

Howe (L)



## Effect of Cocaine upon the Healing of Wounds.

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The anæsthetic effect of cocaine upon the eye, already so well known, suggests an inquiry as to the influence it may also have on the healing of wounds.

A considerable time must necessarily elapse before clinical experience can furnish sufficient data to warrant conclusions which are entirely reliable.

Different individuals, and the circumstances accompanying the operations, vary so greatly that, in spite of the many cases already published, in which cocaine has been used; only a series of those exactly similar would furnish an average for just comparison. In certain rather rare instances, it is true, the same operation is made on each eye of the same individual at the same time, and in these the effect of the drug can be tested. But such cases are by no means numerous. I have, therefore endeavored to determine its influence upon the healing process, by producing equal lesions in both eyes of an animal, and then comparing the one treated with cocaine with the other,—either left to itself or treated with atropine. The principal objects of this inquiry were, to detect any unfavorable influence cocaine might exert upon such wounds, by reason of the irritation produced, or of the effect upon the nerve supply. On the contrary, if its action was advantageous, it was import-

ant to determine what parts of the eye it affected, and, if—for the iris or any other portion—it was as reliable as atropine. It is well to settle such questions as soon as possible after the discovery of an agent like this, whose anæsthetic properties naturally excite unguarded enthusiasm and too great confidence, in a really valuable drug. Accordingly in the laboratory of Prof. Zuntz, in Berlin, a few months since, I noted the healing process in wounds as follows:

- Rupture of conjunctiva in one rabbit.
- Rupture of conjunctiva in two guinea pigs.
- Abrasion of corneal epithelium in two rabbits.
- Abrasion of corneal epithelium in one guinea pig.
- Abrasion of corneal epithelium in one cat.
- Burn of conjunctiva and cornea in two rabbits.
- Puncture of cornea in one cat.
- Iridectomy (simple) in one rabbit.
- Iridectomy (iris being left in wound) in two rabbits.
- Iridectomy (iris being left in wound) in three guinea pigs.
- Traumatic cataract in three guinea pigs.

It would be unnecessary repetition to rehearse in detail the healing of each of these wounds, yet a few examples are not out of place, illustrating not only the process of repair in general, but also, the form of record kept in these cases.

In these tables the eye treated with cocaine is indicated by C, the other by L or R, as it happened to be left or right. For convenience the amount of secretion in the conjunctiva, or the extent of swelling there, or elsewhere, is indicated in degrees, 1 representing the minimum, and 3 the maximum. These figures are, of course, arbitrarily taken, but are preferable to indefinite adjectives. The amount of ciliary injection could also be best shown by counting the large vessels, and giving them in a separate column from the small ones.

Guinea pig.—Extensive tear in conjunctiva reaching from outer to inner canthus.

| DAY. | EYE. | CILIARY INJECTION. |        | CONDITION OF WOUND. |          | Two per cent. Solution used. |
|------|------|--------------------|--------|---------------------|----------|------------------------------|
|      |      | Large.             | Small. | Degree of Swelling. |          |                              |
| 1    | C.   | 2                  | 4      | 2                   | Closing. | 5 times.                     |
|      | L.   | 2                  | 4      | 2                   | Closing. |                              |
| 2    | C.   | 1                  | 2      | 2                   | Closing. | 5 times.                     |
|      | L.   | ...                | 3      | 2                   | Closing. |                              |
| 3    | C.   | 1                  | 1      | 2                   | Closed.  | 5 times.                     |
|      | L.   | ...                | 2      | 2                   | Closed.  |                              |
| 4    | C.   | ...                | 2      | 1                   | .....    | 5 times.                     |
|      | L.   | ...                | 2      | 1                   | .....    |                              |
| 5    | C.   | ...                | 2      | None.               | .....    | 5 times.                     |
|      | L.   | ...                | 2      | None.               | .....    |                              |
| 6    | C.   | Normal.            |        | None.               | .....    | .....                        |
|      | L.   | Normal.            |        | None.               | .....    |                              |

