racy of Eq. 6 is also strengthened by the fact that, after substituting Eq. 6 into Eq. 3, I was able to approximate the η of Hb solutions prepared from dog and goat bloods; 2.8 for the predicted compared to 3.3 for the observed (*7*).

For all values of M, at the low Hb concentrations, an increment in C_{Hb} results in an increase in O_t (Fig. 2). However, at some point, which is peculiar to the molecular weight of the Hb, O_t reaches a maximum value and then decreases with further increments in C_{Hb}. The shape of the curve for O_t lends itself to analysis to determine the components of Eq. 5 that affect the point of $O_{t,max}$; that is, where the slope of the O_t line is zero (*3*). By taking the first derivative of Eq. 5 with respect to Hb and setting the derivative to zero one obtains the conditions at $O_{t.max}$:

$$\delta O_t/\delta C_{Hb} = 0 = 1/k_3 M^a \quad (7)$$

In other words, $O_{t,max}$ is determined by the inverse of M (*3*). Thus, for hemoglobins of lower molecular weight, not only is O_t higher at any given concentration of Hb, but $O_{t,max}$ is also further to the right (Fig. 2). These combined effects of M on O_t result in a fourfold increase in $O_{t,max}$ when M is reduced from 1×10^6 to 7×10^4 (Fig. 2).

The enclosing of the Hb in corpuscles appears to be requisite for a reduction in M. Freely dissolved molecules in the mammalian circulatory system must have a large molecular weight if they are not to be lost via excretory filters. For example, mammalian Hb in solution will pass the glomerular filter. Animals with Hb's of low molecular weight in solution do exist (*1*), but these animals have no excretory filters (*8*). Where fluid filtration does occur, a mechanism that would avoid loss of Hb would be packaging the molecules in corpuscles. An additional problem is that if the Hb in mammalian blood were in solution, the plasma osmotic pressure would be increased approximately threefold (*9*). The effects of such a high osmotic pressure would be profound, because normal fluid distribution and flow could only be achieved by a comparable increase in blood pressure. Through cation impermeability, the corpuscle membrane serves not only to localize the Hb, but to remove it from the plasma osmotic space as well (*9, 10*). Thus, corpuscles appear to be an evolutionary step in obtaining high concentrations of Hb. However, this is not necessarily because of the effects of the corpuscles on η. In fact, it has been suggested that corpuscle suspensions have greater viscosities than do Hb solutions of comparable oxygen capacity (*2*). However, the viscosity of a corpuscle suspension is markedly reduced when flow occurs through tubes of small radial dimensions (*11*). Because in the circulatory system, this is the area where resistance to flow is the greatest, the anticipated high viscosities of corpuscle suspensions are not realized (*12*).

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Congenital Anomalies Induced in Hamster Embryos with Ribavirin

Abstract. *Ribavirin, when given to pregnant hamsters in relatively small single doses, induces congenital anomalies of limbs, ribs, eyes, and central nervous system, as well as fetal deaths, On the basis of these findings, caution should be used in giving ribavirin to women of child-bearing age.*

As recently summarized by Maugh (*1*) ribavirin (1-β-D-ribofuranosyl-1,2,4-triazole-3-carboxamide) has a wide spectrum of antiviral activity. Maugh points out that teratogenicity is a characteristic of antiviral agents that are nucleoside analogs and that ribavirin causes defects after it is ingested by female rodents. Nothing, however, has been published on this subject as far as we are aware. In this report we show that ribavirin (Virazole, ICN Pharmaceuticals) is an extremely effective teratogen when given to pregnant hamsters.

Hamsters of the LVG strain (Lakeview) were purchased from Charles River and injected intraperitoneally on gestation day 8. The single doses used (diluted in 0.5 to 1 ml of buffered saline; 1.25 to 4.2 mg of ribavirin per kilogram of body

Table 1. Effects of ribavirin on fetal development when given to pregnant hamsters in a single dose intraperitoneally on gestation day 8.

Ribavirin (mg/kg)	Number of gestation sacs (22 mothers)	Resorptions		Normal fetuses		Abnormal fetuses	
		Number	Percent	Number	Percent	Number	Percent
1.25	35	4	11	29	83	2	6
2.1	30	1	3	15	50	14	47
2.5	62	13	21	15	24	34	55
3.1	67	9	13	35	52	23	34
4.2	64	24	37	3	4	37	57
6.25	23	23	100				

*Percentages refer to numbers of gestational sacs.

Table 2. Frequency and distribution of malformations in 106 abnormal fetuses of mother hamsters that received ribavirin. CNS, central nervous system.

Parameters	Defects*				
	Limb	Eye	CNS	Rib	Other
Fetuses with malformations	85	32	18	45	27
Frequency (%)	80.1	30.1	17	42.5	25.4

*For details of types, see text.

weight) were well below those used in treatment of viral infections of hamsters by Sidwell *et al.* (*2*).

