EXPERIMENTS ON THE ACTION OF BACTERIA ON OPERATIONS OF THE EYE

BY

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AT the end of a systematic bacteriological course in Koch's laboratory, in Berlin, I received pure cultures of pyogenous microbes — namely, staphylococcus pyogenes aureus, albus, and citreus, bacillus pyogenes fœtidus, and the micrococcus of osteomyelitis. With these I made (first at the Hygienic Institute, afterwards in the Anatomy Building, where Prof. Waldeyer and Dr. Hans Virchow kindly put sufficient room at my disposal, and obliged me besides by manifold instruction, although chiefly in another field) a series of experiments on rabbits, in order to ascertain **how a pure wound differed in its healing process from an infected wound.** The experiments were conducted in this way: first, I made a pure operation on one eye, using, however, no chemical agents but operating on a clean, healthy eye with clean hands and instruments— *i.e.*, aseptically, not antiseptically, and, after the operation, leaving the eye alone without a bandage. The other eye was operated upon in the same way, consequently subjected exactly to the same traumatism, but inoculated one way or other, with a pure-culture of bacteria. In so doing, I imitated the chief operations that are practised on the human subject, and desire to premise the remark **that all eyes operated on aseptically recovered, whereas almost all of those infected with the above-mentioned microbes were lost by suppuration,** only those getting well in which the operations had been superficial and limited. Further, I inoculated several eyes with a fermentation-fungus, that of

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pink yeast. This microbe produced transient parenchymatous inflammation, but no suppuration. The experiments thus furnish illustrations of the action both of pyogenic and non-pyogenic fungi. I will first describe the different operations and their results, and afterward discuss them comprehensively in the light of the literature pertaining to the subject.

a.—EXPERIMENTS WITH A NON-PYOGENIC FUNGUS.

EXPERIMENT I.—*Nov.* 24, 1885.—I contaminated an incision through the cornea of a rabbit with a pure culture of the white pyogenic staphylococcus. On the next day I found the pronounced picture of purulent panophthalmitis. The profuse secretion, containing micrococci, was used for several plate-cultures which developed well and, inoculated on other rabbits, again produced purulent inflammation. Of the plate cultures I took test-tube cultures, which on agar reproduced the staphylococcus in a brighter white color than the original which I had received on gelatine. An agar puncture-culture, taken from the plate after seven days, developed on the surface into a most beautifully pink, inodorous little disc. As it differed from the other cultures only in color, I considered it to be a variety of staphylococcus pyogenes and used it in the following experiment.

Dec. 9, 1885.—After instillations of cocaine (which was used in all experiments), I made with the Graefe cataract-knife an incision through the upper part of the cornea and iris. The iris protruded. The wire speculum was removed, and the eye left so.

The right eye was operated in the same way, but a small quantity of the pink fungus was put into the wound with a loop of platinum wire, previously brought to a glow. This eye, like the other, was left without a bandage.

Next morning both eyes looked materially alike. There was no secretion in the left; a small flake of mucus lay on the wound in the right. No injection; the upper part of both corneæ somewhat diffusely gray; centre and lower part of each was clear. The iris filled both wounds without irritation; the pupils were black, and the irides within the eye normal. Both eyes recovered, with a leucoma along the section, in ten days.

Two puncture cultures in peptonized meat-water gelatine were taken from the flake of mucus on the wound of the

right eye. They developed feebly into several white points. The first test-tube contained a pink coat on the surface and two slightly yellowish points in the interior of the gelatine. Both, examined later under the microscope, proved to be pure accumulations of yeast-cells, which had not yet liquefied the gelatine in the least in nineteen days. Some puncture-cultures, taken from the depth of the wound canal, liquefied the gelatine, and under the microscope were discovered to consist exclusively of cocci.

EXPERIMENT II.—On the same day a guinea-pig was operated on in the same manner. The next day no secretion on the left eye; some mucus on the right; both wounds slightly gaping; the adjacent cornea diffusely gray, more on the right (infected side) than on the left. The wounds closed in five days; the corneal opacity of the left eye disappeared completely; that of the right left a simple speck in the upper part.

Two test-tube cultures, taken from the mucous secretion of the right eye the day after the operation, the one in gelatine, the other on agar, developed into a white thread in the gelatine, and a white, somewhat waxy-looking coat on the agar. The gelatine was liquefied and covered with a dirty white, offensive coat, which in one place looked reddish-yellow and consisted of irregular débris of cells. Microscopically only very small cocci were found, about half of which lay together in pairs.

Some fresh cultures in agar and gelatine were taken from the pink fungus of the puncture in experiment I. They developed quickly and beautifully in the pink color of the original. The gelatine was not liquefied, nor, of course, the agar.

The white coat on the peptonized meat-water agar was a mixture of cocci and short bacilli.

EXPERIMENT III.—*Dec.* 16, '85.—Middle-sized rabbit. On the left side extraction of the lens with extensive prolapse of vitreous, brought about intentionally; on the right side extraction of the lens with section through the iris, without loss of vitreous. A small quantity of the pure culture of the pink fungus on agar was introduced through the wound into the anterior chamber of the right eye. The rabbit drew the nictitating membrane over the cornea causing the corneal flap, raised by the prolapse of vitreous

in the left eye, to apply to the posterior lip of the wound in about an hour.

Next day the wound of the left eye was free from irritation and almost closed. The wound of the right eye was gaping and covered with some mucus. The upper part of the cornea diffusely gray, not white.

Both eyes recovered about equally well in two weeks. No irritation, no ciliary injection,—two test-tube cultures of the limpid liquid in the anterior chamber of the right eye did not develop.

This eye also remaining free from suppuration, the conviction forced itself upon me that the pink fungus must differ from the other kinds and be benign. On examination, under the microscope, I found at the first glance that it was no schizomyces at all but a fermentation-fungus (*Sprosspilz*, sprouting fungus), according to its aspect and all its reactions the common pink torula, the fungus of the pink yeast, which in Koch's laboratory I had cultivated and examined often enough. Nevertheless, I inoculated with a pure culture of it

EXPERIMENT IV.—On *Dec. 17th.*—Another eye after extraction of the lens. To make a test case of this experiment I stroked the whole wound with the fungus and introduced a quantity about the size of a pin-head into the anterior chamber. The next day I found the wound closed, clean, covered with some mucus which consisted of phlegm corpuscles and a few yeast cells. Some mucus on the edges of the lids. No swelling of the conjunctiva. Cornea clear. No blood in the anterior chamber. No suppuration. The eye recovered with formation of a secondary cataract, posterior synechiæ, and bulging iris.