Small white rabbit.—Scraped off epithelium of cornea in each eye from a spot measuring 2 by 2 millimeters.

| DAY. | EYE. | CILIARY INJECTION. |        | CORNEA.                      | No. of times 1 per cent. Solution of Cocaine was used. |
|------|------|--------------------|--------|------------------------------|--|
|      |      | Large.             | Small. |                              |  |
| 1    | C.   | 2                  | 4      | Epithelium partly renewed.   | 5  |
|      | L.   | 2                  | 5      | Epithelium entirely renewed. |  |
| 2    | C.   | 2                  | 4      | Normal.                      | 5  |
|      | L.   | 2                  | 2      | Normal.                      |  |
| 3    | C.   | ...                | 2      | Normal.                      | ...  |
|      | L.   | 1                  | 1      | Normal.                      |  |
| 4    | C.   | ...                | ...    | .....                        | ...  |
|      | L.   | ...                | ...    | .....                        |  |

Comparison of cocaine with atropine in the healing of a burn with lime, involving conjunctiva and cornea of a rabbit.

A sufficient amount of unslaked lime was placed on the upper half of the conjunctiva and cornea to produce an eschar of all the palpebral and ocular portion of the former, and also to whiten the latter over a space measuring 5 by 6 millimeters. Exactly the same was repeated in the other eye, and both were thoroughly washed with distilled water to remove all remaining particles of lime. A solution of cocaine was then dropped into the right and one of atropine into the left. Each being of two per cent. strength.

| DAY. | EYE. | LIDS.      | CONJUNCTIVA. |             | CILIARY INJECTION. |        | Opacity on Cornea, in mm. | Diam. of Pupil, in mm. | Application to each. |
|------|------|------------|--------------|-------------|--------------------|--------|---------------------------|------------------------|----------------------|
|      |      |            | Swelling.    | Secre-tion. | Large.             | Small. |                           |                        |                      |
| 1    | C.   | Open.      | 3            | 2           | 10                 | 13     | 5 x 5                     | 5½                     | 6 times.             |
|      | L.   | Half-open. | 3            | 2           | 12                 | 9      | 5 x 6                     | 8                      |                      |
| 2    | C.   | Open.      | 1            | 1           | 9                  | 10     | 5 x 4                     | 5½                     | 3 times.             |
|      | L.   | Half-open. | 2            | 2           | 10                 | 9      | 6 x 6                     | 8                      |                      |
| 3    | C.   | Open.      | 0            | 0           | 9                  | 8      | 3 x 2                     | 7                      | 5 times.             |
|      | L.   | Open.      | 2            | 2           | 10                 | 9      | 5 x 4                     | 8                      |                      |
| 4    | C.   | .....      | ...          | ...         | 7                  | 10     | 2 x 2                     | 7                      | 2 times.             |
|      | L.   | .....      | 2            | 1           | 8                  | 11     | 4 x 3                     | 9                      |                      |
| 5    | C.   | .....      | ...          | ...         | 2                  | 8      | 2 x 3                     | 6                      | 3 times.             |
|      | L.   | .....      | 1            | 0           | 6                  | 12     | 2 x 3                     | 8                      |                      |
| 6    | C.   | .....      | ...          | ...         | 1                  | 8      | 1 x 1                     | 6                      | 3 times.             |
|      | L.   | .....      | ...          | ...         | 4                  | 10     | 2 x 2                     | 8                      |                      |
| 7    | C.   | .....      | ...          | ...         | ...                | 4      | .....                     | 6                      | 3 times.             |
|      | L.   | .....      | ...          | ...         | 2                  | 10     | 2 x 2                     | 8                      |                      |
| 8    | C.   | .....      | ...          | ...         | ...                | 2      | .....                     | 5                      | 3 times.             |
|      | L.   | .....      | ..           | ...         | ...                | 6      | 2 x 2                     | 7                      |                      |
| 9    | C.   | .....      | ..           | ...         | ...                | 1      | .....                     | 5                      | 3 times.             |
|      | L.   | .....      | ...          | ...         | ...                | 2      | 2 x 2                     | 7                      |                      |
| 10   | C.   | .....      | ...          | ...         | ...                | ...    | .....                     | 5                      | 3 times.             |
|      | L.   | .....      | ...          | ...         | ...                | ...    | 2 x 2                     | 7                      |                      |

