Transient Unilateral Loss of Vision Associated With Oxygen at High Pressure

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Transient, unilateral diminution of vision was produced by exposure for six hours to 2.0 atmospheres (atm) of inspired oxygen in a symptom-free individual with a past history of retrobulbar neuritis. Two distinct processes appear to have been involved in producing the visual disturbance. One is considered to have been an acute expression of oxygen effect on neuronal elements by direct action on enzymes or limitation of nutrient flow. A second process is considered to have been a recrudescence of retrobulbar neuritis. This case emphasizes the need for detailed evaluation of all individuals exposed to oxygen at greater than normal pressures.

OXYGEN at high pressure is both a therapeutically useful and toxic substance. As the number of facilities for treatment and therapeutic research with hyperbaric oxygen increases, the clinical usefulness of hyperoxic therapy must be considered in relation to its various potential dangers. The local toxicity which can lead to death from pulmonary damage[1] can conceivably affect any tissue or organ which receives a high dose (partial pressure) of oxygen for a prolonged period of time. One such organ, for which the rate of development of oxygen toxicity has not been established, is the normal eye. Many studies of the effects of high oxygen pressures on various aspects of human visual system function have been carried out, however, with particular reference to retinal vasoconstriction,[2-8] constriction of peripheral visual fields,[9-11] and the rate of oxygen utilization by the compressed globe.[12,13] The results of these and other studies of the effects of hyperoxia on the normal eye have recently been reviewed.[14,15]

Investigations of the influence of high partial pressures of oxygen on the eye affected by disease processes have been limited to observations of changes in the vasoconstrictive response to transient periods of hyperoxia in diseases with generalized vascular involvement such as atherosclerosis and diabetes mellitus.[4] Additionally, a few cases of retinal artery occlusion,[8,16-18] retinitis pigmentosa,[18] central serous retinopathy,[8] and diabetic retinopathy[8] have been reported which were treated for brief periods with increased partial pressures of oxygen. In none was there any lasting improvement in the vision with oxygen therapy, or was any visual complication of therapy reported. However, the influence of hyperoxia on the eye affected by disease processes is unknown for the periods of time used to treat patients with such conditions as gas gangrene, and the abnormal eye may have quite a different oxygen tolerance from the normal.

The present case, illustrating extreme susceptibility to effects of oxygen, occurred during a study of the pulmonary tolerance of human subjects to oxygen inhalation at 2.0 atm absolute pressure. One individual with a past history of a unilateral retrobulbar neuritis developed a prominent but transient effect upon his vision in the previously affected eye during the period of high-oxygen pressure breathing. The early and gross decrease in vision produced in this individual by oxygen inhalation at 2.0 atm absolute pressure represents a visual effect of oxygen at a level of pressure, and for an exposure time common in diving and in hyperbaric

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oxygen therapy, and at a level where visual disturbance has not been encountered in normal subjects.

Report of a Case

In December 1963, the patient, a 21-year-old male student, noted the onset of a dull pain in his right eye on lateral gaze. Over the following two to three weeks, he found that his ability to read with this eye was diminishing. Tangent screen examination by an ophthalmologist at that time revealed two paracentral scotomas in his right visual field (Fig 1). His left eye was normal, and the result of a neurological examination at that time was also normal. The diagnosis of retrobulbar neuritis of unknown etiology was made. He was treated with corticotropin (ACTH) and cortisone, and states that his vision returned subjectively to normal in two weeks.

Since that time, the patient has noted a similar pain in his right eye two to four times a year, usually associated with periods of stress and lasting several days. Except for one time, there is no record of any visual disturbances

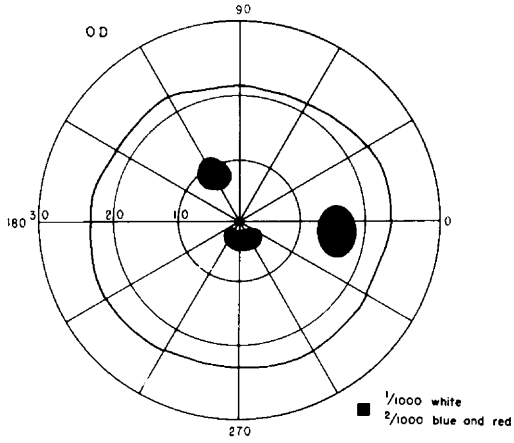


Fig 1.—Tangent screen field of patient in December 1963 during first episode of retrobulbar neuritis. Isopter was obtained with 1-mm white test object at 1-meter with standard illumination. Scotomas were plotted with 1-mm white as well as 2-mm red and blue test objects.

