14331 P

Anoxia Cataract.

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The most vital requirement of tissue is an adequate supply of oxygen. Tissues possessing a blood supply are bathed in a medium containing 13 to 19 vol. % oxygen. This large amount is made possible by the hemoglobin of the red cells which holds the oxygen in a loose chemical combination. The amount of oxygen in physical solution in the body fluids is extremely small. For example, the aqueous humor has only from 0.08 to 0.12 vol. % oxygen (Friedenwald and Pierce[1]). The necessary rapid replenishment of aqueous oxygen is made possible by rapid diffusion from the ciliary body (Pierce, Friedenwald and Freeman,[2] and Friedenwald and Pierce[1]), and by the passage of oxygen from the atmosphere through the cornea (Fischer[3]). From these considerations it is not surprising that there should be adverse effects upon the lens because of a lack of oxygen, an assumption substantiated by our experiments.

Biozzi[4] reported the effects of asphyxia on rats placed singly into 3-liter bell jars. He noted the development of cataract in some of these animals and subsequent regression after a short time in the fresh air.

Experimental. We undertook investigations to determine whether anoxia alone would produce cataract. Rats were placed in a steel chamber in which the pressure was gradually reduced until it was equal to that at an altitude of 30,000 feet or more. When the conditions were severe enough so that 50% of the animals died, about 75% of the dead animals and about 10% of the surviving animals had lens opacities. That the cataracts were due to anoxia and not to pressure was demonstrated by placing rats singly in glass chambers arranged so as to permit the constant flow of a mixture of gases consisting of 5% oxygen and 95% nitrogen at sea level. Again, the rats showed lens opacities. These experiments indicate that cataracts can develop in anoxia and that asphyxia and pressure are not important factors.

Since it is known that the oxidation of the lens is mainly anaerobic and that the lactic acid content in the aqueous humor is ordinarily higher than in the blood, it was thought that lactic acid determination of the aqueous would be of interest. For this investigation rabbits, known to be very resistant to changes in altitude, were employed. The aqueous humor was removed from one eye of each animal under ether. After 2 hours allowed for recovery some were kept in cages as controls; the others placed in the decompression chamber. After 2 hours the latter group were brought down to normal level, anesthetized again, and the aqueous was removed from the second eye. Results were impressive. Whereas the average lactic acid content of the aqueous humor in all of the first eyes and in the second eyes of the controls ranged from 70 to 75 mg per 100 cc of aqueous (a value somewhat higher than normal, probably due to the effects of the ether anesthesia) the average lactic acid value of the aqueous in the second eyes of the decompressed animals was 3 to 4 times as high (250 mg per 100 cc).

In order to determine whether the lenticular changes are due to a shift in the pH of the aqueous, rabbits were decompressed to 30,000 feet. The aqueous humor was removed under oil and the pH determined by glass-electrode method. Since the pH of the aqueous was found to be unaltered, the opacities are due either to a specific action of the lactic acid or, more likely, to an osmotic upset. The latter

1 Friedenwald, J. S., and Pierce, H. F., *Arch. Ophthal.*, 1937, **17**, 477.

2 Pierce, H. F., Friedenwald, J. S., and Freeman, D., *Am. J. Physiol.*, 1933, **104**, 553.

3 Fischer, F. P., *Arch. f. Augenheilkunde*, 1929, **102**, 146.

4 Biozzi, G., *Arch. f. Ophthal.*, 1935, **133**, 423.

was suggested as a possible cause by the work of Bellows and Chinn.[5]

Ocular Findings. After decompression, there is a marked hyperemia of the iris. The light beam in the aqueous, although difficult to observe, is visible. With oblique illumination small diffuse gray opacities are observed in the superficial cortex. The most striking finding is the fact that the anterior superficial suture becomes more readily visible. By use of the higher magnification of the slit-lamp the changes are seen to begin with development of opacity of the anterior sutures from which fine fibrillar opacities extend. In optical section it is seen that the entire opacity is thin and lies in the superficial layers of the cortex. Gradually the opacity extends towards periphery. Similar changes, although less marked, occur in the posterior cortex. In severe cases the fiber structure is lost and a shiny white total cataract is formed.

The cataract lasts from about ¾ to 1 hour and then gradually regresses, exactly reversing the course of its formation, so that the last opacities to disappear are those about the sutures.

Although the author has examined the lenses of human volunteers subjected to decompression to the equivalent of 18,000 feet, it must be pointed out that opacities due to anoxia have been observed only in animals.

[5] Bellows, J. G., and Chinn, H., *Arch. Ophthal.*, 1941, **24**, 979; 1941, **25**, 796.

14332

Distribution and Excretion of Atabrine in Experimental Animals.

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Although a number of workers have reported upon the absorption, distribution, and excretion of atabrine in experimental animals, current interest in this antimalarial drug suggested an extension of these studies.

Methods. The method used for the extraction of atabrine is a modification of Hecht's procedure[1]: One gram samples of tissue or feces were warmed in 10 cc of 30% sodium hydroxide on a water bath for 5 to 15 minutes to emulsify solids. The mixture was cooled and extracted 3 times with 5 cc portions of isoamyl alcohol, centrifuging after each extraction. Ten cc samples of urine were rendered strongly alkaline and extracted directly with isoamyl alcohol without prior heating. Oxalated blood samples were precipitated with 9 volumes of acetone and the acetone filtrates were evaporated to dryness and the residues were taken up in 10 cc of isoamyl alcohol.

Four volumes of benzene were added to the isoamyl alcohol extracts and the basic acridines were extracted with two 5-cc portions of 0.5 N hydrochloric acid. Sodium hydroxide was added to the aqueous extract and the strongly alkaline solution was extracted with an equal volume of isoamyl alcohol. After centrifuging, the alcoholic extract was dried briefly with anhydrous sodium sulfate.

For determinations in blood, the alcoholic extract was read directly in the Pfalz and Bauer fluorophotometer. The instrument was equipped with the Corning filter, red ultra No. 584, across the incident beam, and between the fluorescent solution and the photocell a yellow filter (Corning noviol No. 38) and a blue-green filter (Corning No. 553) were used to permit maximum transmission of the yellow-green fluorescence. Concentrations of atabrine between 0.1 and 1.0 γ per cc can be measured within the limits of instrumental error. For all other determinations, one drop of 6 N hydrochloric acid was added

[1] Hecht, G., *Arch. Exp. Path. Pharmak.*, 1936, **183**, 87.