Small Cat.—Punctured anterior chamber of each eye, evacuating entirely the aqueous humor, and allowing iris to engage in the wound. Right, meanwhile under the influence of cocaine and subsequently treated with it.

| DAY. | EYE. | CONJUNCTIVA. | CILIARY INJECTION. |        | DULL SPOT IN CORNEA.  | WOUND.       | Two per cent. Solution of Cocaine. |
|------|------|--------------|--------------------|--------|-----------------------|--------------|------------------------------------|
|      |      |              | Large.             | Small. |                       |              |                                    |
| 1    | C.   | Normal.....  | ...                | 5      | 2 x 2½ mm. ....       | Closed. .... | 9 times.                           |
|      | L.   | Normal.....  | 2                  | 4      | 3 x 2½ mm. ....       | Open. ....   |                                    |
| 2    | C.   | .....        | 1                  | 3      | As on first day. .... | Closed. .... | 5 times.                           |
|      | L.   | .....        | ...                | 5      | .....                 | Open. ....   |                                    |
| 3    | C.   | .....        | 1                  | 3      | As on first day. .... | Closed. .... | 5 times.                           |
|      | L.   | .....        | ...                | 5      | .....                 | .....        |                                    |
| 4    | C.   | .....        | ...                | 2      | Barely visible. ....  | .....        | 5 times.                           |
|      | L.   | .....        | ...                | 5      | .....                 | .....        |                                    |
| 5    | C.   | .....        | No ne.             | 5      | Barely visible. ....  | .....        | 4 times.                           |
|      | L.   | .....        | ...                | 5      | .....                 | .....        |                                    |
| 6    | C.   | .....        | No ne.             | 5      | Normal. ....          | .....        | 4 times.                           |
|      | L.   | .....        | ...                | 5      | Normal. ....          | .....        |                                    |
| 7    | C.   | .....        | No ne.             | .....  | .....                 | .....        | 3 times.                           |
|      | L.   | .....        | ...                | 3      | .....                 | .....        |                                    |
| 8    | C.   | .....        | No ne.             | .....  | .....                 | .....        | 3 times.                           |
|      | L.   | .....        | ...                | 3      | .....                 | .....        |                                    |

Large Albino rabbit.—Two per cent. solution of cocaine dropped into the right eye until conjunctiva and cornea were

fully under its influence and pupil measured nine millimeters in transverse diameter. An iridectomy was then made, and the two ends of iris allowed to remain in the wound. Exactly the same operation was made on the left eye, without cocaine, the corneal wounds, and pieces of iris removed from each, being as nearly as possible of the same size.