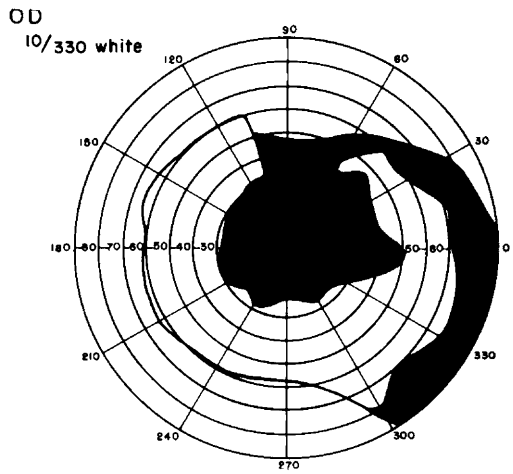
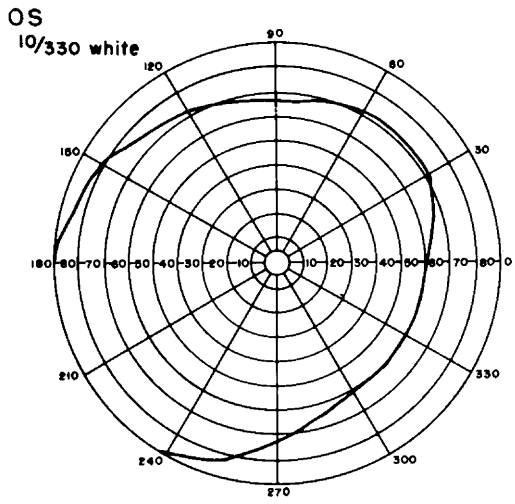
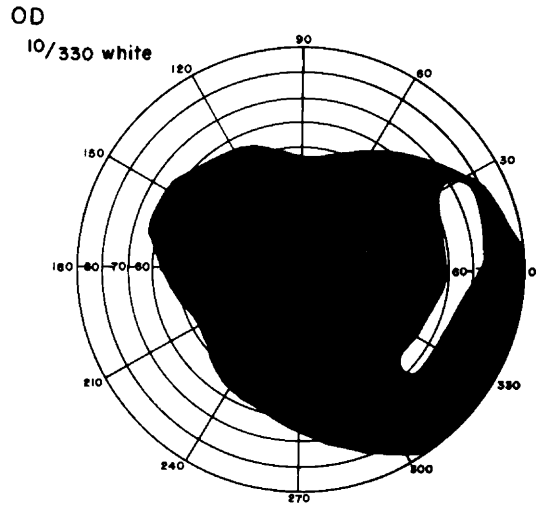


Fig 3.—Perimetric field of right eye 45 minutes after stopping oxygen breathing. This was obtained using 10-mm white object at 330 cm. Left eye was unchanged from that previously recorded.

Fig 2.—Perimetric fields of both eyes obtained after four hours of breathing 100% oxygen at 2 atm absolute. This remained unchanged until oxygen was terminated at six hours. Test object was 10-mm white at 330 cm.





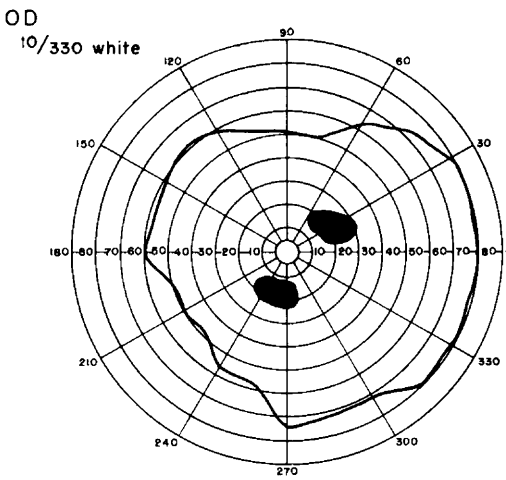
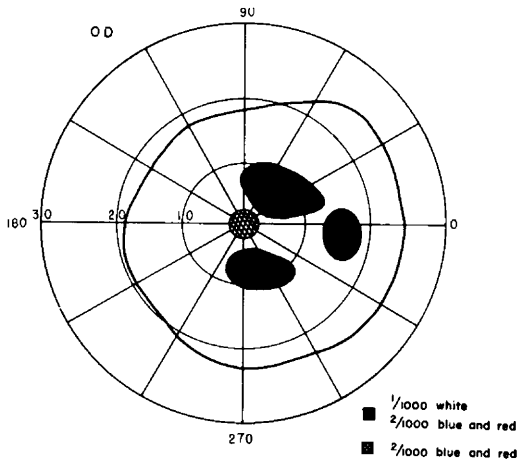