These four experiments show distinctly that the fungus of the pink yeast is not pyogenic. All the wounds infected with it healed in the same way as those which resulted from clean operations done on the fellow eye, with this distinction only that the harmless foreign body was cast off with the formation of a small quantity of mucus. When I spoke to Dr. George Frank, one of the assistants in Koch's laboratory, of the results of these experiments, he told me that the pink torula was abundantly present in the

air of the laboratories in Berlin. Although this widespread fungus entered as a contamination into one of my cultures, I was very much interested by the course of the inoculations I made with it, for it furnished a clear demonstration of the fact that a microbe resembling pyogenic schizomycetes both macroscopically and in cultures (with the exception of not liquefying nutrient gelatine) may totally differ from it in its action on living animal tissues.

b.—EXPERIMENTS WITH PYOGENIC FUNGI.

EXPERIMENT V.—*Discision. Injection of osteomyelitis fungus into the anterior chamber. Panophthalmitis.*

On *Dec.* 18, '85, I made with a Graefe cataract-knife a discision of the lens in both eyes of a middle-sized rabbit. With a Koch's syringe I injected one drop of a fresh emulsion of the orange fungus of osteomyelitis, cultivated on agar, into the anterior chamber of the right eye, letting the animal afterward without bandage take care of itself.

Dec. 19*th.*—*Left*, opacity of the lens without any irritation; *Right*, profuse purulent secretion; cornea white, anterior chamber full of pus.

Dec. 21*st.*—*Left*, no irritation; *Right*, purulent secretion; anterior chamber filled with pus; cornea ulcerous.

Dec. 22*d.*—Eyes in the same condition. The animal is emaciated; its hair shaggy, and it suffers from yellow diarrhœic discharges. Innumerable small cocci are found on microscopic examination of dried and stained cover-glass specimens, taken with a previously heated gelatine wire from the pus in the anterior chamber.

Dec. 23*d.*—Left eye free from irritation; the right cornea partially destroyed; purulent panophthalmitis. The animal looks wretched, and dies in the night.

Dec. 24*th*, AUTOPSY.—The skull was opened with bone scissors. The brain was normal. The optic tracts were severed behind the chiasm. With a small pair of bone-forceps the osseous plates covering the optic nerves were removed and the optic nerves of both eyes carefully laid bare. Neither they nor the chiasm showed any thing abnormal; the internal organs were found healthy with the exception

of the liver which contained numerous small yellowish, dense patches. Gelatine and agar cultures were taken from the interior of the right eye, the chiasm, and the optic nerves close behind the eye. They all developed well. Dry-cover specimens, taken from the same places, and from the blood and the interior of the left eye, were stained with aniline colors, but cocci were found only in the pus which filled the interior of the right eye. They were present in great quantities in the protoplasm of the pus corpuscles, or scattered also in the adjoining free space, or lying in large colonies on a collection of pus cells. They were exactly like the small cocci injected into the anterior chamber. Here and there they were arranged in small chains. Beside these, a sparing quantity of equally or more darkly-stained, larger (about twice the size of the smaller) granules were found single, in small clusters or chains. They have been described as larger cocci, but may be spores of mould. The cultures from the chiasm and the optic nerves had grown but little and were inodorous. Those from the right optic nerve and the chiasm showed under the microscope an innumerable quantity of *short bacilli* with some micrococci interspersed. Surprised at this condition I prepared several specimens from different places of the cultures and examined them carefully: they appeared like short bacilli, not as diplococci. The culture, taken from the left optic nerve near the globe, proved to be pure ordinary cocci, many of them arranged in short chains. A culture taken from the discinded lens of the left eye had developed, and consisted of cocci.

EXPERIMENT VI.—*Discision. Injection of the fungus of osteomyelitis into the anterior chamber. Panophthalmitis.*

Dec. 18*th.*—I made, in a like rabbit, a similar simple discision of the lens in both eyes, and injected into the anterior chamber of the right a drop of an emulsion of osteomyelitis fungus from a test-tube culture which I had taken from the anterior chamber of a rabbit previously inoculated with the same fungus.

Dec. 19*th.*—L, no irritation; lens opaque. R, purulent secretion. Anterior chamber half filled with pus.

Dec. 20th.—L, no irritation. R, intense suppuration ; Cornea sloughing ; anterior chamber filled with pus.

Dec. 22d.—Pus from the anterior chamber contains groups of ordinary cocci in the protoplasm of the cells.

Dec. 26th.—R, still copious discharge ; cornea totally destroyed; iris lying bare. L, lens less opaque ; no irritation.

Dec. 29th.—R eye one mass of pus.

Dec. 31st.—R, cornea and iris having disappeared, a white granular substance protrudes from the depth. The lean but lively animal, the left pupil of which is almost completely clear, is put to death by chloroform.

AUTOPSY.—Opening of the skull as in the preceding case. Brain and inner organs normal, excepting the liver, which contained a number of gray dense patches free from cocci. The right eyeball is small, its sclerotic white, whereas that of the other eye is blackish. The right optic nerve is slighty yellowish, otherwise not different from the (normal) left. Chiasm normal. The left eye, apart from the discision scar, is perfectly healthy. I desire to state particularly that nothing abnormal can be detected in the fundus oculi either with the naked eye or with a magnifier.

Dry-cover specimens and cultures were taken from the interior of the right eye, both optic nerves, the medulla oblongata, the heart-blood, the juice of the kidneys, and the disseminated patches in the liver. The inflammatory changes in the kidneys, which F. Krause describes in his experiments, were absent. The right optic disc and adjacent parts were swollen ; the specimens taken from these parts contained numerous groups of small, apparently shrunken cocci, regularly developed only here and there. The specimens from the optic nerves and chiasm contained no unmistakable cocci.

