Comparative studies of the effect of pilocarpine on the pupil and on the refraction in two species of monkey (Cercopithecus ethiops and Macaca irus)

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It is known that pilocarpine injected into the anterior chamber affects outflow facility in much smaller doses in the vervet (Cercopithecus ethiops) than in the cynomolgus (Macaca irus). The present experiments were performed in order to determine whether a similar species difference, with respect to pilocarpine sensitivity, is present in the sphincter pupillae and the muscle of accommodation. In order to make possible the study of pilocarpine-induced refraction changes, the pupil of one eye was immobilized by a partial excision of the sphincter region of the iris. The other eye was used for studies of the pupil. Pilocarpine was applied to the cornea (in 10 μl), injected into the anterior chamber (in 1 μl), and injected intramuscularly. Dose-response curves were determined for pupillary size and changes in refraction. No important species difference in the sensitivity to pilocarpine of the pupil or of refraction was observed. This was true for all modes of administration. When pilocarpine was applied to the cornea, the dose necessary to effect a half-maximal change in refraction was about 100 times that necessary to cause half-maximal pupillary constriction. This applied to both species of monkey. The ratio between the doses was approximately of the same order when pilocarpine was injected into the anterior chamber. With systemic administration of pilocarpine, no difference could be detected for the effective doses on the pupil and on refraction in either species. If the pilocarpine was injected into the anterior chamber, only about one tenth of the corneal dose was required to obtain the same change in refraction. This applied to both species of monkey.

The mechanism for the facility-increasing effect of pilocarpine in simple glaucoma (glaucoma simplex) has still not been clarified. The common conception is that the pilocarpine acts via the ciliary muscle. On measuring the outflow facility in monkeys, Bárány1 found a conspicuous difference between the African green monkey or vervet (Cercopithecus ethiops) and the cynomolgus (Macaca irus) in their response to pilocarpine injected into the anterior chamber. While the green vervet needed to be given only 2 mcg. of pilocarpine in order to produce a large increase in facility, the cynomolgus required 20 mcg. to produce even a moderate effect. The present investigation was initiated to see if the effect of pilocarpine on the pupil and on refraction in both...
species of monkey showed a corresponding difference. As no method of measuring refraction objectively under miotics was known, one was developed.

Materials and methods

For the experiments, cynomolgus monkeys (Macaca irus), weighing 1.6 to 2.1 kilograms, were used. The eyes were prepared for the experiments by a two-stage operation intended to prevent miosis in the right eye. The sphincter of the iris was excised at two diametrically opposite regions, around 12 o'clock and 6 o'clock, on two separate occasions. These operations were performed under phencyclidine (Sernyl; Parke, Davis & Co.) general anesthesia, 2 mg. per kilogram intramuscularly, and 2 drops of 0.5 per cent tetracaine applied locally. With a keratome an incision was made at the limbus, after which a piece of the iris nearest the pupil was grasped with iris forceps and cut off. The iris was replaced, and the keratome incision sealed itself. After each operation 2 drops of 1 per cent eserine solution were applied. The second iridectomy was made analogously, about one month after the first. The first experiments were made, at the earliest, one month after the last operation. The eyes were then free from irritation, and determination of refraction was possible even with high pilocarpine dosages. A schematic drawing of the appearance of the pupil after two iridectomies is presented in Fig. 1.

In the experiments monkeys were anesthetized with 30 mg. per kilogram of pentobarbital given intraperitoneally as a veterinary pento-barbital solution. Usually an additional 5 to 10 mg. per kilogram had to be given after approximately 2 hours. The animal lay prone on a board, with its head fixed by a head holder. The body temperature was maintained with an infra-red lamp.

Pupil experiments. Measurements of the pupil were made on the left eye of the monkey. The animal was facing a frosted glass screen, placed at a distance of 1 m., behind which was placed a lamp with a bulb (25 W.) fed by a constant voltage transformer. The frosted glass screen was used to minimize the influence of the slow movements of the eye, which occasionally occurred under general anesthesia. The illuminated screen was the only source of light in the room. The eye was held open during the experiment with a thread in the margin of the upper lid, and the cornea was kept moist by pulling the lid down at intervals. The diameter of the round pupil was measured with a pair of vernier calipers held close to the animal's eye, while the investigator's eye was at a distance of 20 cm. from the calipers. The diameter of the pupil was taken as the mean of at least four individual readings. In some of the experiments the size of the pupil was moreover verified photographically with an electronic flash. It was found that the caliper readings and photographic measurements always agreed closely. Shortly after the anesthesia had taken effect, the size of the pupil varied noticeably, primarily in consequence of external stimuli and dependent upon the depth of anesthesia. For this reason the pupil was observed 15 to 20 minutes preceding the administration of pilocarpine. After the pilocarpine had been given, the diameter of the pupil was observed until it had eventually adjusted itself to a new level of contraction; the experiment on the pupil was then considered concluded. During the observations on the pupil, the other (right) eye was closed.

