Pathology and Histology

Mallows were all favourite remedies for all sorts of eye disease; and in our own day rose water is no infrequent ingredient of an eye lotion.

"But to nobler sights
Michael from Adam's eyes the film removed,
Which that false fruit that promised clearer sight
Had bred; then purged with euphrasy and rue
The visual nerve, for he had much to see."

In ancient times, he was probably the best physician who doubted most and did least, leaving the cure of the case to the vis medicatrix naturae; the same is probably true, within limits, of the early ophthalmic quacks, only it is hard to imagine a quack sitting still and doing nothing.

The unpleasant applications of fasting spittle and mother's urine to the eye are only mentioned to be condemned; the first we have seen the results of in a severe case of hypopyon keratitis and the second must undoubtedly have been responsible in the past for a certain amount of ophthalmia neonatorum.

Abstracts

I.—Pathology and Histology


(1) Speidel has been investigating the acceleration in the metamorphosis of tadpoles brought about by feeding them with thyroid. A definite exophthalmos occurs a few days after the first feeding, whereas in a normal tadpole the protrusion of the eye at the same age is only slight. The exophthalmos is due to an increase in the size of the eyeball (this increase occurring chiefly in the anterior part) and to general shrinkage of the adjacent tissues of the face. Histologically the growth is found to be due to proliferation of the cells of the basal layer of the retina in the region of the ora serrata—this proliferation is indicated by a very active mitosis—whereas in the untreated animal no mitosis is observable in this portion of the retina. It is stated as characteristic of the action of thyroid that it stimulates mainly the growth of undifferentiated or embryonic cells, thus explaining the selective effect of thyroid on the eye. Turning to exophthalmic goitre in man, Speidel, assuming that it is an indication of hyperthyroidism, suggests that the protrusion may be partly caused by
actual growth and multiplication of cells in the anterior part of the eyeball. Myopic change occurring in a sufficient number of cases with the onset of exophthalmos would help to establish this theory.

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(2) In this research Hiroishi endeavoured to determine whether the formation of cataract regularly, or indeed certainly, follows the removal of the parathyroids in rats, or is only an occasional phenomenon in the symptom-complex.

His observations were made on nine animals that survived operation. The lens opacities, which were best studied with the aid of the slit-lamp, were always bilateral, and their onset was from six to thirty-five days after the operation—being almost simultaneous in both eyes. The first changes were always visible in the axial area as fine radial striae that soon increased in number and in length towards the equator of the lens. These striae made fairly rapid progress in the first few days, after which they remained stationary and unchanged throughout the period of observation, so that the great mass of the lens remained clear; in no case did the lens become totally opaque.

This limited progress of these opacities is probably due to the fact that the factors producing them were present for only a limited time. The striae formed during that period remained, but no fresh ones developed later. The disappearance of these factors is attributable to the gradual resumption of function by the small accessory parathyroid clumps.

The author concludes by saying that tetania parathyroideopriva in rats runs a relatively mild and chronic course, the symptoms disappearing after a time or, as in the case of the lens, making no further progress. He emphasizes the fact that the development of cataract is the most constant symptom. It occurred in all the animals in which both parathyroids had been with certainty removed. In the cases where only one parathyroid had been excised, the formation of opacities was the exception. The onset of convulsions appears to hasten the development of cataract, but the latter may also occur without them. Changes in the teeth and hair may develop independently of those in the lens or may be absent altogether; no rule could be observed on this point: they seem, however, to be less constant symptoms than the cataract.

THOS. SNOWBALL.
Finoff, William C. (Denver, Colo.).—Changes found in eyes of rabbits following injection of living tubercle bacilli into the common carotid artery. *Amer. Jl. of Ophthal.*, February, 1924, and May, 1924.