In six days, at the temperature of a heated room, only three of the cultures developed—namely, those from the vitreous, optic nerve and optic tract of the right eye. The first two were pure cocci, but that from the right optic tract, and perhaps the adjacent brain substance, into which the inoculating-needle may have dipped, showed short bacilli exclusively. One colony only of this culture, about the

size of a millet seed, in the middle of the needle-track, had developed, whereas a goodly number of dots lined the track from the optic-nerve culture, and the culture from the vitreous had grown luxuriantly.

EXPERIMENT VII.—*Section through cornea, iris, and lens. Painting of the wound with staphylococcus pyogenes albus. Panophthalmitis.*

On *Sept. 24th*, in the bacteriological laboratory of Berlin, I made with a Graefe knife a section, about 9 *mm.* long, through the upper part of the cornea, iris, and lens of both eyes of a full-grown rabbit. The iris prolapsed. A small quantity of a pure culture of the white pyogenic staphylococcus, taken directly from the test-tube with a sterilized platina wire loop, was spread over the wound of the *right* eye.

Dec. 25th.—No secretion, no irritation in the *left* eye. The protruding iris, plugging the wound completely, is covered by a trace of mucus. The upper part of the cornea is diffusely gray, clearing toward the centre. The anterior chamber is reëstablished. The lower half of the cornea, the aqueous humor, iris, and pupil are clear. To finish the description of this eye without interruption I will state that the prolapse of iris diminished from day to day, and finally disappeared without the formation of a staphyloma ; the cornea was clear except at the site of the wound, and the centre of the lens remained transparent.

In the *right* eye profuse purulent secretion had developed. The conjunctiva was red and moderately swollen. The cornea was white in the vicinity of the wound, the iris discolored and swollen.

Dec. 26th.—R eye swollen ; copious purulent discharge ; the wound closed ; the upper part of the cornea white ; the anterior chamber filled with pus ; in short, *the picture of suppurative panophthalmitis in its typical aspect after extraction of cataract.*

Dec. 27th.—Anterior chamber filled with pus ; cornea white, infiltrated all around.

Paracentesis liberated flaky pus, in which I detected no cocci with the microscope, but four needle and three plate cultures taken from it developed pure staphylococcus albus and aureus mixed. They had macroscopically and microscopically the same appearance as the original culture, and

on inoculation manifested the same degree of virulence. Two days later I enucleated the eye and placed it in alcohol. When hardened it was examined with the microscope. Microtome sections discovered cocci in the substance of the cornea but not in the protruding iris. The whole interior was filled with a chalky-white, somewhat granular mass, in which cocci were not detected with certainty.

EXPERIMENT VIII.—*Wound contaminated with virulent pus. No suppuration.*

Nov. 25th.—A section extending to the ciliary region was made through the upper part of both corneæ of a guinea-pig, and pus from the conjunctival sac of the rabbit described in the preceding case was stroked over the wound in the right eye by means of a platina wire loop.

Nov. 26th.—Both corneæ around the wound diffused and opaque, the right somewhat more than the left. No secretion.

Both wounds closed ; the corneæ cleared up ; the left was quite clear in nine, the right in fourteen, days.

EXPERIMENT IX.—*Pyogenic fungi put into the conjunctival sac, then incision made through cornea and iris. No suppuration.*

Nov. 26th.—I put, by means of a wire loop, several drops of a liquefying, very luxuriant culture of staphylococcus pyogenes albus and aureus mixed, from a plate, into the right conjunctival sac of a rabbit. Ten minutes later I thrust a cataract-knife through the cornea, iris, and lens of this eye, after having just before made the same operation on the left, not infected, eye.

Nov. 27th.—The wound of the right eye healed so as to leave scarcely a trace of the injury. In the left a prolapse of iris, clean, disappearing gradually without irritation in two weeks ; cornea and pupil clear.

EXPERIMENT X.—*Corneal section with infected knife. Panophthalmitis.*

Nov. 26th.—On the left side, section with a Graefe knife through cornea, iris, and lens ; on the right, the same operation after the knife had previously been dipped into the liquefied gelatine on a plate of a pure culture of staph. pyog. aur.

Nov. 27th.—L, prolapse of iris ; no secretion ; no irritation

During the following ten days the wound healed in the ordinary way, without irritation, leaving a partial staphyloma. On the *right* side the lids were swollen, closed by dried, purulent secretion, which, on forcible opening of the lids, ran out copiously. Chemosis. Upper segment of cornea white, infiltrated with pus. Pus in the anterior chamber.

Nov. 30*th.*—R, suppuration increased.

Dry-cover specimens of the secretion discovered no microorganisms with certainty, but needle cultures taken from the secretion developed vigorously as staphylococcus pyogenes aureus.

Dec. 5*th.*—The inflammatory symptoms gradually subsided, the wound contracted.

On *Dec.* 10*th* only the upper part of the cornea was yellow, but covered with epithelium.

I made an incision into the yellow, infiltrated portion of the cornea, and used the tissue juice for dry-cover specimens and test-tube cultures. The former discovered no microbes and the latter did not develop, the microbes evidently having all been dead.

Jan. 21, 1886.—The yellow infiltration disappeared completely and the inflammation disappeared, leaving a slightly prominent corneal staphyloma.

EXPERIMENT XI.—*Corneal section, contaminated with staphyloc. pyog. aur. Panophthalmitis.*

Dec. 4*th*—Puncture of the right cornea of a rabbit with a broad needle, enlarged with scissors. Particles of a pure culture of staph. pyog. aur. on agar were put with a wire into the anterior chamber, near the wound, and the wire was passed once over the iris protruding in the wound. L, the same operation with the same instruments, previously brought to a glow in a gas flame. No inoculation.

L, prolapse of iris, but no inflammation. The recovery took place in the usual way.

R, profuse suppuration. Cornea white.

Dec. 9*th.*—The whole right cornea white. Suppuration copious.

Dec. 12*th.*—Upper and central parts of cornea white, lower gray. Termination, total opacity of cornea.

On the second day, cultures were taken from the pus in the anterior chamber. They developed on agar as staphyloc. pyog. aur. pure, in gelatine as st. pyog. aur., and alb. mixed. Cultures from the juice of the inspissated infiltration of the cornea did not develop.