Fig 4.—Perimetric field of the right eye using 10-mm white test object at 330 cm. This was obtained about four hours after oxygen was stopped, and only two dense paracentral scotomas remained.

Fig 5.—Tangent screen fields at 1 meter, 14 hours after oxygen exposure, demonstrated two paracentral scotomas with 1-mm white test object and with 2-mm red and blue test object. Central scotoma was present to colored test objects.



during these periods. In December 1964, approximately one year after the first episode, he had a recurrence of the pain together with a small central scotoma. He was treated with cortisone, and the condition subsided over several days.

In July 1966, four days prior to serving as a volunteer subject for a study of pulmonary oxygen tolerance, the patient's eyes were examined by an ophthalmologist. The study of oxygen tolerance involved continuous exposure to 100% oxygen at 2 atm absolute, to the point of objective evidence of pulmonary oxygen toxicity. Because exposure of subjects to 3 atm

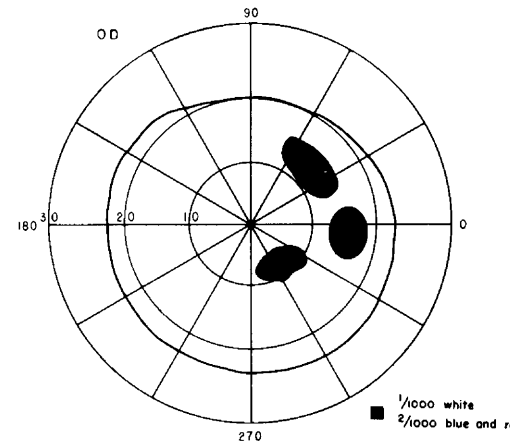


Fig 6.—Tangent screen examination seven days after oxygen exposure could not detect central scotoma to colored objects, and paracentral scotomas using 1-mm white test object at 1 meter were decidedly smaller. Left eye continued to be normal.

oxygen pressure has led to reversible contraction of the visual fields,[9] it was the normal procedure in preparation for this study for all subjects to be examined ophthalmologically, before and after exposure to oxygen. The examination included determination of visual acuity, ophthalmoscopy, and evaluation of the visual fields by tangent screen. The examination of this subject prior to exposure to oxygen was unremarkable except for slight pallor of the right optic disc. Visual acuity was 6/6 (meters/meters) oculus uterque (OU). Examination of the visual field using a variety of both white and colored test objects was prompted by the patient's past medical history; this failed to detect a scotoma. In the absence of influences of oxygen upon the vision of other subjects studied at 2.0 atm pressure, it was elected to proceed with the study.

Before the oxygen exposure commenced, the subject reported that he felt well and had no symptoms referable to retrobulbar neuritis. After breathing 100% oxygen at 2 atm absolute for two hours, he noted a gradual constricting of the temporal field of his right eye, as well as a "bluish haze" before that eye. With his right eye he could see only a blur of letters on the left side of a page of writing, but he could see to read without difficulty with his left eye.

Examinations were begun within the pressure chamber in an effort to identify the nature and degree of the unexpected visual deficit. After four hours of oxygen breathing, he described everything as being dark gray using only his right eye. His visual acuity in this eye was light perception only, while his left eye remained subjectively normal. Perimetry at

this time revealed only a small island of visual function to a 10-mm white test object in his superior temporal field. The left eye was normal (Fig 2). Visual evaluations were continued in the chamber until oxygen breathing was terminated at six hours; the patient then started to breathe room air at 2 atm absolute, and decompression to atmospheric pressure was begun.

