Autoregulation of optic-disk oxygen tension*

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A micro-oxygen sensor was used to monitor the optic-disk oxygen tension in vivo in the cat. The perfusion pressure of the eye, defined as the systemic arterial blood pressure minus the intraocular pressure, was decreased. This was accomplished both by lowering the systemic arterial blood pressure by increasing the expiratory resistance and by elevating the intraocular pressure. The result of lowering the perfusion pressure of the eye was an initial decrease in the optic-disk oxygen tension and then a return to normal within approximately one minute. This autoregulation of the optic-disk oxygen tension was decreased by hypoxia and eliminated by hypercapnia. It was concluded that this autoregulation is a physiologic adjustment for homeostasis of the optic-disk tissue.

Key words: oxygen tension, optic disk, autoregulation, micro-oxygen electrode, intraocular pressure, ocular hypertension, perfusion pressure, hypoxia, hypercapnia, cat.

Autoregulation of blood flow may be defined as the intrinsic tendency of an organ to maintain constant blood flow despite changes in perfusion pressure. This homeostatic mechanism has been demonstrated in many tissues and most recently the phenomenon was shown to occur in the retinal vasculature. It is known that the optic-disk circulation is extremely sensitive to changes in the perfusion pressure (blood pressure-intraocular pressure). Further, a recent study of the blood flow of the optic-disk using radioactively labeled microspheres suggests that the vasculature of the prelaminar portion of the optic nerve does not autoregulate. The study herein reported was undertaken to measure the effect of changes in the perfusion pressure on optic-disk oxygen tension in order to determine if the oxygen tension is autoregulated.

Materials and methods

Thirty-one adult cats, both male and female of mixed breeds, were used. The animals were a part of a separate study of optic-disk oxygen-tension measurement. The animals were prepared and optic-disk oxygen tension measured as previously described. In brief, the technique consisted of placing the tip of an oxygen microelectrode (micro-oxygen sensor No. 721, Transidyne General Corp.) 10 microns from the surface of the center...
Fig. 1. The systemic blood pressure was decreased by increasing expiratory resistance. The oxygen tension of the optic disk decreased but then returned to a level higher than the control value. The time marks are at five-second intervals.

Results

The mean systemic blood pressure was decreased 50 mm Hg and maintained at this level (Fig. 1). The intraocular pressure was held constant so that the perfusion pressure, defined as the mean systemic arterial blood pressure measured in the femoral artery minus the intraocular pressure, decreased to approximately half its control value. The optic-disk oxygen tension initially decreased 8 mm Hg, but then returned to control levels and overshot 2 mm Hg after 30 seconds.

When the perfusion pressure was decreased by elevating the intraocular pressure there was an associated movement of the optic disk because of the expansion of the globe with an increase in the intraocular volume. Fig. 2 is a photograph of a segment of one of the polygraph records obtained when the probe was pulled moving the electrode with the micromanipulator.

Hypoxia was produced by the administration of 10 per cent oxygen in nitrogen from an inflatable bag attached to the respirator. Hypercapnia was similarly induced with a mixture of six per cent carbon dioxide in air.
Fig. 2. The microelectrode was abruptly withdrawn at A and then reinserted to its original position at B.

abruptly back elevating it 0.4 mm. off the optic disk and then moving it back into position. It is evident that the optic-disk oxygen tension falls 7 mm. Hg and remains at this new level until the probe's position is restored. There is only a two to three second latency and there is no overshoot after the tip is repositioned.

When the intraocular pressure was elevated and maintained at a new level, the optic-disk oxygen tension decreased and then returned to normal. The minimal increase in the intraocular pressure that resulted in a measurable decrease in optic-disk oxygen tension was 10 mm. Hg. When the intraocular pressure was returned to control levels, there was an overshoot of the optic-disk oxygen tension. A combination of elevating the intraocular pressure and lowering the blood pressure resulted in a decrease of the perfusion pressure to 10 mm. Hg (Fig. 3). The optic-disk oxygen tension did not return to normal until the blood pressure was normalized, and then there was an overshoot.

The inspiration of 10 per cent oxygen in nitrogen resulted in a decrease in optic-disk oxygen tension of 3 mm. Hg and the response to a decrease in perfusion pressure was diminished. The inspiration of six per cent carbon dioxide in air resulted in an increase of approximately 50 per cent in the optic-disk oxygen tension. During hypercapnia, however, the optic-disk oxygen tension did not recover after decreasing secondary to elevation in the intraocular pressure (Fig. 4). The decreases in the perfusion pressure were less than those which had prevented a recovery of the optic-disk oxygen tension during air breathing.

Discussion

It is evident from the results herein reported that optic-disk oxygen tension is autoregulated in the most strict sense of the term. There is an intrinsic tendency on the part of the tissue of the optic disk to maintain constant oxygen tension despite changes in the perfusion pressure. Whether the perfusion pressure was decreased by lowering the blood pressure or by raising the intraocular pressure, within limits and after a relatively short latency, the average optic-disk oxygen tension returned to normal (Fig. 1). This oxygen autoregulation presumably is a physiologic adjustment on the part of the optic-disk circulation and
perhaps the tissue itself to maintain a constant *milieu intérieur*.