EXPERIMENT XII.—*Section through cornea and iris, contaminated with staphyloc. pyog. alb. Panophthalmitis.*

With a pure culture, derived from the pus in the anterior chamber of the rabbit used in experiment VII., the right eye of a rabbit was infected by means of a wire loop moistened with the culture (albus) and passed over a simple incision through the cornea and iris. In the left eye the same procedure with a wire loop previously heated to a glow. This eye recovered in the usual way without irritation. The other presented next day the well-marked picture of primary suppuration, developing into panophthalmitis.

On the second day, cultures were taken from the pus of the wound. They developed as a mixture of staphyl. pyog. albus, aureus, and citreus. On agar two thirds were aureus, one third albus. In dry-cover specimens the cocci were found abundantly. On the sixth day I killed the animal, found every thing normal, excepting the eyes; in particular, the optic nerves, the chiasm, and the brain were without macroscopic changes.

EXPERIMENTS XIII. AND XIV.—*Extraction. Contamination with bacillus pyogenes fœtidus and staphyloc. pyog. citreus. Panophthalmitis. Vascular parenchymatous keratitis.*

On the 15th of Dec. I made an extraction on both eyes of two rabbits, and contaminated the wound of the right eye of one rabbit with a pure culture of bacillus pyogenes fœtidus, that of the other with staplyloc. pyog. citreus, both discovered by Passet. In order to render the difference between mere traumatism and infection as conspicuous as possible, I made the operations on the left eye in both rabbits most extensive. When the lens was removed, I passed a wire previously brought to a glow, repeatedly over the ciliary processes until a large prolapse of vitreous had occurred and the wound gaped widely. The rabbits left alone drew the nictitating membrane repeatedly over the eye, and in about an hour the prolapse of vitreous had been brushed away. They kept

their eyes open, moving the lids and the nictitating membrane from time to time.

These two, quite coarse operations, were recovered from without a trace of suppuration, with very slight injection, and without secretion.

The two right eyes, on which the extraction had been performed continuously and without accident, presented profuse suppuration of the wound ; white cornea and gray iris on the following day. Subsequently the eyeball swelled, the anterior chamber was filled with pus and the secretion was profuse. The upper part of the cornea gradually sloughed away, the wound filled with inspissated pus and retracted, while the remainder of the cornea became diffusely opaque and covered from the edge with a dense network of blood-vessels (vascular parenchymatous keratitis, Jan. 2, '86).

The secretion of the wound examined by means of cultivation and dry-cover glass specimens contained many bacteria. The cultures of fœtidus were short bacilli, did not liquefy the gelatine, had a blue tinge on the surface, and a bad odor. The cultures of citreus were cocci, they liquefied the gelatine, and were partially white, partially more or less orange, without reproducing the pure lemon-yellow of the original culture.

EXPERIMENT XV.—*Extraction. Contamination with the micrococcus of osteomyelitis. Suppuration. Phthisis bulbi.*

Dec. 16th.—Simple extraction. Contamination of the wound with a three-weeks-old, yellow culture of an emulsion, the micrococcus of *osteomyelitis*, a drop being spread over the wound with a wire loop. The next day profuse purulent discharge, the upper part of the cornea whitish yellow, the wound gaping, anterior chamber filled with pus. During the next few days suppuration continued ; then it gradually disappeared. The cornea cleared from below upward, the hypopyon disappeared, the vitreous was yellowish white, at the closing wound there was a circumscribed purulent abscess of the cornea which disappeared in two weeks after the operation. Eyeball shrinking (*from internal suppuration with partial destruction of the cornea*).

The verifying eye, in which extraction with prolapse of the vitreous had been made, recovered in the usual way without irritation.

In the secretion of the anterior chamber micrococci were freely demonstrated by dry-cover specimens and cultures. The latter developed white at first, but became yellow afterward, liquefied, cone-like, the jelly in the test-tube producing at the lower end a granular (at first white, then yellow) sediment; while on the surface of agar they developed into neat, coalescing orange clusters, the true picture of *staphyloc. pyog. aureus.* These cultures were used for further inoculations. They showed the same properties and the same pyogenic energy as the original.

EXPERIMENT XVI.—*Extraction with an infected knife. Panophthalmitis.*

Dec. 24th.—*L*, extraction, knife introduced three times, iris in the wound.

R, section with a single introduction of a Graefe knife, previously moistened with an emulsion of osteomyelitis coccus. The culture was orange-colored, and showed under the microscope small cocci—single, double, and in short chains.

Dec. 25th.—*L*, wound clean, plugged with iris. Upper part of cornea profusely gray. Neither congestion nor secretion. *R*, purulent secretion, wound gaping, in it a black bead of vitreous. Lower two thirds of cornea filled with pus.

The left eye recovered smoothly. In the right panophthalmitis developed with total destruction of the cornea.

EXPERIMENT XVII.—*Discision with an infected needle. Panophthalmitis.*

Dec. 24th.—*L*, discision of lens with a needle. *R*, the same, the needle having previously been moistened with an emulsion of the fungus of osteomyelitis.

Dec. 25th.—*L*, opacity of lens without irritation, puncture of cornea clean, iris normal. *R*, closed, purulent discharge on separating the lids. Cornea around puncture swollen, infiltrated with pus. Streaky, purulent exudation in the shallow anterior chamber. Eye swollen.

Dec. 25th.—*R*, profuse sanguino-purulent discharge on forcible separation of the swollen lids. Eye swollen, cornea opaque. Pus in the pupillary space and in the lower part of the anterior chamber.

Jan. 2, 1886.—Right eye lost from panophthalmitis; the left has remained free from inflammation.

EXPERIMENT XVIII.—*Extraction. Pressing out of the lens with infected lids. Panophthalmitis.*

Dec. 28th.—*L*, ordinary extraction. *R*, the same; after an emulsion of osteomylitis coccus had been freely applied to the conjunctival sac and over the edge of the upper lid. When the corneal section, which at the same time had opened the capsule, was completed, the lens was pressed out with the edges of the lids, and the remnants of the lens were wiped out of the wound with the edge of the upper lid.

Dec. 29th.—*L*, large prolapse of iris, covered with a streak of mucus which, when drawn away with a pair of forceps, left a smooth, clean surface. Cornea in the neighborhood of the section diffusely opaque. Pupil and iris clear. The eye recovered without irritation. *R*, excessive purulent secretion; thin, turbid liquid escaped even from the nose. The whole cornea white; the wound and protruding iris white, bathed with pus.