The patient described improvement in his visual field in about 15 minutes from the time of discontinuing oxygen breathing, with the peripheral fields returning first. Perimetry 45 minutes after oxygen was stopped showed a large central scotoma with breakthrough to the periphery superiorly (Fig 3). The fields continued to expand over the next three hours, but two paracentral scotomas remained (Fig 4). The result of the ophthalmoscopic examination at this time was normal except for the slight temporal pallor of the right optic disc noted previously.

The patient was examined repeatedly during the postexposure period. Fourteen hours after exposure, the subject complained of pain on movement of his right eye and difficulty reading with that eye. On ophthalmologic examination, the right eye had a visual acuity of 6/7.5, preexposure acuity of 6/6, and an abnormal visual field on tangent screen examination. Two paracentral scotomas to a 1:1,000 white test object, as well as to 2:1,000 blue and red test objects, and a small central scotoma to the colored objects were found (Fig 5). Examination of the left eye was normal. He was subsequently given corticotropin (ACTH), 40 units per day intramuscularly for ten days, with methylprednisolone, 40 mg/day orally.

In daily examinations during the five days after exposure to oxygen, the visual acuity and fields of the right eye remained unchanged. Two days later, however, the examination showed that the central scotoma had cleared and the paracentral scotomas were smaller (Fig 6). Repeated examinations over the next two weeks revealed an increase in the visual acuity of the right eye to 6/6 and clearing of the paracentral scotomas. The methylprednisolone dosage was then decreased progressively over the next week. Under the same conditions, an examination approximately two months after the experiment again showed normal visual fields, but ophthalmoscopy demonstrated a larger area of temporal pallor than had been observed in the initial examination.

Comment

The development of unilateral loss of vision in the case described in this paper is considered to represent the result of concurrent activity of more than one process. One, related to metabolic effects of high oxygen pressures, presumably was responsible for the progressive decrease in the visual field in one eye which cleared within an hour after he began to breathe air. This differed from the symmetrical contraction of the visual fields described by Behnke et al[9] in being unilateral, in the persistence of a small temporal island of vision and in the complete loss of vision around fixation. This contraction of the visual fields is felt to result from enzyme inactivation, with possibly an associated decrease in nutrient flow to the retina.[14] The second process presumably was the recrudescence of a retrobulbar neuritis which became evident after recovery from the acute, oxygen-induced constriction of the visual field. It had the characteristic features described by Kestenbaum[19] of rapid onset, pain, central scotoma, and no immediately detectable change on ophthalmoscopic examination. An increase in the amount of the previous temporal pallor was noted later. It is further considered that the occurrence of unilateral, gross reduction of vision while breathing oxygen at only 2.0 atm represents an exaggerated expression of oxygen effect, brought about by the existence of an underlying defect, neuronal, vascular, or both. Since the reduction of vision occurred in one eye, previously affected with two episodes of retrobulbar neuritis, it will be desirable ultimately to determine the basis for the gross exaggeration of oxygen effect. Aside from a form of increased susceptibility to direct action of oxygen upon enzymatic systems of abnormal neurons, oxygen may conceivably also interfere with neuronal metabolism and function in an abnormal retina or optic nerve indirectly, by way of vascular constriction, with resultant decreased nutrient flow.

The previous history of two episodes of retrobulbar neuritis and the presence of temporal pallor make the existence of some degree of vascular limitation likely in the case presented here. It is not possible to state whether the acute, transient diminution of vision was an expression of a form of oxygen toxicity, was the result of a temporary further restriction of metabolite (eg glucose) delivery to neuronal tissue already

poorly supplied by blood, or was due to a combination of these physical and chemical effects. If only such acute processes had been involved, full restoration of vision could have been expected within minutes or a few hours after terminating exposure to high oxygen pressure. The multiday time course actually required for recovery indicates that the subject had developed a recurrence of his retrobulbar neuritis. It is not possible to state whether this recurrence was induced by oxygen administration, exaggerated by it, or was independent and completely coincidental.

It is clear from this case that high oxygen pressure can induce acute changes in vision where an apparently inactive neurological defect exists. This effect may prove to have considerable clinical usefulness. However, until it is established that oxygen does not, in fact, reactivate a dormant process, patients with a history of retrobulbar neuritis should be considered as hypersensitive to the visual effects of oxygen, and the use of high oxygen pressures as a clinical diagnostic aid in ophthalmology must be explored with care.