Finoff injected clumps of living tubercle bacilli into the common carotid artery of 46 rabbits, and lesions developed in all the animals inoculated. Bovine bacilli proved to be more pathogenic than human. The quantity injected varied from 0.2 to 10 mg. Ocular lesions developed on the side injected and the majority of the animals developed pulmonary, hepatic and a more or less generalized tuberculosis which usually caused death, before the eye condition had run its full course. The average incubation period of ocular tuberculosis was a little over six days, the shortest being one day, and the longest thirteen. The first sign of disease was contraction of the pupil in the eye corresponding to the side which had been injected. Then came changes in the iris; in the more acute form, there were haemorrhages and a turbid aqueous. These changes were probably the reaction to an irritant, and were not specific. After the fourth day there developed “ridged iritis,” wedge-shaped thickenings of the iris with their apices at the pupillary margin. Serous exudation occurred, and in severe cases greyish yellow nodules developed at the bases of the wedges, protruded into the anterior chamber and became vascularized. These nodules showed the histological picture of a typical tubercle. In the fulminating cases, the cornea was affected, becoming stippled, then dense white and later vascularized. Histologically, there was necrosis in the centre and inflammatory change in the periphery. This type of keratitis occurs after the injection of other substances which alter the nutrition of the cornea, and changes simulating the human type of tuberculous keratitis did not occur. Conjunctivitis occurred when the cornea was involved. Red and yellow nodules appeared, in some cases resembling phlycten, which broke down to form small irregular ulcers. In nine smears out of 20, tubercle bacilli were found in the secretion. Episcleritis appeared in three animals after the fourteenth day. Choroiditis, when the condition of the media permitted ophthalmoscopic examination, ran a fairly typical course, ill-defined oval patches becoming yellow in colour, and later pigmented and circumscribed. Later still, the pigment moved to the periphery of the lesions, which themselves became brilliantly white. Histologically, there was first an infiltration with epithelioid cells, round a clump of bacilli, then small round cells appeared and the pigment epithelium showed signs of degeneration and proliferation. On disintegration of the retina, the pigment cells migrated forward. The last stage was caseation of the centre of the lesion with complete atrophy of the retina and disappearance of some of the pigment.
in the centre. In most animals there was a severe generalized uveitis with clouding of the vitreous. Tubercle of the retinal vessels was observed in only one case, and appeared as a grey perivascular exudate. The presence of this was confirmed by histological examination which also showed endothelial proliferation in the veins. Finoff concludes that haematogenous eye infections with living tubercle bacilli are of a severe and progressive type and with a few exceptions do not correspond with human ocular tuberculosis. He also finds that dead tubercle bacilli can produce similar lesions, with this essential difference, however, that the lesions can be followed through their whole course, as the animal does not die from tuberculosis of other parts. Clump emulsions of bovine bacilli grown on glycerine agar and killed by boiling were injected into the common carotid artery in amounts varying from 0.2 to 10 mg. The size of the dose had no influence on the nature of the lesions or the frequency of infection. Early phenomena, due to irritation, occurred as in the series injected with living bacilli. Ridged iritis was not so common and, when it did appear, underwent retrogression, the iris returning to its normal condition or becoming atrophic. Synechiae and pupillary exudates were common. The iris nodules also occurred, becoming white about the sixth week and frequently discharging their contents into the anterior chamber; occasionally they fused, producing massive conglomerate tubercle. The smaller nodules were sometimes absorbed, leaving grey atrophic patches. The early changes in the cornea were similar to those observed in the first series, but, as the animals survived, it was possible to watch the disappearance of the vascularization. There was first a diminution of the fine peripheral vessels and the formation of a few large vascular trunks presenting arborescent branching. The periphery of the cornea then cleared gradually, leaving finally no trace of the vessels or only some fine strands of scar tissue. The later changes appeared after the eighth week. They comprised sclerosing keratitis beginning at the limbus, non-vascular lardaceous infiltrates in the substantia propria, and mutton fat precipitates. Conjunctivitis was seen similar to that in the first group and in one case a typical phlycten. In all except three severe cases the conjunctiva regained its normal appearance within ten days of the onset. In ten cases, nodules developed in the lids, which broke down to form crateriform ulcers; in one case a cold abscess formed. Episcleritis occurred once; it appeared on the seventh day, and lasted ten days. Tubercles of the choroid appeared as in the first series; they were always multiple and scattered irregularly over the fundus. A detailed account is given of their histological and ophthalmological changes. Vitreous haze developed in eight cases and cleared in a short time. One animal
developed a tubercle on the optic disc and in one there was an isolated tubercle on the retina. There was no case of tubercle of the retinal vessels.