Jan. 2, 1886.—Most pronounced panophthalmitis.

The pus taken from the wound the day after the operation, presented under the microscope an immense quantity of cocci.

EXPERIMENT XIX.—*Needle inoculation with the micrococcus of osteomyelitis. Circumscribed abscesses. Recovery.*

Dec. 28th.—Three punctures of the corneal substance, without perforation, were made with a Graefe knife, the point of which had been previously dipped into an emulsion of the coccus of osteomyelitis.

Dec. 29th.—Moderate discharge. The three punctures are white, raised, from two to four millimetres in diameter.

Dec. 30th.—The three points have developed into prominent corneal abscesses. Hypopyon filling the lower third of the anterior chamber.

Dec. 31st.—Abscesses smaller, cornea clearing; no secretion.

Jan. 4, 1886.—Abscesses very small, circumscribed opacities.

Under cocaine a small quantity of the contents of the absorbing abscess was removed with a needle and examined in dry-cover glass specimens, stained with aniline. It showed an immense quantity of small, feebly-stained, somewhat irregular granules (cell detritus and dead cocci).

EXPERIMENT XX.—*Five needle-pricks in the cornea, fungus of osteomyelitis painted over them ; only one develops into a pustule, which gradually disappears.*

Dec. 28th.—With a clean Graefe knife the cornea is pricked in five points and then repeatedly painted with an emulsion of the coccus of osteomyelitis by means of a wire loop.

Dec. 29th.—The whole cornea clouded, but only one prick is white. Slight secretion.

Dec. 30th.—The white, infiltrated point somewhat larger than the day before ; the remainder of the cornea clearer.

Dec. 30th.—The circumscribed infiltration smaller.

Jan. 1, 1886.—Still smaller and covered with epithelium.

Its contents scraped out with a needle and microscopically examined showed the same detritus as in the preceding case.

EXPERIMENT XXI.—*Painting of a healing scar with micrococci of osteomyelitis. No reaction.*

Dec. 28th.—An emulsion of recently cultivated osteomyelitis cocci, which, in other experiments, had proved very efficient, was spread by means of a wire loop repeatedly over the iris, which filled the clean extraction-wound of the left eye of a rabbit operated on twelve days previously (Expt. XV., verifying eye). Absolutely no reaction followed. The next day the eye looked whiter and the scar was cleaner and smoother than before.

EXPERIMENT XXII.—*R, extraction with an infected knife ; L, extraction with the same knife, over which a current of water had been running a quarter of a minute. Panophthalmitis on both sides.*

Dec. 29th.—On the right eye, extraction with a Graefe knife previously dipped into an emulsion of micrococci of osteomyelitis. On the left eye the same operation, with the same knife, over which a stream of ordinary water from a hydrant had just before been running for a quarter of a minute.

Dec. 30th.—Purulent iridokeratitis in both eyes, *L* even more than *R*. Purulent secretion marked.

Jan. 2, 1886.—Infiltration of the flap limited in both eyes, right almost disappeared. Both corneæ and anterior chambers opaque. Irides and pupils not to be seen. The purulent inflammation extends no doubt to the deeper parts.

Jan. 4, 1886.—Panophthalmitis in both eyes with preservation of the cornea.

Examination of the secretion of the wound showed the leucocytes loaded with cocci.

EXPERIMENT XXIII.—*R, extraction with an infected knife. Panophthalmitis. L, extraction with the same knife after it had been washed with water and wiped clean with a towel. Recovery without irritation.*

Dec. 29th.—*R*, extraction with a Graefe knife previously dipped in an emulsion of the coccus of osteomyelitis. *L*, the same operation with the same knife which had just been washed in ordinary hydrant water, washed clean, and polished with a recently washed ordinary towel of the anatomical laboratory.

Dec. 30th.—*R*, suppuration in the wound marked as usual; *L*, no secretion, no irritation. Iris in the wound clean. Upper part of cornea cloudy, the lower two thirds, the pupil and iris clear.

Jan. 2d.—*R*, panophthalmitis; *L*, no irritation.

Jan. 4th.—*L*, smooth recovery.

EXPERIMENT XXIV.—*Emulsion of pyogenic cocci put into the conjunctival sac. Extraction and paracentesis with a clean knife. Suppuration in both cases.*

Dec. 29th.—An emulsion of a fresh culture of the fungus of osteomyelitis is dropped repeatedly into the upper and lower parts of the conjunctival sac and painted over the cornea. Two minutes later the lens is extracted from the left eye with a sterilized Graefe knife, and with the previously heated blade of the same a paracentesis of the anterior chamber and a puncture into the substance of the cornea of the right eye are made. By the next day the left eye presented the usual wound suppuration, and the right well-marked abscesses as the punctures. Purulent secretion in both. The extraction-wound causes panophthalmitis; the corneal abscesses cause hypopyon in the next few days, burst on the outer surface, and disappear, leaving cicatrices.

Jan. 4th.—The contents of the abscess, obtained with a needle, show in the dried and stained cover-glass specimen distinct colonies of irregular, evidently decaying cocci.

EXPERIMENT XXV.—*Squint-operation; infected. Phlegmon. Recovery.*

Dec. 23d.—I made a subconjunctival tenotomy of the upper straight ocular muscle of a rabbit and introduced with a wire loop a very small quantity of a culture of osteomyelitis coccus.

Dec. 24th.—Purulent secretion on the lids and in the conjunctival sac. The regions of the wound swollen, whitish yellow, its neighborhood congested, cornea clear.

Dec. 25th.—No secretion, cornea clear, region of the divided muscle greatly swollen (abscess).

Jan. 2, '86.—The phlegmon discharged a good deal of thick yellow matter. The cornea clear, and the region of the wound less swollen and red.

Jan. 4, '86.—Swelling and suppuration have almost disappeared.

Cultures of the pus taken the day after the operation grew luxuriantly and showed on Jan. 4th pure cocci.

