not end in temporary recovery. The presence of the second, or megakaryocyte type, is of grave significance, and no case in my experience has lived beyond a few days from its appearance.

REFERENCES.

- ¹ Cooke, W. E.: *The Arnetb Count*, 1914, 19. ² Cooke, W. E.: *Journ. Path. and Bact.*, xix, 496. ³ Arnetb, J.: *Deut. med. Woch.*, Leipzig, 1904, Bd. xxx, S. 54. ⁴ Lewis, M. R.: *Arch. exper. Zellforsch.*, 1926, 2, 228-243. ⁵ Barta, E.: *Ibid.*, 1926, 2, 6-30. ⁶ Walterhöfer, G., and Schramm, O.: *Arch. f. klin. Chir.*, 1921, cxviii, 794-811.

THE EXPERIMENTAL BASES OF PROPHYLAXIS IN GONORRHOEA.

BY

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THE study of the initial stages of gonococcal urethritis is of extreme importance from the point of view of prophylaxis. Knowledge of the pathology of acute gonococcal urethritis is almost entirely derived from the observations of Finger, who inoculated moribund patients with gonococci and made a detailed examination of their urethrae thirty-six to forty-eight hours afterwards. His description is as follows:

"The gonococci begin to proliferate on the surface of the epithelium which they are about to attack; they are not spread diffusely, but in small groups. At the end of thirty-eight hours they have scarcely as yet penetrated into the epithelium; at the most they have slipped in among the superficial coils at the points presenting the feeblest resistance. If the epithelium is denuded at any point, exposing the connective tissue, the organisms penetrate there more rapidly. They invade the lumina of the crypts of Morgagni with extreme rapidity, and are found in them, lying free on the surface of the epithelium. From this moment, and, indeed, well before this, diapedesis has commenced, the leucocytes are everywhere numerous in the superior layers; a certain number have gained the surface, and one already finds intracellular gonococci."

Finger's observations would lead us to believe that until at any rate thirty-eight hours after inoculation very little penetration of the epithelium by the gonococci has taken place, and that the adoption of appropriate prophylactic measures would stand every chance of success if carried out within this period.

Experimental work has, however, been carried out by other observers using organisms other than gonococcus, which suggests that the diffusion of organisms within the urethra might be more rapid than Finger's observations on the gonococcus would lead us to suppose. Notable among these experiments are those of Palladino Blandini. This observer placed a loopful of *Bacillus prodigiosus* within the meatus of a guinea-pig, and twelve hours later made a necropsy under aseptic conditions and investigated the fate of the organisms since their introduction into the urethra. His choice of *B. prodigiosus* was determined by the fact that on account of its brilliant colouring matter it could easily be recognized. Palladino Blandini found that a widespread diffusion of prodigiosus from the urethra had taken place within twelve hours of inoculation, but that if the animal were allowed to survive for more than twenty hours these diffused organisms were destroyed by the tissues. That the method of diffusion was not through the blood stream was proved by the fact that blood cultures taken from the heart were sterile. In 1909 I repeated and confirmed these findings, and four years later Teale and Embleton proved that what occurred in the urethra was equally true of organisms placed on other mucous surfaces or inoculated into serous cavities. The prodigiosus is capable, therefore, of passing through uninjured mucous membrane, and may be carried from thence along the lymphatic stream and eventually into the thoracic duct. Teale and Embleton's experiments showed, therefore, as mine had already done, that with regard to the generative tract the spread of organisms is into the submucous tissues rather than along the surface. At the necropsy of a guinea-pig killed twelve hours after a loopful of organisms had been placed within the meatus no infection of the surface of the posterior urethra, bladder, ureter, or pelvis was found, although extensive dissemination by the lymphatics had taken place. The organism employed for this experi-

ment was, however, *B. prodigiosus*, and it is possible that what is true of that organism is not true of the gonococcus. *B. prodigiosus* is a non-pathogenic organism, whereas the gonococcus, at any rate in the human being, provokes immediate and intense reaction of the tissues. Nevertheless, on repeating this experiment with a mixture of *Staphylococcus aureus* and diphtheroids I obtained similar results, and these organisms, unlike *B. prodigiosus*, are pathogenic to guinea-pigs.

In the light of these experiments Finger's contention that there occurs little or no penetration of the human urethral mucous membrane by the gonococcus for thirty-eight hours seemed open to doubt, and for many years I awaited an opportunity of throwing new light on the situation. Would organisms placed within the meatus of a human being behave in the same way as organisms inoculated into the urethra of a guinea-pig? Two years ago a chance of carrying out a somewhat similar observation on a human being presented itself.