Refraction experiments. In the experiments in which pilocarpine was applied to the cornea or injected into the anterior chamber, the refraction experiments were performed after those concerned with the pupil were completed but during the same anesthesia. When pilocarpine was given intramuscularly, alternate measurements on the pupil of the left eye and on the refraction of the right eye were made after each dose. The determination of refraction was made by a Thorner optometer (Emil Busch, A-C., Rathenow). First, the initial value of the refraction in a horizontal meridian was determined as the mean of at least four readings. After pilocarpine had been given, the refractive power in the horizontal meridian was read until a definite maximum was observed for the pilocarpine dose in question. Each refraction value was always calculated by taking the mean of at least four individual readings made in rapid succession. The refractive power was also read in the vertical meridian during the experiments.

Fig. 1. Schematic drawing of the arrangement for injection into the anterior chamber. Notice the shape of the pupil.
Fig. 2. Changes in refraction in relation to time after pilocarpine given onto the cornea (200 μg), into the anterior chamber (10 μg), and intramuscularly (0.5 mg per kilogram). All curves are from the same animal (vervet).

Pilocarpine administration. Pilocarpine was given in three ways. When pilocarpine was applied to the cornea varying quantities of pilocarpine HC1 were dissolved in distilled water. The solutions were never more than 3 days old. The pilocarpine, always in the same volume of water (10 μl), was applied to the cornea with an Agla micrometer syringe (Burroughs Wellcome & Co., London). The drug was given intermittently during 2 minutes, 1 to 1.5 μl every 15 seconds. These small droplets were applied so as to avoid the pilocarpine reaching the limbus region. When all the pilocarpine had been given, the eyelid was held back for another 2 minutes, whereupon the intermittent closures were resumed. With use of this method of application never more than one experiment was made during the same anesthesia.

When pilocarpine was injected into the anterior chamber, a thin, stainless steel needle (0.45 mm. outer diameter) was used. Without local anesthesia this needle was shot through the cornea near the limbus at 9 or 3 o'clock with a needle gun. The needle was attached to an Agla micrometer syringe by means of thin polyethylene tubing (Clay-Adams, PE 20). The tubing was supported near the eye so as to minimize the deformation of the cornea. The point of the needle was not allowed to reach the optical zone. Shortly before the needle was shot into the eye, the tubing was loaded with a series of drops: 2 μl of 0.9 per cent NaCl and increasing doses of pilocarpine, each dissolved in 1 μl of 0.9 per cent NaCl (Fig. 1). The saline and pilocarpine solutions were separated by air bubbles of approximately 1 μl. Beginning with the weakest, the solutions were drawn up into the tubing. When all the solutions had been drawn up, the tubing was turned around so that the highest concentrations came nearest the syringe and the lowest close to the needle. With this arrangement the stronger solutions did not contaminate the weaker ones when they were successively injected. After 2 μl of physiologic NaCl solution, there were, as a rule, 2 to 3 doses of pilocarpine of increasing concentration injected at the same experimental occasion. The ratio between successive doses was never less than 5:1. The effect of a former dose was neglected when the next was given. The whole experiment was done aseptically.

In some experiments pilocarpine was injected intramuscularly. Varying doses were dissolved in physiologic saline solution so that 0.5 ml. pilocarpine solution per kilogram of body weight was always given. The intramuscular injections were made into the arm. One to 2 doses of pilocarpine were given on each occasion. When a second dose followed, the effect of the first was neglected. The ratio between successive doses was never less than 5:1. All pilocarpine doses refer to pilocarpine HC1.

Calculations. The effect of pilocarpine on refraction was expressed as the largest change in refraction, i.e., the difference between the refraction before the drug was given (initial value) and the refraction when the pilocarpine dose in question had its largest effect (final value). These initial and final values were calculated as the mean of at least four individual readings. The changes in refraction obtained for the respective pilocarpine doses were entered on a graph, and the responses of each individual animal to the different doses joined by straight lines (Figs. 3, 4, 5, and 6). When the same dose had been administered several times to the same animal, the lines were drawn to the point which corresponds to the mean value for the dose in question.