Reviewing these cases in groups we arrive at the following results:

1. **Two cases of discision with injection of a drop of an emulsion of pyogenic cocci into the anterior chamber** (exp. V. and VI.). The operation was immediately followed by the most intense primary suppuration in the anterior chamber with purulent maceration of the cornea and of all interior parts of the eye. Both animals looked ill, the one died on the sixth day, the other recovered and was killed on the thirteenth. Under the microscope and by cultivation cocci were discovered in the pus, the cornea, and inner membranes; besides that, cultures developed from the optic nerves, the chiasm, one optic tract, and the lens of the other eye, though I did not succeed microscopically in demonstrating cocci in these and other parts of the body, nor in the blood. It surprised me to see short bacilli develop in some cultivations that were taken from parts behind the eye, while others reproduced the injected micrococcus of osteomyelitis, which I cannot but consider to be identical with the staphyl. pyog. aureus on account of the indentical morphological, biological, and pathogenic properties they have in common. I desire to mention here the interesting experiments of Deutschmann,[1] who after injection of large

[1] Experimenteller Beitrag zur Pathogenese der sympathischen Augenentzündung, *Graefe's Arch.*, Bd. xxvii., ii., pp. 291–300, 1882. Zweiter Artikel, *Ibidem*,

quantities of pyogenic fungi into the vitreous of one eye could observe their migration with concomitant inflammation through the optic nerve of the infected eye, the chiasm, and the optic nerve of the other eye into the posterior segment of the latter. All his animals died in a few days. I would dwell on these interesting and suggestive investigations as well as on Deutschmann's bacteriological researches of enucleated human eyes if it lay within the scope of my subject. The object of my experiments is not to find the paths by which micro-organisms travel through the organs of the body, but to determine their pyogenic properties with special reference to the operations of the eye. These properties manifest themselves most strongly when the organisms are injected through a small wound into the interior of the eye and are there retained, a fact which is in harmony also with the experiments of Deutschmann.

2. **A discision with an infected needle** (exp. XVII.) was followed by severe primary suppuration in the track of the needle through the cornea and in the anterior chamber, and loss of the eye. It is evident from this observation that, under certain conditions, the quantity of the infecting material may be small, the traumatism insignificant, and yet the suppuration marked and extensive. Cases of suppuration from discision, especially in old secondary cataracts, have occurred several times in my own practice ; I have also seen them (even last year) in the practice of others that operate antiseptically, so that an introduction of pyogenic germs could, it seems, be excluded. To enter more deeply into this question would, in this place, lead me too far. I desire only to remark that these cases resembled those in which a foreign body, a scar, a small prolapse of iris, or an iridencleisis not visible exteriorly may have existed without irritation for many years, and then suddenly produce suppuration after very insignificant traumatism, or, indeed, without assignable cause. Recent investigations seem to make it probable that, in some cases, the suppuration after discision is not due

Bd. xxix., iv., 261–270, 1883. Dritter Artikel, *Ibidem*, Bd. xxx., iii., pp. 77 to 122, 1884. Erster Nachtrag, *Ibidem*, Bd. xxx., iii., pp. 331–336, 1884. Zweiter Nachtrag, *Ibidem*, Bd. xxx., iv., pp. 315–317, 1884. Vierter Artikel, *Ibidem*, Bd. xxxi., ii., pp. 270–290, 1885.

to fresh introduction of pyogenous elements with the needle, but to older, latent local deposits of cocci, or to their presence in the humors of the organ or the whole body, so that the traumatism is to be regarded only as one of the conditions by forming a locus minoris resistentiæ. Among these investigations I may mention those of Becker,[1] F. Krause,[2] and Rosenbach,[3] who, after simple fractures in animals, have seen suppuration occur only when osteomyelitis micrococci were injected into the veins. Also the experiments on ulcerous endocarditis recently communicated by Orth,[4] at the Society of Naturalists and Physicians, at Strasburg, may serve to lend weight to this supposition. When he and Dr. Wyssokowitsch pierced the aortic valves from the carotid with a blunt-pointed probe, neither endocarditis nor thrombotic deposits occurred at the injured place; but when pyogenic organisms were injected into the vein of the ear simultaneously, or one or two days later, acute endocarditis with metastatic abscesses developed, of which the animals died in from two to five days. The organisms did not settle at certain places arbitrarily but only where a previous disturbance had caused a predisposition. This tendency may be produced by very insignificant mechanical injuries, for the organisms did not settle on the lacerated valves only but also on the large vessels over which the knob of the probe had slid. By such and similar experiments the old doctrine of "impure humors" gains a visible form. If we call this process constitutional or indirect infection of a wound, the possibility of which, according to what has been said, can scarcely be denied, our experiments positively demonstrate the importance of direct infection even by instruments of the smallness of a division needle.

3. Three cases (XIX., XX., and XXIV.) of **inoculation by pricks of a needle, and paracentesis.** These inoculations caused circumscribed corneal abscesses with so much the

[1] Vorläufige Mittheilung, etc., von Struck, *Deutsche med. Wochenschr.*, 1883, No. 46.

[2] *Fortschritte der Medicin*, 1884, No. 7 u. 8.

[3] Wundinfectionen des Menschen, Wiesbaden, 1885.

[4] *Tageblatt*, page 58, Strasburg, 1885.

more certainty as the micro-organisms were introduced the more directly and probably also the more plentifully and deeply into the corneal substance. The paracentesis with an infected needle caused the largest abscess, the inoculation pricks with an infected needle produced well-developed pustules, whereas, of the five punctures with a clean needle, after which the emulsion of microbes was immediately painted over the cornea, only one developed into a circumscribed purulent exudation which soon disappeared. I may mention in connection with this that I painted an emulsion of pyogenous bacteria over the corneæ of a guinea-pig and some rabbits after I had made superficial scratches in the cornea with a knife, but produced no more than a transient opacity without suppuration.

Inoculations of the cornea have been made by F. Krause and Passet. Krause[1] says: "If the cornea is inoculated by making a small pouch into the corneal substance with a division needle, previously brought to a glow, an infiltration of the cornea occurs, which in most cases disappears in a short time. In two eyes out of twelve hypopyon formed. In the pus of the enucleated eye no micro-organisms were found and the planting of pus from the hypopyon on agar-agar yielded a negative result." I can say the same of a case in which hypopyon formed three weeks after an extraction that had healed with a smooth scar. In the pus, aseptically obtained by paracentesis of the cornea, no micro-organisms could be detected in dry cover specimens and four gelatine plates charged with it showed no trace of growth. These observations harmonize with the investigations of R. Koch, A. Ogston,[2] and others who found cocci in the pus of acute abscesses only.