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(4) Owing to the difference of opinion still existing as to the value of tuberculin therapy in tuberculous diseases of the eye Davids returns to the discussion of the subject after twenty years’ experience of this method of treatment, and cites a few of a series of cases including various types of this disease to show its efficacy, particularly in the form of bacillary emulsion. All these cases were treated with B.E. and atropin only, after a preliminary positive test with O.T., mostly ambulant and even as far as possible while continuing their work, with uniform success after other lines of treatment had failed. These results, together with those of other writers, prove beyond doubt the value of tuberculin, and especially of B.E., as a curative agent.

He regrets that doubt should still be cast on this method of treatment on the grounds that relapses may occur and that tuberculin in certain cases fails to effect a cure.

Relapses do occur, but the fact of their disappearance on repeating the course of tuberculin when the primary attacks had yielded to its use he regards as further proof of its specific action. Moreover, they are best avoided by continuing it after the case is clinically cured.

Failures in cases of true tuberculous disease, he says, are very few.

Tuberculin treatment gives the best results in iritis with formation of nodules seen in young individuals, in tubercular choroiditis, keratitis, and scleritis; it is good in most cases of severe iritis without nodules occurring in the later decades of life, and the recurring vitreous haemorrhages of young persons, while in the class of chronic quiet iridocyclitis it can only be used with great caution.

The author utters a warning against the use of mercury in these cases as often harmful, and against a too hasty iridectomy.

As to scrofulous affections he recommends the preliminary test with O.T. followed by B.E. to cases of severe phlyctenular disease, but in cases where the O.T. test has produced an intense local reaction he advises that treatment should be pursued with caution.

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All the experiments in this exhaustive investigation were made on the staphylococcus pyogenes aureus. For the details of the skilful technique and the interesting and instructive experiments, which do not lend themselves to abstracting, the reader is referred to the originals which occupy no less than sixty pages of the Arch. f. Augenheilk.

As regards the direct action of light on bacteria Passow's findings are as follow:

1. Infra-red, red, yellow, and green rays even of high total intensity had no effect whatever on the staphylococci.

2. Of the blue, violet and ultra-violet rays of low intensity, the extreme ultra-violet rays between λ 300 and 250 μμ were by far the most effective.

3. In this stretch of the spectrum the quartz and ferro-carbon arc acted more intensively than the carbon-arc light.

4. The effects of light on the bacteria, on the photometer paper and on the thermopile were altogether different and bore no relationship to one another.

5. Therefore, the action of light on bacteria is specific and depends mainly on the capacity of the bacteria to absorb particular rays.

6. In general, sources of light whose rays are the most intensive in the spectral parts which are best absorbed by the bacteria will be the most suitable for their destruction.

7. Given good capacity of the bacteria to absorb a particular radiation, a low total intensity of this radiation suffices to kill them; but if their capacity for absorption is defective, even a considerably increased total intensity of the radiation is uncertain of success.

8. In light-therapy of infectious diseases of the eye without the aid of biological sensitization, on account of their richness in intense ultra-violet rays, the quartz and ferro-carbon lamps are preferable to the carbon-arc lamp, and whenever possible the extreme ultra-violet radiation from 300 μμ downwards should be used unfiltered.

The second part of the research concerns the photo-dynamic action on bacteria. The findings are:

1. The bacteria can, without harm to themselves, absorb stains.
2. For photo-dynamic action it is essential that the bacteria should be capable of absorbing the photo-dynamically effective substances.

3. All the stains that were non-toxic to the staphylococci and coloured them well were also photo-dynamically effective except toluylen-red and indigo-carmin.

4. "Rose bengal" was the best sensitizing substance for the staphylococci; phloxin came next. Diod-fluorescein, eosin erythrosin and acid fuchsin also produced good photo-dynamic action. The other substances of this kind experimented with produced very weak effects.

5. With the help of rose bengal, the photo-dynamic action in the yellow and green regions of the carbon-arc lamp spectrum appears quicker than the direct action of light in the ultra-violet region of the spectrum from the same source of light and with diiod-fluorescein, eosin, erythrosin, phloxin and acid fuchsin as quickly as in the latter.

6. Through suitable sensitizing—especially with rose bengal—all the rays except red and infra-red could produce bactericidal action.

