, N. Kretchmer, *Science* 127, 86 (1958); N. Kretchmer and H. McNamara, *J. Clin. Invest.* 35, 1089 (1956); A. Brown and W. Zuelzer, paper presented before the 27th annual meeting of the Society for Pediatric Research, Carmel, Calif., June 1957.
3. W. E. Knox, *Brit. J. Exptl. Pathol.* 32, 462 (1951).
4. The research described in this report was supported by U.S. Public Health Service grant No. A-1314.
5. W. E. Knox, in S. P. Colowick and N. O. Kaplan, *Methods in Enzymology,* Academic Press, New York, 1955, vol. II, p. 242.
6. G. A. Jervis, *Proc. Soc. Exptl. Biol. Med.* 82, 514 (1953); G. T. Cori, Harvey Lecture Ser. 48, 145 (1954); N. Kretchmer, S. Z. Levine, H. McNamara, *Am. J. Diseases Children* 93, 19 (1957).
7. D. N. Baron, C. E. Dent, H. Harris, H. Hart, J. B. Jepson, *Lancet* 2, 421 (1956).
* Postdoctoral fellow, U.S. Public Health Service.

29 May 1958

Psychological Brightness Reduction of Simulated Flashes from a Polyhedral Satellite

Abstract optical properties (such as brightness, frequency, and duration) of solar flash reflections to be expected from a polyhedral satellite have been discussed extensively elsewhere (*1*). However, since a leading advantage of such design for an artificial satellite would be the relative ease and certainty of visual observation of it, there remain to be studied further the human visual reactions which might result from such optical properties. In particular, one might ask how the apparent brightness or conspicuousness of the satellite would be affected by the reflected sunbeam's consisting of intermittent pulses having a frequency of perhaps 10 per second and a pulse duration of less than 0.001 second.

Visual response to intermittent illumination is generally described by two psychological theories (*2*). First, Talbot's law states that, for flash rates greater than the "critical flicker frequency," the fused image always appears fainter than a steady source, and of brightness equal to the time-mean brightness (*3*, p. 118). For example, if the image appeared fused at flash frequency of 10 per second, and the flash durations were 0.001 second, the image brightness would be 0.001/0.1, or 1/100 of its steady brightness—that is, it would be reduced by five stellar magnitudes.

But the proper applicability of Talbot's law depends on the flash rate's being above the critical frequency. This critical rate has been extensively measured for various colors and intensities of light. Curves plotted by Hecht (*4*) show that, for night (rod) vision, the critical flicker frequency is about 15 per second, while for fainter and redder sources it may decrease to 10 or below. Hence, although Talbot's law giving a time-mean brightness would hold for polyhedral satellites flashing more than 15 times per second, for lower flash rates it would not be strictly applicable.

It has been shown (*3*, p. 138) that for such flash rates below the fusion frequency the apparent brightness of the flickering light increases continuously with decreasing frequency. Indeed, for day (cone) vision and light-to-dark ratios of at least 1 to 1, the enhancement effect, discovered by Bartley, gives, for a frequency of about 9 per second an apparent brightness actually greater than the steady brightness, by a factor equal to the reciprocal of that given by Talbot's law. However, the Bartley effect for a light-to-dark ratio as low as the expected 1 to 100 of a polyhedral satellite seems not to have been investigated by the psychologists.

Nevertheless, it appears certain that, for frequencies below that of fusion, the brightness above the time-mean would generally increase with decreasing frequency, so that, for zero frequency, it would always equal the steady brightness. As an approximation hypothesis one might assume, for a constant light-to-dark ratio, a linear logarithmic increase of brightness with decrease of frequency—that is, a linear variation of apparent stellar magnitude in proportion to frequency below that of fusion. Thus, for the above example in which brightness at the fusion frequency of 10 per second was reduced by five magnitudes, the reduction at a frequency of 4 per

Table 1. Diminution of the intermittent image for three typical flash rates.

Star	Steady magnitude	Flashing magnitude	Dimming
Run No. 1 (frequency, 3.3/sec; duration, 0.00152 sec)			
Jupiter	−1.4	+1.2	+2.6
Vega	+0.1	+1.8	+1.7
Arcturus	+0.2	+1.2	+1.0
Saturn	+0.5	+2.7	+2.2
Altair	+0.9	+1.8	+0.9
Spica	+1.2	+3.8	+2.6
Mean dimming			+1.8 ± 0.2
Run No. 2 (frequency, 6.2/sec; duration, 0.00081 sec)			
Jupiter	−1.4	+0.7	+2.1
Arcturus	+0.2	+1.9	+1.7
Spica	+1.2	+3.4	+2.2
Mean dimming			+2.0 ± 0.1
Run No. 3 (frequency, 7.7/sec; duration, 0.00065 sec)			
Jupiter	+1.4	+1.4	+2.8
Arcturus	+0.2	+2.2	+2.0
Spica	+1.2	+3.3	+2.1
Mean dimming			+2.3 ± 0.2

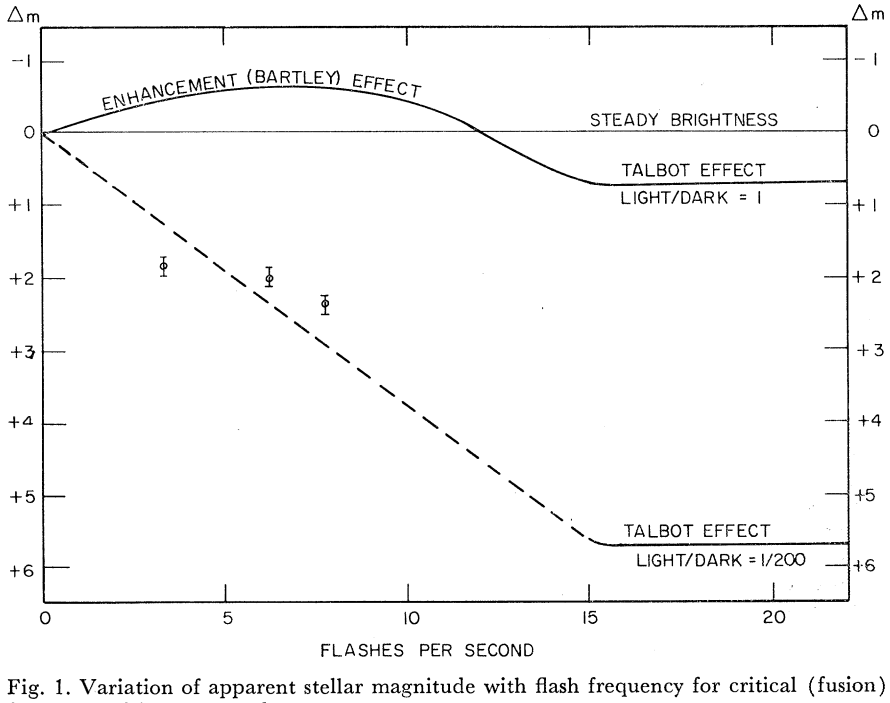

Fig. 1. Variation of apparent stellar magnitude with flash frequency for critical (fusion) frequency of 15 per second.