R. Koch, in his classical monograph, "Investigations on the etiology of diseases by wound infection,"[3] describes the whole process of the formation of abscesses in a very clear manner. The bacteria are met with in large numbers in the abscess wall and the near vicinity whereas the caseous con-

[1] *Fortschritte der Medicin*, 1884, p. 228.

[2] Ueber acute Abscesse, *Archiv f. klin. Chirurgie*, Bd. xxv., Heft 3, p. 588, 1880, und an verschiedenen Orten im *Brit. Med. Journ.*

[3] Leipzig, 1878, p. 51, u. f.

tents are made up of cell detritus and dead, scarcely recognizable cocci.

Passet [1] noticed, after inoculation punctures with staphyloc. pyog. aureus (*l. c.*, p. 21), albus (p. 25), and citreus (p. 27), whitish-gray, circumscribed exudations which disappeared in from four to ten days, leaving a speck.

The necessity of a certain quantity that must not be too small to render inoculations efficient, is not only demonstrated by my experiments but has been noticed and distinctly pointed out by many others. F. Krause [2] says: "No reaction occurs if a small quantity of a pure-culture is put, without attenuation, into a pouch in the skin of a rabbit, guinea-pig, or mouse, with a platinum needle previously heated.

4. **Negative experiments with pyogenic material** (exp. VIII., XXI., and XXIII.). Pus was put into an incision through the cornea and iris of a guinea-pig. It was taken from a rabbit affected with acute corneal suppuration and certainly was not sterile, for at the same time much smaller quantities of it were used for needle cultivations which not only developed vigorously, but wounds inoculated with these cultivations suppurated freely. There remains no other possibility than to assume that the inoculated quantity was insufficient at least for this guinea-pig.

A very strong emulsion of osteomyelitis fungus (expt. XXI.) was painted freely over the cicatrizing wound of a rabbit, without any effect. The wound may have been entirely covered with epithelium and thus protected, but I have recently seen (in the above-mentioned case of hypopyon, where the pus contained no cocci) the apex of a corneal flap become white about twelve days after a cataract-extraction, the cicatrix up to that time having been perfectly free from irritation. The infiltration disappeared in three or four days, but a week later hypopyon made its appearance without any abnormity to be noticed in the cornea or iris. The patient suffered from chronic conjunc-

[1] Untersuchungen über die Ætiologie eitriger Phlegmone des Menschen. Berlin, 1885.

[2] *Fortschritte der Medicin*, 1884, p. 227.

tival catarrh, but had been treated and operated on under strict antiseptic precautions. The other eye, operated on shortly before by a very skilful hand, had been lost through intense iritis and iridocyclitis. If we are loath in this anæmic patient to accuse impure humors, we are forced to assume that pyogenous fungi from the conjunctival sac must have subsequently infected the incompletely closed or partially reopened wound, and migrating through the fresh scar to the ciliary body produced a purulent cyclitis. How much the susceptibility varies in different species of animals, even in different individuals of the same species, has long been known. The most striking example of this fact with reference to bacteriology is the observation made by R. Koch and reported in his "Diseases by Wound Infection," 1878, that the smallest quantity of the bacillus of mouse septicæmia kills the house-mouse, but has no influence on the field-mouse. Expt. XXIII. shows a regular primary suppuration after an infection of the blade of the knife, whereas an extraction made on the other eye with the same blade, after it had been washed and polished with a clean towel, healed without irritation. The instrument after this simple cleansing proved sterile with reference to the inoculation of this rabbit. I do not venture to maintain that this kind of sterilization suffices for all rabbits or all men, but according to recent investigations[1] this seems to be the case for surgical instruments in general and especially for polished ones.

5. **Insufficient cleansing of an instrument.** In connection with the preceding remarks the following observation (expt. XXII.) is of particular importance. The right eye of a rabbit was lost by primary suppuration after extraction of the lens with a Graefe knife that was contaminated with an emulsion of osteomyelitis fungus. The extraction of the lens of the left eye with the same knife, though after the operation on the right a stream of hydrant water had been

[1] *Gärtner* u. *Plagge:* Ueber die desinficirende Wirkung wässeriger Carbolsäurelösungen. Verhandl. der Deutschen Gesellschaft für Chirurgie. Berlin, Hirschwald, 1885, II. p., 1–11.

H. Kümmel: Die Bedeutung der Luft- u. Contactinfection für die practische Chirurgie. *Ibidem*, II., p. 430–446.

running over it, produced a suppuration no less intense. The water of the new Berlin water-works, which at present is remarkably pure, can scarcely have been the cause of the suppuration, and we must assume that the micrococci adhered so firmly to the steel as not to be swept away by a simple stream of water, whereas washing of the blade with the fingers and polishing it with a towel removes them thoroughly enough.

Experiments on that point, with special reference to ophthalmological practice, would be highly desirable. How surely is sterilization effected, 1. by ordinary cleansing? 2. heat, of what degree, and how long? 3. absolute alcohol? 4. carbolic acid? 5, corrosive sublimate? 6. boric acid, etc. How surely do these chemicals sterilize, with or without previous ordinary cleansing of an infected instrument? The examination should be made according to the different methods of cultivation, inoculation, and operations, of course with strict observance of the rules of bacteriology. The above-mentioned experiments of Gaertner, Plagge, and Kümmel might be used for comparison.

6. **Incisions through cornea, iris, and adjacent part of the lens.** Inoculation with different pyogenic bacteria. Four cases (exp. VII., X., XI., and XII.), all lost by primary suppuration.

7. **Four cases of extraction, the wound infected with different pyogenic bacteria** (exp. XIII., XIV., XV., and XVI.). Suppuration in all. The verifying operations in these two groups, though performed in the most extensive and unsparing manner, were followed by prolapse of iris, transient diffuse gray opacity of the flap, but no suppuration.

