temperatures which approach the upper limits of their physiological range, membrane addition may already be proceeding at a near-maximum rate which cannot be further accelerated by light stimulation.

I thank Donna Medford and Mary E. Rayborn for their assistance with the autoradiography and Luan Pearson for typing the manuscript.

From the Cullen Eye Institute, Baylor College of Medicine, Houston, Texas. This study was supported by a grant from the Retina Research Foundation, Houston, Texas, and by NIH grants EY 02362 and EY02363. Joe G. Hollyfield is the recipient of Research Career Development Award EY00112. Submitted for publication March 30, 1979. Reprint requests: Joe G. Hollyfield, Cullen Eye Institute, Baylor College of Medicine, Houston, Texas 77030.

Key words: photoreceptors, membrane renewal

REFERENCES


Polychlorinated biphenyls poisoning in monkey eye. YOSHITAKA OHNISHI AND TOSHIHIKO KOHNO.

Poisoning by polychlorinated biphenyl(s) (PCB) in humans leads to cutaneous and ocular findings. A white, cheesy-like secretion issuing from the orifice of the Meibomian gland duct when the eyelid is squeezed is one sign of this intoxication. In the rhesus monkey, abnormal hyperkeratosis of the ductal epithelium was observed histopathologically.

Polychlorinated biphenyl(s) (PCB) have been extensively utilized in industry as materials for electric current transformers, condensers, carbonless copy papers, printing ink, and many other uses.1 The extensive use of these compounds, coupled with their stable structure, has resulted in their gradual accumulation in nature. Environmental pollution by PCB poses a problem of grave concern throughout the world.2, 3 In 1968 in western Japan, an outbreak of PCB (commercial brand: Kanecroh 400) poisoning occurred in those who ingested contaminated rice oil. PCB had accidentally been mixed with the oil in the manufacturing process.4 Over 1600 cases of food poisoning (referred to as "Yusho" disease) due to this compound were registered by 1978. Many still suffer from the symptoms of this intoxication. The main ocular manifestations are hypersecretion of Meibomian glands and abnormal pigmentation of the conjunctiva.4 Despite the fact that almost all Yusho patients exhibit ocular involvement,5, 6 few investigations concerning the eye have been reported.4, 7

Materials and methods. Twelve adult rhesus monkeys, six male and six female, weighing 4.1 to
Fig. 1. Lower eyelids. A, Normal monkey eyelid. The Meibomian glands (G) and hair follicles (H) are well developed. F, Follicle of cillum; S, skin; M, muscle; C, palpebral conjunctiva. B, Eyelid of monkey fed 86.6 mg of PCB in 1 month. The Meibomian glands have atrophied. The ducts of the glands (D) are filled with hyperkeratotic cell debris. Although the follicle of the cillum appears intact, no hair follicle is seen. (x34.)

6.5 kg were used in these experiments. Eight animals were each day fed a banana injected with PCB (0.5 mg/kg body weight) dissolved in salad oil. During the 1 to 5 months duration of the experiment the animals were given a dose of 79.2 to 253.6 mg of PCB. Two out of eight animals were also fed a diet containing PCB with polychlorinated dibenzofuran (PCDF; 2.5 μg/kg body weight) which had contaminated the rice oil ingested by Yusho patients. Four untreated animals were used as controls.

Experimental animals were killed at 1, 2, 3, and 5 months. The eyelids and globes were excised and dissected. One half of each specimen was fixed in 10% neutral formalin for light microscopy, and the other half in 4% glutaraldehyde followed by 1% osmium tetroxide for electron microscopy. After dehydration the specimens were embedded in paraffin or Epon 812, as the case might be, and studied morphologically.

Results. One month after the first ingestion of PCB, there was a 17.3% reduction in the body weight in the experimental animals. There was little spontaneous discharge from the eyes, but when pressure was applied to the eyelids of experimental animals, white secretions extruded. Within 3 months, three experimental animals had hair loss from the head and upper extremities. Swelling of the eyelid and acneform eruptions were present but not conspicuous in these animals. Since histopathological changes of eyelids were identical in PCB-fed animals and PCB + PCDF-fed animals, the results will be described together.

