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## **Response to Dr. Blakemore's Assertion that Work Involving Nonhuman Animals has Led to Significantly Greater Understanding and Treatment of Amblyopia.**

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I will not repeat the points made in Dr. Gill Langley's excellent response to Dr. Blakemore's claims, entitled "Blinded by Science."<sup>1</sup> Being skeptical that a non-ophthalmologist might have misconstrued some of the information, I independently verified each of her references and representations. I could find nothing that detracted from her conclusion that Dr. Blakemore's claims were specious at best. Her work should put to rest any claims by Dr. Blakemore that his or similar work is responsible for improved diagnosis or treatment of amblyopia or strabismus. Additional references confirm that there has been essentially no change in concepts or in treatment methodologies over the last 100 years or more.<sup>2,3</sup>

It is my professional opinion that Dr. Blakemore's work has essentially no applicability to the human situation. His research involves nonhuman animals that have *major* differences from humans in the development and structure of their visual systems.<sup>4-7</sup> For example, cats do not have a macula or fovea, two regions of the retina of primary importance for human vision. These areas account for essentially all useful vision occurring in the human. The area of the brain responsible for vision and the circuitry of the nerves are considerably different between the human and the cat. Although there are some general similarities between humans and cats, the differences are so great that the results obtained in this work do not appear to have had any meaning for humans.<sup>8,9</sup> The cat "model" cannot predict what changes may occur in humans when vision is deprived either monocularly or binocularly. Furthermore, the experimental situation in the cat is entirely artificial, a perturbation of an otherwise normal animal. Spontaneously occurring visual deprivation in human children, however, is often associated with other developmental defects which tend to modify

and confound the situation.

The information necessary to help humans with disorders related to vision development have been derived from human work and will continue to be most effectively studied in humans. For example, we have learned a great deal by studying people who have lost an eye early in life, who have had untreatable or untreated opacification of the ocular media early in life, or who have had other perturbations of their developing visual system for reasons unrelated to the eye.<sup>9</sup> These conditions are not uncommon and would provide the necessary perturbations to understand how vision develops in the human being. There have been many of these studies done in humans,<sup>8-16</sup> and these, not studies such as those of Dr. Blakemore, have led to the most important information on vision in humans.

When reviewing Dr. Blakemore's statements and work, one must bear in mind that his research is neurophysiological with some anatomical correlation; he records from cells in the brain. This work does not measure vision and actually has little to do with vision in terms of behavior and function. He even alludes to this in his own publications.<sup>17</sup>

I will next address specific inaccuracies in Dr. Blakemore's publication, "A reply to criticism of experiments involving visual deprivation," dated September 1987.

On page one, he states, "The surgical procedures carried out on the eyes of animals are essentially similar to those employed in human patients - closing the lids (tarsorrhaphy) is commonly performed in people to protect injured eyes; eye-muscle surgery is used to straighten the eyes in humans with squint (strabismus)."

It should be obvious that a serious flaw in his argument is that the procedures being done in humans are being done for their benefit. This is not the case for the nonhuman animals in his experiments for they are normal and the procedures are entirely unnecessary. Furthermore, his method of tarsorrhaphy is to excise (cut away) the entire eyelid margin and suture the skin and conjunctivae separately.<sup>18</sup> This is most certainly *not* the manner in which it is done in humans, for it would lead to permanent closure of the eyelids, a condition incompatible with sight.

Later on page one, Dr. Blakemore explains that amblyopia "...was poorly understood until about 25 years ago when experimental research involving animals began to tackle the question of its origin ... in the absence of

any real knowledge of the cause of the disease there was no single agreed method of treatment." This is a preposterous statement that simply denies or ignores the facts. As Dr. Langley has shown, treatment for amblyopia had been successfully accomplished many years before the experimental work was even considered.<sup>1</sup> Furthermore, there is no question that essentially all of the hypotheses examined by experimental work were known by physicians in this field years before the experimental work was done. These hypotheses were developed and confirmed in human patients. Moreover, the experimental work did not have anything to do with vision per se because it was primarily neurophysiological rather than behavioral in nature. It is most immodest of Dr. Blakemore to claim for himself or his contemporaries the credit for discoveries that were made years before by others.