Inoculated animals were killed with ether and examined on gestation day 14. Tables 1 and 2 show that ribavirin had a potent effect in inducing fetal deaths (resorptions) as well as malformations. The most common abnormalities were limb defects. Others listed in Table 2 were eye malformations, ranging from microphthalmia to complete absence of the eye (anophthalmia), encephaloceles, exencephaly, rib defects, and one case of occult spina bifida.

The range of abnormalities of the extremities (single missing digit to complete amelia) were similar to those induced by cadmium in the same animal model (*3*) as well as to those which resulted from the unfortunate use of thalidomide in early human pregnancies (*4*). Should ribavirin be licensed for marketing, warning to prevent its use in the pregnant woman would seem mandatory for, if the findings in hamsters are applicable to man, ribavirin might cause either fetal death or congenital anomalies.

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Monocular Deprivation: Morphological Effects on Different Classes of Neurons in the Lateral Geniculate Nucleus

Abstract. *Retrograde axonal transport of horseradish peroxidase from areas 17 and 18 of the cat's visual cortex labels, principally, the small (X) and large (Y) cells, respectively, of the lateral geniculate nucleus. Quantitative analysis of the sizes of these morphologically identified neurons after monocular deprivation shows that the arrest of cell growth in the deprived laminae involves mainly Y cells.*

The lateral geniculate nucleus (LGN) of the cat contains neurons of widely varying sizes and shapes (*1*, *2*). In particular, there is a small population of very large cells, which is clearly visible in Nissl-stained sections.

If one eye of a kitten is deprived of vision by suturing the eyelids together within a sensitive period during the first 3 months of life there is a retardation of neuronal growth in the laminae of the LGN innervated by the deprived eye, compared with the laminae receiving axons from the experienced eye (*3*), and very large cells are not detectable in the deprived laminae. However, it is not clear whether there is an overall lack of growth of cells of all sizes, or whether the large cells are affected specifically and become indistinguishable from the small cells.

There is physiological evidence that the responses from a specific cell type become harder to record in the deprived laminae of the LGN of cats with monocular lid suture (*4*). The hypothesis that LGN cells can be divided into different types stems from the observation that retinal ganglion cells which project to the main laminae of the LGN can be classified, on the grounds of their response properties, into X and Y cells (*5*). This classification has a morphological basis: Y cells in the retina probably correspond to the largest ganglion cells, and X cells to the smaller ones (*6*). Furthermore, retinal Y cells conduct rapidly to the thalamus where they relay with Y-type cells in the LGN, which have fast conducting axons to the visual cortex; retinal X-type cells, however, influence geniculate X cells, and thence the cortex, by slower axons (*7*). Rapid conduction is a feature of large axons, derived, presumably, from large neuronal somata. The specific loss found after monocular deprivation was in the percentage of recordable Y cells in the LGN, and it has been postulated that the lack of morphologically large cells after monocular lid closure is correlated with these findings (*8*). We now have morphological evidence that monocular deprivation does indeed cause a selective failure of growth among the Y cells of the LGN.

We sought a method of labeling X cells and Y cells selectively in the LGN of the cat, based on the observation that lesions of area 17 of the visual cortex cause retrograde cell degeneration mainly in small or medium cells, while after lesions of both areas 17 and 18 the large cells are also involved (*9*). This suggests that the small cells project mainly to area 17 and the Y system to both 17 and 18, a hypothesis supported by physiological evidence (*7*).

In the present study, horseradish peroxidase (HRP) (Sigma type VI or Boehringer grade 1) was injected into the visual cortex of five cats anesthetized with Althesin or Ketamine. One of these animals (N1) was a normal adult and the others were kittens 10 to 12 weeks old which had undergone suture of the right eyelids at the age of 1 week (MD1, MD3, and MD4) or 40 days (MD2). The injections were restricted to area 17 on one side of each brain and to area 18 on the other. A total of 1 to 2 μl of 30 percent HRP distributed over three or four penetrations was injected by pressure in each hemisphere, either through a Hamilton microsyringe needle or a glass micropipette. After a survival time of 1 to 3 days, the animals were perfused through the heart with a buffered mixture of aldehydes. A block containing the visual cortex and the LGN was washed in buffered sucrose, frozen, and sectioned coronally at 40 μm; the sections were incubated in di-

Table 1. Results of measurements of cross-sectional areas of LGN neurons.

Animal	Injection (side and area)	Mean cell areas in LGN ipsilateral to cortical injection (μm^2)					
		All cells sampled			Labeled cells		
		Undeprived lamina	Deprived lamina	Difference* (%)	Undeprived lamina	Deprived lamina	Difference* (%)
MD1	Left 17	328	190	42	317	241	24
MD3	Left 17	399	266	33	402	291	28
MD4	Right 17	361	278	23	350	301	14
MD1	Right 18	317	204	36	401	188	53
MD2	Right 18	506	333	34	682	344	50
MD3	Right 18	491	274	44	532	255	52
MD4	Left 18	522	279	47	592	216	64

*Difference as percentage of larger figure. All differences are significant at $P < .005$ (Student's t-test).