The mean curves in the figures were constructed from the graphs in the following way: The logarithms of the pilocarpine doses corresponding to preselected changes in refraction were determined by interpolation and averaged. The values for the mean log pilocarpine doses were subsequently joined by straight lines. Thus the mean curves represent geometric means.

In the pupil experiments the smallest diameter (final diameter) observed after a given pilocarpine dose was taken to illustrate the effect of pilocarpine. Diagrams and mean curves were drawn in analogy to what has been described for refraction (Figs. 7, 8, 9, and 10). In the figures each individual animal within a species has been designated by the same symbol throughout.

Reliability of the methods. The optometer was tested with positive and negative lenses of known strength and never showed errors of more than 0.25 diopters. The optometer gives the refraction as the dioptric power (D.) of a correcting lens placed 12 mm. from the eye.
The standard deviation of successive differences between the single readings at any one occasion was calculated. The standard deviation of the single reading due to error of the method ($\sigma_w$) is obtained by dividing with $\sqrt{2}$. These standard deviations of single readings, when the pilocarpine was administered onto the cornea, were for: pupillary diameters before pilocarpine (291 readings) $= \pm 0.12$ mm.; final diameters smaller than 2 mm. (112 readings) $= \pm 0.07$ mm.; refraction values before pilocarpine (519 readings) $= \pm 0.42$ D.; final refraction values in experiments where myopia between 15 and 20 D. was obtained (58 readings) $= \pm 0.93$ D. In the experiments in which the myopia obtained was less than 15 D., $\sigma_w$ of the final values was lower than $\pm 0.93$ D.

Upon intramuscular administration of pilocarpine the $\sigma_w$ of the observations on both the pupil and

![Figure 3](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/932895/)

**Fig. 3.** Changes in refraction after pilocarpine given onto the cornea. Five cynomolgus monkeys and geometric mean curve (dashed) for 6 vervets. In the upper right-hand corner the changes (maximum obtainable) in refraction after large doses of pilocarpine are indicated for the 5 cynomolgus monkeys.

![Figure 4](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/932895/)

**Fig. 4.** Changes in refraction after pilocarpine given onto the cornea. Six vervets and geometric mean curve for 5 cynomolgus monkeys (dashed). In the upper right-hand corner the changes (maximum obtainable) in refraction after large doses of pilocarpine are indicated for the 6 vervets.
the refraction readings were somewhat less than when pilocarpine was applied locally to the cornea. When pilocarpine was injected into the anterior chamber the \( \sigma_m \) values were for: pupillary diameters before pilocarpine (52 readings) = \( \pm 0.19 \) mm.; final diameters smaller than 2 mm. (40 readings) = \( \pm 0.09 \) mm.; refraction values before pilocarpine (56 readings) = \( \pm 0.70 \) D.; final refraction values in experiments where myopia between 15 and 20 D. was obtained (31 readings) = \( \pm 1.25 \) D.

Because no significant differences in method error between the species of monkey were found, the figures represent combined values for both species. Since never less than four readings were taken at any one occasion, the standard deviation due to reading errors of any point was half the quoted values or less.

**Fig. 5.** Changes in refraction after pilocarpine given into the anterior chamber. Four cynomolgus monkeys and geometric mean curve for 4 vervets (dashed).

**Fig. 6.** Changes in refraction after pilocarpine given into the anterior chamber. Four vervets and geometric mean curve for 4 cynomolgus monkeys.

**Fig. 7.** Pupil diameters after pilocarpine given onto the cornea. Five cynomolgus monkeys and geometric mean curve for 6 vervets (dashed).

**Influence of the iridectomies.** In 4 cynomolgus monkeys and 3 vervets the refraction of both the right and left eyes was examined under phencyclidine anesthesia (1.5 mg. per kilogram of body weight) with 1 per cent atropine solution applied locally. The refraction in the horizontal meridian had a mean value of -1.4 D. (range -0.3 to -2.3 D.) in the 7 eyes operated upon, and a mean of -1.2 D. (range -0.6 to -2.3 D.) in the 7 eyes not operated upon of the same animals. The astigmatic aberration amounted to a mean of 0.5 D. in the operated eyes as against 0.4 D. in the unoperated eyes. Accordingly, the iridectomies have not caused any important changes in the refraction of the eyes.