7. As no fluorescence was recognizable in the case of acid fuchsin, pending further investigation, photo-dynamic action without the manifestation of fluorescence appears possible.

8. Even with the long-waved rays of low intensity of the 110-volt quartz-light—although only after about two to three times longer exposure than with the 16-amp. carbon-arc lamp—a strong photo-dynamic action is attainable.

9. Both the direct and the photo-dynamic action of light on the staphylococci occurred in the absence of oxygen. Consequently the photo-dynamic action on bacteria may be regarded as (a) a sensitization, i.e., accentuation of light-action; and (b) not dependent on a process of oxidation.

10. Whether or not sensitization of bacteria is a pure process of absorption requires further investigation.

From these two sets of findings the author derives the following conclusions:

(a) In the application of rays to bacterial diseases of the eye, sensitization with rose bengal, phloxin, diiod-fluorescein, eosin, erythrosin or acid fuchsin—the stains are given in the order of preference—is to be recommended, provided that the stain is equally photo-dynamically active against the bacteria to be killed as against the staphylococci and is harmless to the tissues of the eye. It has been found that rose bengal diffuses well through the cornea while being just as harmless to the eye as fluorescein which is photo-dynamically ineffective.
(b) Besides the short-waved rays which are in themselves bactericidal, by means of sensitization the more penetrating long-waved rays could also be rendered bactericidal, so that an appreciable summation of effect results.

c) For the direct action of light the quartz and ferro-carbon lights are preferable to the carbon-arc light and for photo-dynamic effect the latter is superior to the former.

(d) With the reservations mentioned under (a), to obtain a harmless and effective light-therapy the employment of photodynamic action by means of the carbon-arc lamp is more suitable than the direct action of ultra-violet rays as: (1) the latter may damage the tissues of the eye; (2) by sensitization the bacteria could, to say the least, be as quickly killed by the yellow-green rays as by the ultra-violet; and (3) the long-waved rays penetrate deeper into the tissue than the short-waved, and thus hold out the possibility of killing bacteria even when deep-seated, as for example in the cornea.

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(6) Woodruff notes that the nocardia are familiarly known as streptothrices, which is incorrect as there are marked differences between the two groups. Comparatively few cases have been recorded of infections with this type of organism, but it has been found in pneumonic areas, in cerebral abscesses and in meningitis. The lesions often resemble those produced by the tubercle bacillus. Microscopically, the organisms are curved and thread-like, the threads varying in length and thickness. The thicker ones show deeply stained globules and irregular bodies. Branching, which is only seen occasionally, is irregular, the branches being placed at a wide angle, sometimes at right angles. Nocardia would appear to occupy a position intermediate between certain of the bacteria and the hyphomycetes. Woodruff's case occurred in a girl, aged 19 years, who for six years had had a round circumscribed mass about 12 x 4 mm. under the skin of the left eyebrow. This was removed. During the operation the wall of the tumour was ruptured allowing a small quantity of pus to escape. The tissue removed showed many small lobules composed almost entirely of epithelioid cells with the thread-like organisms in compact groups at or near their margins. A small amount of tissue was left at the first operation and in consequence an abscess developed a week later which was opened and drained. The smears from this showed long and short threads of uniform thickness, with some branching. The appearances were quite different from those of the organisms in the tissue removed at the first operation.

F. A. WILLIAMSON-NOBLE.
(7) Grüter, Wilhelm (Bonn).—The mode of propagation of the herpes virus in the animal body and its significance in the problem of sympathetic ophthalmitis. (Der Verbreitungsmodus des Herpesvirus im Tierkörper und seine Bedeutung für das Problem der sympathischen Ophthalmie.) Arch. f. Augenheilk., February, 1924.

(7) In this communication Grüter discusses the findings of v. Szily, Mariani, Dörr and Schnabel, Bastai and Busacca, v. Prowazek, Marinesco and Draganesco, Rehbock and himself, in experiments on rabbits with the virus of herpes.

It has been found that the propagation of the virus may occur either by the blood and lymph streams, or by the preformed nerve paths, or both. In the case of the nerve paths the spread may be either centripetal or centrifugal according as the initial site of infection is central or peripheral. In rabbits the virus shows a definite elective affinity to the nerve paths along which it spreads by continuity, though it is not improbable that to a small extent the blood stream is responsible for its propagation.