The Meibomian glands in the normal eyelid consist of groups of acini, formed by numerous secretory cells, and ducts passing through central zone (Fig. 1, A). One month after the PCB intoxication, the glands in the experimental animals were compressed by a keratin cyst and had atrophied (Fig. 1, B). Squamous metaplasia and hyposecretion of the glands (Fig. 2) were also observed. Five months after the intoxication, no acini remained. On the other hand, epithelial cells of the ducts of Meibomian glands were hyperplastic. Although in normal ducts there were four to
Fig. 2. Secretory cell in the Meibomian gland of monkey fed 88.1 mg of PCB and 440.5 μg of PCDF in 1 month shows hypofunction. Nu, Nucleus; SG, secretory granule. (×10,700.)

Fig. 3. Epithelial cell in the duct of the Meibomian gland of monkey fed 88.1 mg of PCB and 440.5 μg of PCDF in 1 month. Many keratohyalin granules (K) are seen in the cytoplasm. Note the abnormal keratinization. (×19,800.)
five layers of stratified squamous epithelial cells, in the duct of an experimental animal seven to 10 cell layers were observed by 1 month of experimental treatment. In the basal layer of the epithelium, there were many mitotic cells, and in the superficial layer irregular shaped keratohyaline granules were evident in the cytoplasm (Fig. 3). The lumen of the duct was enlarged and was filled with keratinized cells. The orifice of the duct was also enlarged. Because of the variety of the pigment granules in the conjunctiva of the control animals, it was difficult to determine whether abnormal pigmentation had been induced. The retina and choroid of the experimental animals were morphologically similar to those of the control animals.

Discussion. Since the outbreak of PCB poisoning in humans, numerous experiments in small animals have been reported. However, none of the small animals has had findings similar to those observed in humans. In the monkey, Allen et al.7 have reported a decrease in body weight, hair loss, swollen eyelids, purulent discharge from the eyes, acne, and hyperplasia of the gastric mucosa. Our study shows that the cause of the discharge from the eyes of PCB-intoxicated monkey is not hypersecretion of the Meibomian glands but rather hyperkeratinization of the epithelial cells of the duct. This explains the "sticky" nature of the discharge of the Yusho patients prior to visual loss. Ocular symptoms in Yusho patients appeared first; 2 or 3 months later, acneform eruptions and the pigmentation of the skin became evident. Therefore, the secretion of white, cheeselike material from the ducts of Meibomian glands when the eyelid is squeezed by fingers is the first clinical sign. A primary loss of Meibomian substance might result in a secondary keratinization.

It is generally held that a cyst of the human Meibomian gland follows obstruction of the duct and that the cystic contents differ from the keratin material filling an epidermal inclusion cyst. 8,9 Therefore the keratic cyst of this gland may be considered one of the characteristic findings of PCB-intoxicated mammals. On the basis of our experiments, the photograph of the eyelid reported by McNulty and Griffin as “Possible polychlorinated biphenyl poisoning in rhesus monkey” does indeed identify the cause as PCB. 10

We are grateful to members of a Study Group of Yusho.

From the Department of Ophthalmology, Faculty of Medicine, Kyushu University, Fukuoka, Japan. This work was supported by a Yusho grant from Ministry of Health and Welfare in Japan. Submitted for publication March 23, 1979. Reprint requests: Yoshitaka Ohnishi, M.D., Department of Ophthalmology, Faculty of Medicine, Kyushu University, Fukuoka, 812, Japan.

Key words: polychlorinated biphenyls, polychlorinated dibenzofuran, Meibomian gland, hyperkeratosis, squamous metaplasia

REFERENCES


Effect of iontophoretic and topical application of antiviral agents in treatment of experimental HSV-1 keratitis in rabbits.* BYOUNG SE KWON, LOUIS P. GANGAROSA, NO-HEE PARK, DAVID S. HULL, EDWARD FINEBERG, CAROL WIGGINS, AND JAMES M. HILL.

Cathodal (−) iontophoresis of 9-β-D-arabinofuranosyladenine 5′-monophosphate (idarubicin monophosphate; Ara-AMP) was performed once daily for 3 days for the treatment of experimental herpes simplex virus type 1 (HSV-1) keratitis in rabbit eyes, and the therapeutic efficacy was compared with that of topical treatment of Ara-AMP and idoxuridine (IDU) administered five times daily for 4 days. With the treatment initiated 24 hr after viral inoculation, Ara-AMP cathodal iontophoresis resulted in significant suppression of epithelial and an-