| DAY. | EYE. | SWELLING OF CONJUNCTIVA. | CILIARY INJECTION. |        | UPPER PART OF CORNEA. | WOUND.                  | ANTERIOR CHAMBER.                   | PUPIL. |            | IRIS.               | Two per cent. Solution of Cocaine. |
|------|------|--------------------------|--------------------|--------|-----------------------|-------------------------|-------------------------------------|--------|------------|---------------------|------------------------------------|
|      |      |                          | Large.             | Small. |                       |                         |                                     | Size.  | Form.      |                     |                                    |
| 1    | C.   | 3                        | 1                  | 4      | Dull.                 | Open (iris prolapsed)   | Blood in upper $\frac{1}{8}$ .      | .005   | Irregular. | Swollen.            | 1 in R.                            |
|      | L.   | 3                        | 2                  | 3      | Dull.                 | Open (iris prolapsed)   | Blood in upper $\frac{1}{8}$ .      | .005   | Irregular. | Swollen.            |                                    |
| 2    | C.   | 2                        | 3                  | 2      | Dull.                 | Closed (iris prolapsed) | Blood in upper $\frac{1}{8}$ .      | .005   | Irregular. | Less swollen.       | 2 in R.                            |
|      | L.   | 2                        | 2                  | 8      | Dull.                 | Open (iris prolapsed)   | Blood in upper $\frac{1}{8}$ .      | .005   | Irregular. | Less swollen.       |                                    |
| 3    | C.   | Normal.                  | 3                  | 2      | Clearer.              | Closed (iris prolapsed) | Blood in upper $\frac{1}{8}$ .      | .005   | Irregular. | As on 2d.           | 4 in R.                            |
|      | L.   | Normal.                  | 4                  | 6      | Dull.                 | Open (iris prolapsed)   | Blood in upper $\frac{1}{8}$ .      | .005   | Irregular. | As on 2d.           |                                    |
| 4    | C.   | .....                    | 3                  | 2      | Still more clear.     | Closed (iris prolapsed) | Blood in upper $\frac{1}{8}$ .      | .008   | Irregular. | As on 2d.           | 4 in R.                            |
|      | L.   | .....                    | 4                  | 6      | Clearer.              | Closed (iris prolapsed) | Blood in upper $\frac{1}{8}$ .      | .005   | Irregular. | As on 2d.           |                                    |
| 5    | C.   | .....                    | 1                  | 2      | As on 4th.            | .....                   | Blood all absorbed.                 | .005   | Irregular. | Normal.             | 2 in R.                            |
|      | L.   | .....                    | 3                  | 6      | As on 4th.            | .....                   | B'ld&Lymph in upper $\frac{1}{8}$ . | .005   | Irregular. | As on 2d.           |                                    |
| 6    | C.   | .....                    | 1                  | 1      | As on 4th.            | .....                   | As on 5th.                          | .005   | Irregular. | Normal.             | 2 in R.                            |
|      | L.   | .....                    | 2                  | 3      | As on 5th.            | .....                   | As on 5th.                          | .005   | Irregular. | Still less swollen. |                                    |
| 7    | C.   | .....                    | 2                  | 2      | As on 4th.            | .....                   | As on 5th.                          | .005   | Irregular. | Normal.             | 2 in R.                            |
|      | L.   | .....                    | 4                  | 4      | As on 5th.            | .....                   | As on 5th.                          | .005   | Irregular. | Normal.             |                                    |
| 8    | C.   | .....                    | 2                  | 2      | As on 4th.            | .....                   | As on 5th.                          | .005   | Irregular. | Normal.             | 2 in R.                            |
|      | L.   | .....                    | 2                  | 2      | As on 5th.            | .....                   | As on 5th.                          | .005   | Irregular. | Normal.             |                                    |
| 9    | C.   | .....                    | 1                  | 1      | Cicatrix only.        | .....                   | As on 5th.                          | .005   | Irregular. | Normal.             | 2 in R.                            |
|      | L.   | .....                    | 2                  | 2      | As on 5th.            | .....                   | As on 5th.                          | .005   | Irregular. | Normal.             |                                    |
| 10   | C.   | .....                    | .....              | .....  | Cicatrix only.        | .....                   | As on 5th.                          | .005   | Irregular. | Normal.             | .....                              |
|      | L.   | .....                    | .....              | .....  | Cicatrix only.        | .....                   | As on 5th.                          | .005   | Irregular. | Normal.             |                                    |

Large brown rabbit.—A linear wound at the corneo-scleral margin six millimeters long was made in the left, and the prolapsing iris allowed to remain. Exactly the same operation was then made in the right. A piece of cotton was placed on each eye, that of the left being saturated with a two

per cent. solution of cocaine, and that on the right with water merely, in order that both might be kept equally moist. They were then covered with thin India-rubber, and the animal placed with his head resting easily but firmly so that the covering could not be scratched off.