8. **Subconjunctival squint-operation** (exp. XXV.). This operation also, after inoculation with the pyogenous fungus, was followed by primary suppuration. Fourteen years ago I made a subconjunctival tenotomy in a boy who, after the operation, on a cold winter day, travelled three hours in a carriage, vomiting frequently (he had been anæsthetized with chloroform) and held his head out of the carriage. On the third day I was called, and found a phlegmonous inflammation like the one in our rabbit, which was recov-

ered from, but left a divergent strabismus. At the time I attributed this to the influence of the long drive in the cold. Last summer I saw a subconjunctival tenotomy followed by a small pustule at the upper end of the wound canal, under the unbroken conjunctiva. It burst and disappeared without inconvenience in a few days. In drawing the attention of the assistants and students to this case, I remarked that scarcely any other explanation could be given than infection by the introduction of germs with the instruments. I do not recall other cases of suppuration after tenotomy (I have made about 3,000), and certainly no loss has occurred. Be the number ever so small, our experiment and the just-mentioned cases demonstrate that primary suppuration from infection may occur even after a simple conjunctival squint-operation.

9. **Operations after infection of the conjunctival sac** (exp. IX. and XVIII.). In addition to the above-cited cases of extraction and paracentesis (exp. XXIV.), and the case reported on sub. 3, two others are still to be mentioned. In exp. IX. small quantities of a staphyloc. growth were put into different parts of the conjunctival sac by means of a wire loop. A section through cornea and iris made several minutes later healed without any reaction by immediate union. In the second case I put an emulsion of staphyloc. freely into the conjunctival sac, spreading it especially over the free edge of the upper lid. After the section and the simultaneous opening of the capsule, I pressed the lens ont with the lids, and wiped the remnants out of the wound with the edge of the upper lid. The operation had been cautiously done, the removal of the lens was complete, the wound closed admirably, but there was intense suppuration the next day.

Among all the faulty manipulations of which in the course of years, in explanation of the failures in my cataract-operations, I have accused myself, I consider, from a bacteriological point of view, none so prejudicial as this apparently so gentle and innocent manœuvre of rubbing the remnants of the lens out of the wound with the upper lid. It is certainly very rare that many pyogenic micro-organisms lodge on a healthy eye and its appendages, but if any

are present they are in all probability located on the edges of the lids more than anywhere else, and carried in the most direct manner into the wound by this mode of wiping away the remnants of cataract. If we hesitate to give up these external manipulations on account of their efficiency in removing remnants, we should take care not to let the edge of the upper lid come in contact wlth the open wound, how carefully soever it may have been bathed inside and out with corrosive sublimate.

To finish I may be allowed to make some

CONCLUDING REMARKS.

It has been on my part, as on that of many others, a great mental struggle to abandon the mechanical theory of suppuration. From the beginning I have appreciated the advantages of antiseptics in surgery so highly that in 1871 I went to Edinburgh for the special purpose of acquainting myself with Lister's method by personal observation. When I asked the great surgeon whether much benefit might be derived from this method in ophthalmic surgery he answered that he did not think so. The operations on the eyeball are mostly small; the territory is so well protected that after the closure of the lids the conditions resemble pretty closely those of a pure subcutaneous operation; furthermore, the conjunctival sac is constantly bathed in an antiseptic fluid, the tears; there is little occasion to contaminate the wound with hands, dressing materials, or instruments difficult to keep clean; the operations are soon over, and, therefore, exposed to injurious influences for a short time only;—all this explains why the results obtained by careful operations without the use of antiseptic agents have not been inferior to the results of those that have imitated the antiseptic methods of general surgery. In ophthalmology, as in general surgery, operations and dressings may be antiseptic without the employment of chemical means, antiseptics—witness the unsurpassed results of Lawson Tait. Moreover, it is to be borne in mind that a new idea thrown into the world commonly causes more harm by having its proper limits of application

transgressed than would come from disregarding it, a fact which is illustrated by the first period of antiseptics in ophthalmology. In the course of years, however, the antiseptic method has not only brilliantly maintained its principle, but divested itself of much that was burdensome and immaterial, and it has conquered more and more ground. Its triumphs have been an incentive to thorough scientific researches in the domain of bacteriology. Although it was a number of years ago that some surgeons made the startling statement: "No suppuration without micro-organisms," and in spite of the recent investigations of Orthmann,[1] J. A. Ruys,[2] Scheuerlen,[3] Klempener,[4] and others, do we not yet find many pathologists who are prepared to accept this statement without reserve? It is sure, however, that the other causes claimed for suppuration are steadily losing ground, and even conservatively disposed natures that have followed the discussion of this highly important scientific question must ask themselves: Will not the pyogenic fungi control their domain as uncontestedly in future as the fermentation fungi control theirs now? Certainly nobody has ever doubted that micro-organisms may produce suppuration, but the microbes were believed to be one of many irritants that have this effect. The above experiments, made according to the methods used in the bacteriological laboratories of Berlin, have had for their object to ascertain by plain demonstration how far mere traumatism carried to its utmost limits can be made responsible for the formation of pus in the limited field of eye operations, and how far the pyogenic species of bacteria that have been purely cultivated during the last few years are concerned in suppuration. The experiments without exception have sustained the bacteriological influence on the formation of pus. I have reported them as they have appeared, leaving it to the reader to draw practical conclusions from them. Yet I should not omit to point out that this field of experimenta tion, already so happily cultivated by Eberth, Leber,

[1] Virchow's *Arch.*

[2] *Deutsche med. Wochenschr.*, No. 48, Nov. 26, 1885.

[3] *Arch. f. klin. Med.*, Bd. xxxii., p. 500.

[4] *Zeitschr. f. klin. Med.*, Bd. x., 1 u. 2.

Deutschmann, and others, is likely to yield the most important results, particularly now that the methods of investigation have gained accuracy and system chiefly through the genius of R. Koch.[1]

[1] To those that wish to make themselves acquainted with the present standpoint of practical bacteriology the following works may be recommended: Hüppe, "Methoden der Bacterienforschung." 3 Aufl. Wiesbaden, 1886. Hüppe, "Formen der Bacterien." Wiesbaden, 1886. De Bory, "Vorlesungen über Bacterien." Leipzig, 1885. J. S. Woodhead and W. H. Hare, "Practical Mycology." Edinburgh, 1885. Cornil-Babes, "Les Bactéries." Paris, 1885.

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