**Induced astigmatism.** The refraction was observed in a horizontal as well as a vertical meridian. Astigmatism with oblique axes was not seen. With drop application to the cornea and upon intramuscular injection of the pilocarpine, no important astigmatism could be recorded. When pilocarpine was injected into the anterior chamber, 2 cases of rather strong astigmatism were seen (4.7 D. and 7.3 D., respectively); otherwise the astigmatism was less than 2 D. Astigmatism
always occurred when the needle was shot into the eye, and most often it increased the refraction in the meridian which coincided with the direction of insertion. The astigmatism thereafter remained unaltered during the whole experiment.

Results

Changes in refraction when pilocarpine was dropped onto the cornea. When the pilocarpine was applied to the cornea the peak effect was reached after approximately 25 to 40 minutes (Fig. 2). The mean initial value for the 5 cynomolgus monkeys was -1.7 D. (range -0.8 to -2.4 D.). For the 6 vervets the mean initial value was -1.1 D. (range +0.3 to -3.3 D.). The maximum obtainable change in refraction after the drop application of pilocarpine in large doses (30 to 40 mg.) to the cornea was determined for all these animals and was found to be 14.1 D. (range 10.5 to 18.0 D.) for the cynomolgus monkeys and 17.9 D. (range 16.3 to 20.0 D.) for the vervets. The differences might be due to age or species differences, but might also be fortuitous. Fig. 3 shows the relation between the change in refraction and the pilocarpine applied as drops to the cornea for the different cynomolgus monkeys. In order to facilitate comparison of the species, a mean curve showing the effect of pilocarpine in the vervets has been drawn on the same figure (this curve has been interpolated from the individual curves in Fig. 4). Fig. 4 shows the changes in refraction after different corneal doses for the 6 vervets and, for comparison, the corresponding mean curve for the cynomolgus monkeys (interpolated from the individual curves in Fig. 3). Both figures show that there is no considerable difference between the species. How close the mean curves are to each other can be seen in Fig. 13.

Changes in refraction after the injection of pilocarpine into the anterior chamber. The injection of the first pilocarpine dose into the anterior chamber was always preceded by an injection of 2 μl of physiologic saline solution. In no case did this solution cause any demonstrable effect on the refraction. With this type of administration, the full effect on the refraction was reached in both species 8 to 15 minutes after the injection of pilocarpine (Fig. 2). The experimental results are presented in Fig. 5 (i.e., the results for the 4 individual cynomolgus monkeys together with the mean curve for the 4 vervets) and Fig. 6 (the results for the 4 vervets as well as the mean curve for the 4 cynomolgus). The scatter is evidently much smaller with this method of application. No difference between species is found. How close the mean curves are can be seen in Fig. 13. This illustration also shows that, for the same effect on refraction, doses approximately 10 times as large are required on the cornea as are required in the anterior chamber.

Changes in the pupil when pilocarpine was dropped onto the cornea. When the pilocarpine was dropped onto the cornea, the full effect on the pupil was reached after 20 to 30 minutes in both the cynomolgus monkeys and the vervets. The average

![Fig. 8. Pupil diameters after pilocarpine given onto the cornea. Six vervets and geometric mean curve for 5 cynomolgus monkeys (dashed).](image_url)
diameter of the pupil before the application of pilocarpine was 3.2 mm. (range 2.6 to 3.8 mm.) in the 5 cynomolgus monkeys and 3.4 mm. (range 2.9 to 3.8 mm.) in the 6 vervets. Doses of less than 0.5 mcg. of pilocarpine applied to the cornea caused little or no effect, while doses larger than 10 mcg. always caused considerable miosis, many times causing a final diameter of the pupil of less than 2.0 mm. In all the mon-

![Graph](image1)

**Fig. 9.** Pupil diameters after pilocarpine given into the anterior chamber. Four cynomolgus monkeys and geometric mean curve for 4 vervets (dashed).