A patient was admitted under my care into the Royal Northern Hospital suffering from an impassable stricture in the bulbar urethra and an early carcinoma of the glans penis. At 11 a.m. I placed two loopfuls of *B. prodigiosus* within his meatus. At 6 p.m. I opened the urethra on the bladder side of the stricture without having previously attempted to pass any instrument. After dividing the stricture through the wound in the perineum, a sterile cotton-wool swab on a holder was passed along the urethra from the opening in the perineum to a point 2 inches from the meatus and an agar plate inoculated. A second swab was similarly passed until it reached a spot 1 inch from the meatus, and another plate inoculated. My object in doing this was to ascertain whether in the seven hours' interval the organism had spread along the surface of the urethra towards the bladder. The fact that both plates remained sterile showed that no surface spread had occurred. I then carried out a partial amputation of the penis. Later multiple transverse sections were made through the amputated penis. These sections were stained with methylene blue and carefully examined under an oil immersion objective for organisms within the tissues. On the surface of the urethra no organisms could be found, but in the submucous tissues large clumps of small bacilli morphologically resembling *B. prodigiosus* were visible. These collections of bacilli were either in the form of more or less circular colonies or else were spread out along a line, and although no proof could be furnished of this, their distribution suggested that they were lying within the submucous lymphatics.

This observation, therefore, so far as it went, led me to believe that what was true of the behaviour of *B. prodigiosus* within the urethra of a guinea-pig was equally true of its behaviour when placed within the meatus of a human being.

By the courtesy of Dr. Mervyn Gordon I was able to repeat my observations in a monkey. Similar results were obtained.

A loopful of Hoffmann's bacillus and *Staphylococcus aureus* was placed within the meatus, care being taken to inflict no damage whilst the inoculation was being made. Eight hours later the monkey was killed by means of chloroform. Transverse sections were then prepared through the urethra at different levels and organisms searched for. In this case a few Gram-positive bacilli and cocci were found lying in the lumen of the urethra and also deep to the epithelial cells, but further up, an inch from the meatus, larger clumps were found in the submucous layers.

The above experiments suggest, although they do not prove, that in any infection of the urethra there is an immediate dissemination of organisms through the lymphatics as well as a slower spread which is associated with the signs of inflammatory reaction. In the majority of cases the tissues are able to deal with the immediate lymphatic invasion provided that it is not too liberally reinforced by fresh supplies from the surface. The chief point of practical interest is the bearing of these observations on prophylaxis in gonorrhoea.

Clinical observations, and particularly those carried out at the prophylactic stations established by the American Army in Paris during the war, showed that the chances of success of any prophylactics are directly proportional to the time that has elapsed since exposure. Since the gonococcus is easily destroyed by weak disinfectants while lying on the surface of the urethra, irrigation with weak permanganate solution is found to be effective in the great majority of cases, provided the patient presents himself for disinfection within a few hours of exposure. The longer the interval between exposure and disinfection, the more often does the disinfection process fail. No absolute time limit, however, can be laid down to guide us in arriving at a decision as to

when a prophylactic measure is likely to be of use, and the evidence given before the Trevethin Committee on this point by different authorities was conflicting in the extreme. Individuals vary in their susceptibility to gonococcal infection, and for this reason it is advisable to wash out the urethra even although twenty-four or forty-eight hours have elapsed since exposure.

From the fact that irrigation is successful in safeguarding the patient in the great majority of cases, provided it is carried out within three to four hours of exposure, it may be surmised that the tissues are generally capable of dealing with the more rapid dissemination of organisms occurring through the lymphatics, for if this were not so prophylactic measures would be of little avail. But it is within the experience of most urologists that from time to time prophylactic measures fail, even although carried out within an hour of exposure. I can remember several instances in which the urethra was washed out immediately after exposure, either by a competent orderly or else by the patient himself, and yet gonorrhoea developed. It is possible that these failures of prophylaxis are to be explained by an inability of the patient's tissues to deal with the rapid lymphatic dissemination. The problem is complicated, however, for we know that not only do individuals vary in their resistance to the gonococcus, but also that different strains of the organism exist with different grades of virulence. The reaction of the tissues to these different strains varies, as is shown, not only by the acuteness of the attack that develops, but also by the length of the latent period.