Dr. Blakemore does previous ophthalmologists a grievous injustice concerning the treatment of amblyopia. All available evidence clearly indicates that there has been no improvement in the treatment of amblyopia since the early part of this century. In addition to the information brought to light in Dr. Langley's work,<sup>1</sup> Abraham makes the following comments concerning Claud Worth, an ophthalmologist who retired from practice in 1918:

Here, almost 80 years later, we are given a chance to evaluate his work. It is surprising how little change seems indicated, how little has been added to the major store of knowledge as he presented it, at least from the practical viewpoint ... Worth's emphasis on *early treatment of the error of refraction and the amblyopia is still the keynote of the most rational approach to the treatment of the strabismic child...*<sup>2</sup>

Along the same lines, on page two Dr. Blakemore contends that the several associations of certain conditions with amblyopia were first made in the early 1960s. However, these associations were known at least 50 years previously, as has been adequately documented by Dr. Langley<sup>1</sup> and others.<sup>2,3</sup>

Later on page two Dr. Blakemore states that "...before the animal research began it was not known whether squint could *cause* amblyopia or whether the existence of poor vision in one eye *causes* the squint." This simply is not true. For example, Claud Worth, mentioned previously, had

made the proper association in the nineteenth century.<sup>2</sup> Dr. Blakemore then implied that experimental work provided the answer, because there was "...no clear view about the time of onset or duration of the period of sensitivity to the disease." Even if this were true, and it is not, how could experimental work in monkeys or cats on something as species-specific as development provide any answers for humans? Dr. Blakemore's own work has shown that there is wide disparity concerning the sensitive period between nonhuman primates and humans.

On page three, Dr. Blakemore uses von Noorden's name in an attempt to support his position. However, von Noorden has been critical of vision deprivation research done in the cat because it is scientifically unsound.<sup>8,16,19</sup>

Then, Dr. Blakemore lists several findings with respect to amblyopia which are incorrectly attributed to experimental work. For example, ophthalmologists had known long before Dr. Blakemore was alive that they must alternately patch eyes or else amblyopia would develop in the better eye.<sup>1</sup> Similarly, ophthalmologists have been recommending early diagnosis and operation for strabismus (squint) long before any experimental work had been done.<sup>1-3</sup> Clinicians recognized that there was a sensitive period in childhood before a sensitive period was demonstrated in nonhuman animals. Also, ophthalmologists have encouraged early diagnosis of anisometropia (unequal refraction between eyes of the same individual) for decades.

On page four, Dr. Blakemore states that "...removal of an eye ... is much less common than it used to be because of progress in the understanding of such diseases that have come through animal experimentation."

This is untrue and illustrates a lack of understanding by someone not trained as a clinician. Eyes still are removed (enucleated) for the same pressing reasons that justified removal in the past. I can think of no condition involving nonhuman animal experimentation that has led to a reduction in the need for enucleation. For example, eyes with cancerous conditions are frequently removed in order to save the patient. Decades of research, artificially induced ocular cancer in nonhuman animals has had essentially no effect on this group of conditions.

There is one situation in which there has been a reduction in enucleation, but not because of experimentation of any type. This is the situation known as visceral larva migrans, a condition caused by the migration of

*Toxocara canis* larvae in young humans. The organism cannot establish itself in humans because humans are not the proper host. Therefore, the larvae migrate throughout the body, sometimes ending up in the eye to cause a granulomatous inflammatory response, which was often confused with a childhood cancer known as retinoblastoma. Because retinoblastoma is highly malignant, ophthalmologists tended to enucleate the involved eye if there was a suspicion of cancer. A worker in a pathology laboratory recognized, however, that many of these eyes did not have the cancer. Rather, they had inflammation centered around a parasite, which she could not recognize. She called upon a veterinarian for help, and a diagnosis of visceral larva migrans was made. Subsequently, more circumspection was used in diagnosing retinoblastoma in children and many eyes were saved. Therefore, there is no information to support Dr. Blakemore's statement. Indeed, experimentation was not involved in one discovery that did prevent some unnecessary enucleations.

Dr. Blakemore does make some irrefutable statements in his critique of September, 1987. On page six, he states, "Animal experimentation is an important moral and scientific issue, worthy of the most serious debate. That debate is not advanced by deliberate distortion, misrepresentation and trivialization..." Unfortunately, he clearly is guilty of his own charges, as is seen by his comments in his critique. And, in a letter to one of my associates, dated October 18, 1988, he embarrasses himself further by chastising Animal Aid, an organization vitally concerned with human and nonhuman animal health, with allegations of which only he is guilty: "...misrepresentation, distortion and straight factual inaccuracies..."

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