![Graph](image2)

**Fig. 10.** Pupil diameters after pilocarpine given into the anterior chamber. Four vervets and geometric mean curve for 4 cynomolgus monkeys (dashed).

keys the minimum diameter obtainable was determined with very large doses of pilocarpine dropped onto the cornea (approximately 10 mg.). A mean diameter of 1.4 mm. (range 1.4 to 1.5 mm.) was obtained for the cynomolgus monkeys, and a mean of 1.4 mm. (range 1.3 to 1.6 mm.) for the vervets. Fig. 7 shows the relation between the diameter of the pupil and different doses of pilocarpine for the 5 cynomolgus monkeys. The dashed curve in the figure is a mean curve for the 6 vervets which had been given pilocarpine in the same manner. Their individual results are presented in Fig. 8, where a mean curve for the cynomolgus monkeys has also been introduced. These figures show that, for the cynomolgus specimens employed here, 1.2 to 4.0 mcg. of pilocarpine applied locally to the cornea were needed in order to give a pupil diameter of 2 mm. For the vervets, 4 to 20 mcg. were needed to obtain the same diameter. A comparison between the mean curves is shown in Fig. 13. The cynomolgus monkeys required somewhat smaller doses than the vervets.

A comparison between the doses acting on the pupil and refraction can be made as follows: The half-maximum effect on the pupil when pilocarpine was applied to the cornea of the cynomolgus monkeys corresponds to a diameter of 2.3 mm. (halfway between the mean of the initial values and the mean of the values for maximal miosis). Half the maximal effect on refraction in the cynomolgus can be calculated to be 7.1 D. (half the mean of the maximal change in refraction). By interpolating in Fig. 13, it can be seen that a dose approximately 100 times greater is needed to obtain the half-maximal effect on refraction than is needed for a similar effect on the pupil. The same comparison for vervets gives approximately the same ratio. (Compare the doses necessary for a pupil diameter of 2.4 mm. and for a change in refraction of 9.0 D.)

**Changes in the pupil after injection of the pilocarpine into the anterior chamber.**

An injection of 2 µl of physiologic saline...
was always made before pilocarpine was injected into the anterior chamber. Apart from 2 cases, where a slight but transient dilatation occurred, the physiologic saline caused no demonstrable effect on the pupil. The full effect on the diameter of the pupil was reached about 5 to 12 minutes after the administration of pilocarpine. The results found are given in Fig. 9 (the final diameter of the pupil after different pilocarpine doses for 4 cynomolgus monkeys, with a mean curve for 4 vervets) and Fig. 10 (the final diameter for 4 vervets, with the mean curve for the 4 cynomolgus monkeys). In order to obtain a pupil diameter of 2 mm., approximately 0.4 to 1.0 mcg. of pilocarpine for the cynomolgus monkeys and 0.3 to 1.5 mcg. for the vervets were required in the anterior chamber. The effective doses with this method of application appear to be about the same for both species.

From Fig. 13 can be seen that for the pupil diameter the anterior chamber administration is more effective than the corneal (as was the case for the change in refraction). Fig. 13 also shows that the ratio between effective doses on the refraction and on the pupil diameter is nearly the same (100:1) with this administration, as when pilocarpine was given onto the cornea. This applies to both species of monkey.

**Pilocarpine injected intramuscularly.**

From the experiments it has been shown that when pilocarpine was applied as drops to the cornea, as well as when it was injected into the anterior chamber, much larger doses were required to obtain a moderate effect on the refraction than were required to affect the diameter of the pupil. In order to see whether this is due to an inherently greater sensitivity of the iris, the drug was injected intramuscularly in 3 patients.
cynomolgus monkeys and 3 vervets. A full effect on both the pupil and the refraction in both species of monkey was reached 5 to 15 minutes after the injection (Fig. 2). In Figs. 11 and 12 the continuous lines show the diameter of the pupil and the dashed lines the changes in refraction in relation to the intramuscularly injected doses expressed in milligrams per kilogram of body weight. No important difference in sensitivity seems to exist between the ciliary muscle and the sphincter pupillae in either of the species.

Discussion

Methods giving greater accuracy in determining the size of the pupil do exist, but, as it has not been the primary aim of the present investigation to study the pupil, the methods employed were considered accurate enough. The data for the individual animals show, it is true, a large scatter, especially those for the drop-application to the cornea. However, this scatter is probably due mainly to shortcomings in the method of application.

A perfectly satisfactory method of determining refraction in animals with miosis is, to my knowledge, not known. In this investigation the difficulty was circumvented by severing the sphincter of the pupil in two places. No significant change in the state of refraction after the operation was observed.

The mean refractions in both species turned out to be myopic already before the administration of pilocarpine. As all the monkeys used in the experiments were confined to relatively small cages and small rooms, it is possible that the restricted visual space was a contributory factor in producing the myopia. Since the animals were given pilocarpine on only few occasions and with long intervals, it is improbable that the pilocarpine could have caused the myopia.