| DAY. | EYE. | SWELLING OF CONJUNCTIVA. | CILIARY INJECTION. |        | CORNEA.        | WOUND.  | ANTERIOR CHAMBER.   | PUPIL. |            | SWELLING OF IRIS. | Cocaine, 2 per cent. |
|------|------|--------------------------|--------------------|--------|----------------|---------|---------------------|--------|------------|-------------------|----------------------|
|      |      |                          | Large.             | Small. |                |         |                     | Size.  | Form.      |                   |                      |
| 1    | C.   | 3                        | 8                  | 10     | Dull above.    | Open.   | Small clot above.   | 6 mm.  | Regular.   | 3                 | 10 times.            |
|      | R.   | 3                        | 8                  | 10     | Dull above.    | Open.   | Smaller clot above. | 4      | Irregular. | 3                 | .....                |
| 2    | C.   | 2                        | 6                  | 7      | Clearer.       | Closed. | Clots equal.        | 6      | Regular.   | 2                 | 3 times.             |
|      | R.   | 3                        | 7                  | 8      | Dull above.    | Closed. | Clots equal.        | 4      | Irregular. | 3                 | .....                |
| 3    | C.   | Normal.                  | 3                  | 4      | Clearer.       | Closed. | As on 2d day.       | 6      | Regular.   | 1                 | 4 times.             |
|      | R.   | 2                        | 6                  | 8      | Clearer.       | Closed. | As on 2d day.       | 3.5    | Irregular. | 3                 | .....                |
| 4    | C.   | Normal.                  | 2                  | 4      | Normal.        | Closed. | Normal.             | 6      | Regular.   | Normal.           | 3 times.             |
|      | R.   | .....                    | 3                  | 4      | Almost normal. | Closed. | As on 2d day.       | 4      | Irregular. | 2                 | .....                |
| 5    | C.   | .....                    | 1                  | 2      | Normal.        | Closed. | Normal.             | 6      | Regular.   | Normal.           | 3 times.             |
|      | R.   | .....                    | 1                  | 3      | .....          | Closed. | As on 2d day.       | 4      | Irregular. | 2                 | .....                |
| 6    | C.   | .....                    | 1                  | 1      | .....          | Closed. | Normal.             | 6      | Regular.   | Normal.           | 3 times.             |
|      | R.   | .....                    | 1                  | 3      | .....          | Closed. | As on 2d day.       | 4      | Irregular. | Normal.           | .....                |
| 8    | C.   | .....                    | .....              | 1      | .....          | Closed. | Normal.             | 6      | Normal.    | Normal.           | 3 times.             |
|      | R.   | .....                    | .....              | 3      | .....          | Closed. | Band of Lymph.      | 4      | Irregular. | Normal.           | .....                |
| 14   | C.   | .....                    | Normal.            | .....  | .....          | Closed. | Normal.             | 4      | Normal.    | .....             | .....                |
|      | R.   | .....                    | Normal.            | .....  | .....          | Closed. | Band of Lymph.      | 4      | Irregular. | .....             | .....                |

No attempt has been made in any systematic manner to verify these experiments by a similar series upon the human subject. One is not justified in subjecting an eye recently operated upon—for iridectomy for example—to the manipulation, or even violence which such an exact examination often demands, but the great majority of clinical experience, thus far, seems to be in perfect accord with the results reached by experiments upon the animals mentioned.

The conclusions may be briefly stated as follows:

1st—In lesions of the conjunctiva perfect solutions of the hydro-chlorate of cocaine have no appreciable effect, beneficial or otherwise, in the healing process. When the solution is

imperfect a slight additional hyperæmia is produced which persists longer than in the other eye, but this is ordinarily of no practical importance.

2d—In lesions of the cornea, it has a beneficial effect like other mydriatics, but inferior to that of atropine. In imperfect solutions a perceptible abrasion of the epithelium is produced, and, though, this is quickly renewed, the healing is thereby delayed by the cocaine.

3d—In wounds of the iris the mydriatic action of cocaine is evident, but here, again, it is inferior to atropine, and is of little value in detaching firm synechia. Imperfect solutions, however, do not appear to hinder the healing process any more than when applied to the conjunctiva or cornea.