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Key Words.—Hyperbaric oxygenation; oxygen, adverse effects; retrobulbar neuritis; vision loss.

Generic and Trade Names of Drugs

Corticotropin—*ACTH.*
Cortisone—*Cortogen, Cortone.*
Methylprednisolone—*Medrol.*

References

1. Fuson, R.L., et al: Clinical Hyperbaric Oxygenation With Severe Oxygen Toxicity, *New Eng J Med* **273**:415-419 (Aug) 1965.

2. Campbell, J.A., and Hill, L.: Concerning the Amount of Nitrogen Gas in the Tissues and Its Removal by Breathing Almost Pure Oxygen, *J Physiol* **71**:309-322 (March) 1931.

3. Cusick, P.L.; Benson, O.O., Jr.; and Boothby, W.M.: Effect of Anoxia and of High Concentrations of Oxygen on the Retinal Vessels: Preliminary Report, *Mayo Clin Proc* **15**:500-502 (Aug 7) 1940.

4. Sieker, H.O., and Hickam, J.B.: Normal and Impaired Retinal Vascular Reactivity, *Circulation* **7**:79-83 (Jan) 1953.

5. Dollery, C.T., et al: High Oxygen Pressure and the Retinal Blood Vessels, *Lancet* **2**:291-292 (Aug 8) 1964.

6. Saltzman, H.A., et al: Retinal Vascular Response to Hyperbaric Oxygenation, *JAMA* **191**:290-292 (Jan 25) 1965.

7. Gallagher, T.J., et al: The Effects of Various Oxygen Partial Pressures on Scotopic and Photopic Vision, US Naval Air Engineering Center Report NAEC-ACEL-530, Philadelphia, July 26, 1965.

8. Haddad, H.M., and Leopold, I.H.: Effect of Hyperbaric Oxygenation on Microcirculation: Use in Therapy of Retinal Vascular Disorders, *Invest Ophthal* **4**:1141-1149 (Dec) 1965.

9. Behnke, A.R.; Forbes, H.S.; and Motley, E.P.: Circulatory and Visual Effects of Oxygen at 3 Atmospheres Pressure, *Amer J Physiol* **114**:436-442 (Jan) 1936.

10. Donald, K.W.: Oxygen Poisoning in Man, *Brit Med J* **1**:712-716 (May 24) 1947.

11. Rosenberg, E.; Shibata, H.R.; and MacLean, L.D.: Blood Gas and Neurological Responses to Inhalation of Oxygen at 3 Atmospheres, *Proc Soc Exp Biol Med* **122**:313-317 (June) 1966.

12. Carlisle, R.; Lanphier, E.H.; and Rahn, H.: Hyperbaric Oxygen and Persistence of Vision in Retinal Ischemia, *J Appl Physiol* **19**:914-918 (Sept) 1964.

13. Anderson, B., Jr., and Saltzman, H.A.: Retinal Oxygen Utilization Measured by Hyperbaric Blackout, *Arch Ophthal* **72**:792-795 (Dec) 1964.

14. Nichols, C.W., and Lambertsen, C.J.: Effects of O_2 at High Pressure on the Eye, to be published.

15. Beehler, C.C.: Oxygen and the Eye, *Surv Ophthal* **9**:549-560 (Dec) 1964.

16. Patz, A.: Oxygen Inhalation in Retinal Arterial Occlusion: A Preliminary Report, *Amer J Ophthal* **40**:789-795 (Dec) 1955.

17. Anderson, B., Jr.; Saltzman, H.A.; and Heyman, A.: The Effects of Hyperbaric Oxygenation on Retinal Arterial Occlusion, *Arch Ophthal* **73**:315-319 (March) 1965.

18. Anderson, B., Jr.; Saltzman, H.A.; and Barbee, J.Y.: "Retinal Vascular and Functional Response to Hyperbaric Oxygenation," in Brown, I.W., Jr., and Cox, B.G. (eds.): Hyperbaric Medicine, publication 1404, National Academy of Sciences-National Research Council 1966, pp 276-279.

19. Kestenbaum, A.: *Clinical Methods of Neuro-ophthalmologic Examinations,* ed 2, New York: Grune & Stratton, Inc., 1961, p 133.