Pilocarpine causes difficulties in determining refraction, not only as a result of the miosis but also by the secretion of tears and mucus. The tear flow affects the efficiency of the corneal dose, and the secretion of mucus the optics of the eye. Because of the increased tear flow, the lacrimal pathways also influence the efficiency of the dose. The interindividual variability of the results with the drop-application of pilocarpine may therefore partly depend on individual differences in the function of the lacrimal pathways. Different degrees of presbyopia may also have caused interindividual differences.

How much the present standardized method of application to the cornea differs from the clinical methods of topical application in efficiency and variability is unknown. Presumably it is more efficient and less variable.

As has been described in the section on methods, the accuracy of observation as such was somewhat poorer when the pilocarpine was injected into the anterior chamber than when it was applied as drops to the cornea. However, even though astigmatism sometimes occurred, the refraction readings in the eye with a needle shot into the anterior chamber did not involve great difficulties. Both when pilocarpine was given onto the cornea and into the anterior chamber, the sphincter pupillae was approximately 100 times more sensitive than the ciliary muscle. This was true for both species of monkey (Fig. 13). Lommatzsch²

Fig. 13. Average data (geometric mean curves) showing the effect on pupil diameter and refraction of pilocarpine given into the anterior chamber (4 cynomolgus, 4 vervets) and onto the cornea (5 cynomolgus, 6 vervets).
has published in vitro experiments on the eyes of cats and humans in which he found that $10^2$ times larger doses of pilocarpine are required for contraction of the isolated ciliary muscle than for the contraction of the isolated sphincter pupillae. His experiments would then, at first sight, seem to agree with the values found in the present experiments. However, when pilocarpine was administered systemically, no such differences could be shown in the size of the doses causing pupillary contraction and changes in refraction, neither in the 3 cynomolgus monkeys nor in the 3 vervets examined. As Lommatzsch himself points out, the difference observed is probably due to an imperfection in the technique. In the present experiments the intramuscular administration of pilocarpine was chosen to obtain a protracted effect. A few experiments with intravenously injected pilocarpine gave essentially the same results.

The observations of higher sensitivity of the pupil than of the ciliary muscle in experiments with topical application may be caused by the fact that the sphincter of the pupil is more easily reached from the anterior chamber. Moreover, the portion of the ciliary muscle responsible for accommodation is shielded by the interposition of vascularized tissue, the blood in which washes the pilocarpine away continuously.

When the pilocarpine was applied to the cornea and when it was injected into the anterior chamber, the ratio between doses producing an effect on the pupil and on the refraction remained approximately 1:100. This suggests that with the technique used, pilocarpine applied as drops to the cornea enters by way of the anterior chamber.

The dose of pilocarpine dropped onto the cornea must be about 10 times larger than the one injected into the anterior chamber in order to obtain approximately the same effect on refraction in both the cynomolgus monkeys and vervets (Fig. 13). Something similar applies to the effect on the pupil (Fig. 13), where a 4 to 10 times larger corneal dose is required for the same degree of miosis as when the pilocarpine is injected into the anterior chamber. A similar ratio was found by Müller, Hockwin, and Kleifeld, who administered 2 drops of 2 per cent pilocarpine (approximately 2 mg.) into the conjunctival sac of human eyes and found the concentration in the aqueous humor after 20 minutes to be 0.2 per cent (approximately 0.4 mg. of pilocarpine in the anterior chamber). However, proof of specificity of their polargraphic method for the determination of pilocarpine is lacking.

One aim of this investigation has been to establish possible differences between the cynomolgus monkey and the vervet in respect to the effect of pilocarpine on refraction. Fig. 13 shows that the corresponding dose-response curves for the two species lie close together. Barany found marked differences between the cynomolgus monkey and the vervet in their ability to react with increased outflow facility after the injection of pilocarpine into the anterior chamber. The cynomolgus monkeys were much more insensitive. No corresponding difference in sensitivity was found in the present experiments, neither for the pupil nor for the refraction. With regard to the latter it is improbable that the iridectomy improved the possibility for the pilocarpine to reach the ciliary muscle more in the cynomolgus than in the vervet, since the iridectomies were performed in the same way in both species. Therefore, the greater reduction of outflow resistance in the vervets cannot be caused by differences in the sensitivity of the two smooth muscles involved in pupillary constriction and accommodation.

After this paper was sent for publication, it was incidentally found that iridectomies were used in refraction studies already in the nineteenth century and first by Trautvetter.

REFERENCES