The anatomical investigation of animals which died of encephalitis after corneal inoculation has shown that the virus penetrates along the ciliary nerves into the ciliary ganglion, further into the Gasserian ganglion, and from there into certain seats of predilection in the brain: optic thalamus, hippocampus the nuclear region of the pons and medulla oblongata; it also spreads within the vascular layers of the meninges and the peri-neural sheaths of the optic nerve.

In some instances inoculation keratitis in the one eye was followed by spontaneous keratitis in the other. In one case in which the animal died of encephalitis after inoculation, an infiltrative perineuritis in both eyes extending to the chiasma was noted; in another, after subdural (not intracerebral) inoculation, encephalitis followed by a descending uveitis and keratitis occurred and, from the keratitis, inoculation into another animal proved positive.

These results inclined v. Szily to surmise some affinity between the herpes virus and that of sympathetic ophthalmitis and to hint at the possibility of sympathetic disease occurring by the passage of the virus from the one eye to the other by way of the chiasma.

The author differs from v. Szily. Neither v. Szily's experiments nor his own nor those of others support the view that the herpes virus or a virus biologically akin to it is the cause of sympathetic ophthalmitis. The mode of spread of the herpes virus is comparable to a septic infection of the brain by a visible germ. In man sympathetic ophthalmitis after superficial infection of the cornea does not occur. The migration theory of sympathetic ophthalmitis in man demands the spread of the herpes virus
exclusively by way of the optic nerves and chiasma and this condition is put out of court by its peculiar diffuse mode of propagation in the brain. Further, while the virus is mainly a neurotrope in the rabbit, it is an outspoken dermatrope in man. He gives credit to v. Szily for having shown the possibility of a spontaneous transmission of inflammation from the one eye to the other by the blood and nerve paths and agrees with Axenfeld that probably an invisible virus is the long looked-for cause of sympathetic ophthalmitis.

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II.—MISCELLANEOUS

(1) Howard, Harvey, J. (Peking).—Role of the epithelial cell in conjunctival and corneal infections. Amer. Jl. of Ophthal., December, 1924.

(1) This important paper by Howard, covering 26 pages and illustrated with 18 microphotographs will be of great interest to all who are concerned with the bacteriology of conjunctival infections. The first four pages are concerned with details of technique—space does not allow of their being transcribed in full. Scrapings were taken with a sterile platinum spatula from the palpebral conjunctiva and with a slightly dull discussion knife, from the bulbar conjunctiva and cornea of numerous cases of conjunctivitis—the eyes being previously anaesthetized with cocain. Smears were also made from the conjunctival secretion. The scrapings included epithelial cells, so that the relationship between these and the infecting organisms could be made out. When it was desired to know what was taking place in the tissue as a whole, a small piece of conjunctiva was removed by squeezing down a pair of de Wecker scissors over it and cutting off the tissue between the blades. The staining was done principally with Lindner's contrast stain and both dry and wet fixation were used for the specimens examined.