It is important to consider the possible sources of error arising from the methods used to reduce the perfusion pressure. It has already been stated that increasing the expiratory resistance did not decrease the partial pressure of oxygen in the systemic arterial blood. It might be expected that the intraocular venous pressure would decrease (although systemic venous pressure increased slightly) but no movement of the probe relative to the disk was observed. When the intraocular pressure was elevated, however, the tip of the probe moved away from and over the optic disk. To determine the significance of this movement, an experiment was carried out in which the probe was purposefully moved. The results indicate a relatively small change in the optic-disk oxygen tension and no overshoot (Fig. 2). Another problem encountered with the use of the oxygen microelectrode is its temperature sensitivity. As previously reported, there is a six per cent change in the current for each 1° C. change in the temperature.\(^5\) It has been previously shown, however, that the temperature decrease with elevations of the intraocular pressure of the magnitude used in this study were on the order of 0.01° C. and thus did not appreciably affect the oxygen measurements.\(^6\)

Classically, autoregulation refers to the maintenance of a constant blood flow. The cerebral blood flow autoregulates if the blood pressure decreases or if the spinal fluid pressure increases.\(^7\) Although the optic disk of the cat appears on ophthalmoscopy to be avascular, there is a thick network of capillaries in front of the lamina cribrosa.\(^*\) Further, there is some evidence that the circulation of the optic disk is able to respond to stress by a hyperemia. In a previous study of the intraocular pressure-induced alterations in optic-disk blood flow measured by a thermocouple, a transient hyperemia was shown to occur when the intraocular pressure was normalized.\(^3\) This overshoot in the optic-disk circulation was similar to the overshoot in oxygen tension following normalization of the perfusion pressure (Fig. 3). For technical reasons the temperature measurements in

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Fig. 3. The intraocular pressure was increased and the optic-disk oxygen tension decreased and then returned to normal. The perfusion pressure was further lowered by decreasing the blood pressure. The optic-disk oxygen tension did not overshoot and return to normal until the blood pressure was normalized.
Optic-disk oxygen tension

Fig. 4. Hypercapnia eliminated the return to the base-line of the optic-disk oxygen tension normally seen when perfusion pressures were reduced to similar levels during air breathing.

The previous study could not be used to obtain further information about the regulation of the optic-disk circulation. Nonetheless, lack of blood flow to the tissues is known to cause vasodilation and this is a form of autoregulation.

Hypoxia, which might be expected to cause dilation of the vasculature in response to tissue factors, and hypercapnia which is known to be a strong vasodilator, inhibited autoregulation. This suggests that the factors responsible for autoregulation are at least partly vascular. The recent optic-disk blood-flow studies with radioactively labeled microspheres, however, suggests that the circulation does not autoregulate. Part of the interpretation of the microsphere data is based on the idea that the peripapillary choroid is the source of the vasculature to the prelaminar portion of the optic nerve. It is hypothesized that elevations in the intraocular pressure cause a decrease in blood flow in the relatively low-pressure choroidal vascular system and that this is related to a loss of optic-disk circulation and accounts for the functional loss seen in glaucoma patients. The anatomic evidence, however, for a significant peripapillary choroidal vascular contribution to the prelaminar optic nerve is not completely clear. Further, there is fluorescein angiographic evidence that the peripapillary choroid does not contribute to the vasculature of the optic disk. Further studies are obviously needed on the circulation of the optic disk.

The restoration of normal blood flow by a decrease in vascular resistance after the perfusion pressure is lowered is only one of the ways in which oxygen may be autoregulated. The extraction of oxygen from the blood could increase and thus maintain the tissue oxygen tension in spite of a decreased perfusion pressure. It is not known if this occurs and the information would be very difficult to obtain since the disk venous drainage is into the central retinal vein along with the entire inner retina. A third possible mechanism for the autoregulation of tissue oxygen tension is a more efficient distribution of the local blood flow. With a reduction in perfusion pressure presumably the blood flow decreases, but if there was an associated increase in the number of capillaries perfused, the average tissue oxygen tension...
could remain constant. To obtain information about the distribution of oxygen in tissue, it is necessary to obtain simultaneous recordings from a battery of microelectrodes placed in close approximation to the capillaries. Changes in the resulting histogram would give information about the distribution of the tissue oxygen tensions while the single electrode herein described gave only average values.

Finally, and most important to consider, is the possibility that the average extracellular oxygen tension remained normal at the expense of cellular utilization of the oxygen. There is evidence from work on the brain using intracellular oxygen electrodes that certain nerve cells cease firing and essentially go into a resting state when the extracellular oxygen tension decreases.\textsuperscript{15} If this is taking place in the retinal ganglion cell axons at the optic disk, there could be nerve destruction even though the average extracellular oxygen tension was normal.

REFERENCES