At the outset, Howard emphasizes the fact that all the cells in the epithelium of a mucous membrane, such as the conjunctiva, are alive, in contrast to the epidermis of the body generally, where the superficial cells are dead. Hence organisms which are found growing on the epithelial cells of the conjunctiva are to be regarded as parasites, while those which grow only on the desquamated cells are saprophytes. It is interesting to note that of the bacteria, only the gonococcus, pneumococcus, b. Koch-Weeks, b. diphtheriae and b. influenzae can be regarded as parasites, staphylococcus, b. xerosis, etc., being only saprophytes. The bacillus of Morax
and Axenfeld while it grows as a saprophyte, yet produces an exogenous toxin which causes an irritative conjunctivitis. Taking the parasitic organisms: The gonococcus. Smears made immediately after a definite infection with gonorrhoeal discharge show the presence of the organism; a few hours later however none can be found. If, 24 hours later, scrapings are taken from the areas showing commencing inflammation, turfs of gonococci are seen on the surface of some of the epithelial cells, though none can be found in a smear. In 36 to 48 hours the turfs of growth are more extensive and, when they cover several cells, the most extensive concentration of germs occurs at the cell boundaries. Even at the end of the third or fourth day the gonococci found in smears are scanty while vast numbers of them are seen in epithelial scrapings. From the fifth to the tenth day, the superficial cells are found to be smaller and more cylindrical in shape, because the old flattened cells have been thrown off and those replacing them have only recently been derived from the basal cells. At the third day the gonococci dissolve the intercellular cement substance, penetrate the superficial epithelial layer at the cell borders and begin to grow on the posterior surface of these cells. They seldom penetrate beyond the deepest epithelial cells, though in some cases the whole conjunctiva is thrown off in certain areas, leaving only a few firmly attached basal cells. Phagocytosis occurs in the epithelial cells at the end of the first week, and is most active between the tenth and fourteenth days. Ten to twenty organisms are usually present in each cell, and they can be seen undergoing various stages of degeneration and digestion, down to the stage at which the organism is represented by a little area of cloudy granular material. In no case was a leucocyte found in the conjunctiva, acting as a phagocyte of gonococci, i.e., they are effective only against germs which have been torn loose from their living hosts, the epithelial cells, and are lying in the secretion. Leucocytic phagocytosis of gonococci begins at the end of the first week. The density of growth on the corneal epithelium was about half that found in conjunctival specimens removed at the same time. Where there is an ulcer, gonococci are found in the surrounding epithelium, but in the substance of the ulcer there are only a few free ones, mixed with the detritus. There is no evidence of the proliferation of gonococci in the substance underlying the ulcer.

The pneumococcus: Proliferation occurs first on the bulbar conjunctiva, then on the palpebral; the process is rapid and reaches its maximum on the second day. Penetration does not occur below the third layer of cells and epithelial phagocytosis is well under way by the second day. Leucocytic phagocytosis is a very minor process. Scrapings from the cornea on the second day show an astonishing number of germs though the clinical appearance
is not abnormal. On the third day, the scrapings from cornea and conjunctiva are negative and the disease has disappeared by crisis. Pneumococcic ulcers rarely begin with pneumococcic conjunctivitis, but in ulcus serpens the organisms are found in the substance of the cornea beneath the ulcer. In the new born, pneumococcic infections are more persistent.

Koch-Weeks infections follow much the same course as those due to pneumococci; the infection is at a maximum on the second day, declines considerably on the third day and by the fourth day the scrapings are negative, though from time to time during the following three weeks small tuft growths are found in the scrapings.

B. influenzae differs from Koch-Weeks in the slightness of its proliferation and the shallow depth to which it penetrates, though the secretion contains an abundance of bacilli. In diphtheria, epithelial cell phagocytosis was not observed.

In acute trachoma and inclusion blenorrhoea, Lindner's contrast stain showed the presence of small epithelial cell inclusions of "initial bodies" about the end of the first week. They appear as dark blue cocci-like bodies. Some are also found lying free, but to bring these out well Giemsa's stain is required; they are present in all stages of division and in a great variety of sizes. In the cells, the most prominent inclusion generally covers the nucleus at one end like a cap, in more advanced stages the entire protoplasm of the cells may be filled with blue initial bodies. Later, they are found to stain a pink colour and are then called elementary bodies. In some cells the bodies can be seen in the act of being extruded through a gap in the cell wall. Morphologically they are identical in inclusion blenorrhoea and trachoma, both acute and chronic, though in the latter they are far less numerous. In one case of mixed infection, epithelial cells were found with gonococci on the surface and inclusion bodies inside. Two cases of spring catarrh were examined; in the first, of pericorneal type, with pavement stone granulations on the palpebral conjunctiva, a few were found. B. Morax-Axenfeld was found only on dead epithelial cells which were present in greatest amount on the lid margins or at the canthi. The same was true of b. xerosis and staphylococcus, but there was no sign of any irritation being caused by either of them. The pneumococcus, though it can act as a parasite is more frequently found as a saprophyte growing on dead cells or shreds of mucus, and producing no irritation. It was found present as a saprophyte in 40 per cent. of normal individuals; the reason why it should suddenly become parasitic is not known. With regard to saprophytes in general, the toxins of b. xerosis and staphylococcus exert a non-pathogenic rôle and only that of the diplobacillus is pathogenic. They are never phagocytated by epithelial cells, and by leucocytes only after an acute conjunctivitis due to
one of the pathogenic organisms. With the parasitic organisms, proliferation usually begins on the bulbar conjunctiva and extends rapidly over its surface and over the cornea by the creation of many separate foci. The proliferation then extends more slowly over the palpebral conjunctiva. The bacteria disappear from the bulbar area by crisis, whereas turfs of them may be found growing here and there on the palpebral conjunctiva for quite a long time. Several factors are concerned in bringing about the disappearance of the organisms.

1. The ectotoxins produce a dissolution of the intercellular cement substance, and so breaks occur in the superficial epithelial layer of the conjunctiva through which the bacteria grow. This dissolution continues until all the epithelial layers are affected, but at the same time, an abnormal proliferation occurs, the superficial cells with their dense turf being cast off. Layer after layer of cells is removed until in a very few days the conjunctiva is composed of entirely new cells which are actively phagocytic and digest the bacteria. This was proved microscopically and it is interesting to note that whereas the germs can thrive parasitically on the surface of the epithelial cells, once they are inside they become digested and broken up.

2. The ectotoxins cause subconjunctival hyperaemia and oedema, with formation of pus cells. These act merely as "camp followers" and act only against bacteria which are no longer parasites, i.e., against those which have been cast off and washed into the secretion. Not a single leucocyte was found showing phagocytosis in all the wet-fixed specimens of conjunctival tissue.

The cornea, though covered with the same kind of bacteria which are so toxic for the conjunctiva, showed no clinical symptoms whatever. The explanation is probably three-fold: (1) In the absence of blood-vessels sudden and active proliferation of the deeper epithelial cells does not occur; (2) the cells being less "viable" react to all external injuries and stimuli in much slighter degree; (3) the cells being dryer and flatter, are less nutrient and the germs disappear from lack of nutrition. No epithelial cell phagocytosis was observed in the cornea. When an ulcer occurs, except in gonococcal ophthalmia and ulcus serpens, it is due to some trauma producing a breach in the epithelium. Discussing the findings in trachoma, Howard notes that the difference between the parasitic rôles of inclusion bodies and bacteria, is that the former proliferate in the substance of the cells, the latter on their surface. These bodies are not derived from nuclear material, because with Lindner's stain they are dark blue, as are the bacteria, while the nuclei and cell protoplasm are not stained blue at all. Moreover, cellular degeneration bodies do occur in various forms of conjunctivitis including trachoma, but they are not stained blue
by the contrast method. Hence bacteria and initial bodies are closely allied and have a biologic similarity; Noguchi and Cohen were able to cultivate them. In wet-fixed specimens they are seen on the periphery of spaces containing fluid, sticking to the cytoplasm and feeding on it. The degree of proliferation is in direct proportion to the amount of available protoplasm, and when this is all consumed they break through their thin cell wall and other cells as yet unaffected take them in. From some cells, however, the initial bodies appear to be unable to escape so that they remain within their host and die. Other types of so-called cell inclusions such as molluscum contagiosum, vaccinia, herpes, etc., are cellular reaction products, and not true inclusions.

In his summary Howard notes that the following factors are concerned in terminating infections of the conjunctiva: (a) The early casting off of the superficial layer with its dense turf of bacteria; (b) the out-pouring of exudates against whose current the bacteria must grow; (c) extensive proliferation of the deeper cells, which results in continuous exfoliation of cells, as layer by layer the deeper ones become superficial; (d) phagocytosis by the epithelial cells of the deeper layers; (e) a local acquired immunity where the toxins have stimulated the generation of an entirely new conjunctival structure.

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BOOK NOTICES


The first edition of this book was published thirteen years ago as a volume of Pyle's "System of Ophthalmic Practice." The present work is produced independently. It is a welcome revision of a well-known and useful book. It has been considerably enlarged by about one hundred and eighty pages and now contains seven hundred and thirty pages. The number of illustrations has also been increased considerably, from two hundred and thirty-seven to three hundred and six. The coloured illustrations in the text are a new feature. Some are good, viz.: Fig. 112, angioma of the conjunctiva, and Fig. 194 of subhyaloid haemorrhage in pathological section, but Fig. 288 has not been reproduced at all well and shows hardly any trace of the reticular opacity of the cornea,