It has been proved by experiment and by clinical practice alike that the ideal fluid for prophylactic irrigation is of a non-irritating nature with the maximum power of penetration. Could a bactericidal fluid be obtained which was capable of being absorbed to some extent by the lymphatics, it is possible that a still higher ratio of success might be achieved, and that the small percentage of cases in which prophylactic measures miscarry might be abolished. But before these ideals can be reached more research is necessary, and it is possible that the knowledge which will be of the greatest use will be that which throws light on the part played by the lymphatics in disease and in health.

REFERENCES.

- Finger, Gohn, and Schlägenhauser: *Archiv. für Dermatologie und Syphilologie*, 1894, xxviii, 3-24, 277-344. See also Motz: *Ann. des Mal. des Org. gen. urin.*, 1903, xxi, 419-441.
Palladino Blandini: *Ann. des Mal. des Org. gen. urin.*, 1900, xviii, p. 1009.
Teale and Embleton: *Proc. Roy. Soc. Med.*, 1913-14, vii, Path. Sect., p. 69.
Walker, Kenneth: *Lancet*, 1915, i, p. 435; *Proc. Roy. Soc. Med.*, March 30th, 1922, p. 45.

NYSTAGMUS IN AN INFANT.

BY

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THE following case has been under our observation for about two years and seems worth recording.

The patient is a child with paralysis of the third nerve and nystagmus. The mother has five children living, but she has also had two that were stillborn, and one that died shortly after birth. Several of her confinements have been "instrumental," the history of these suggesting some maternal malformation. When the patient was born instruments were again required, and soon after birth it was observed that "the right eye was too much closed." There was also a suggestion that the right side of the face was paralysed, but, if so, it soon passed away. It was further observed that the right eyeball diverged. At the end of two months the drooping of the right upper eyelid disappeared.

When first seen the child was 9 months old; there was no evidence of ptosis, but the reverse, for the lid was now unnaturally drawn up, exposing part of the sclerotic above the cornea. The right eye could only be closed imperfectly, and the child seldom closed it; even when in sleep the eye remained open. The right eyeball was still divergent; it could be moved up to, but not beyond, the middle line, and it could not be raised or lowered. The right pupil was dilated, and did not seem to react to light. Moreover, this eye had rotatory nystagmus. The left eye seemed normal, except that it also exhibited rotatory nystagmus.

A year later both upper eyelids seemed normal. The mother stated that the child now closed both eyes, but that the right

tended to open during sleep. The right eye was still divergent, but came in when the left was covered—not, however, beyond the middle line. The pupils were now equal. There was still rotatory nystagmus in both eyes, but the range was less. The child tended to turn the head to the left, as if endeavouring to use both eyes. The fundus in both eyes was normal.

A few months later the condition was much the same. When the child looked down, the right upper eyelid did not come so far down as the left.

Here, then, we have a lesion that in effect produces abeyance of function of the greater part of the higher area of the brain that controls the oculomotor apparatus of the right eye, and with this is associated nystagmus affecting both eyes. It is interesting to note that the paralysis of the levator palpebrae was replaced by spasm, thus resembling the cyclic affections of the third nerve.

Nystagmus occurring in a miner is not an entity by itself, and should not be considered in a detached manner. The neurasthenia that attends the later stages in the miner is in great measure fostered by the legal recognition of injury received and the elaborate provisions made for dealing with compensation.

Imperfect retinal images are common to all cases of nystagmus, or there is interruption of the transmission of these as afferent impulses. The miner straining to see while at work at the black and dark coal face has very imperfect images to guide his labours, while often the actual onset of the disorder is occasioned by a blow.

In the case here recorded there is interruption of the associated efferent impulses, with loss of some higher control. Nystagmus is sometimes associated with mental defect, and it is sometimes a terminal manifestation in exhausting diseases. In the background of all these there is probably loss or enfeeblement of the higher control, with consequent release phenomena.

SYMMETRICAL HYPERKERATOSIS OF THE
EXTREMITIES.

(? KERATODERMIA BLENNORRHAGICA.)

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THE following case of symmetrical hyperkeratosis of the extremities is of interest because of its association with the gonococcus.

A married woman, aged 51, presented herself at the dermatological clinic of the Royal Infirmary, Cardiff, on October 16th, 1925. She stated that the condition started as a horny mass under the left great toe about a month previously and soon spread over the sole of the foot, simultaneously appearing on the sole of the right foot. There were soreness and burning sensations, and the mass of horny tissue caused pain on walking. Immediately previous to the attack her left ankle swelled and became painful; later, shortly before she came to the clinic, there were pain and swelling in the left knee.

On examination the soles of both feet, including the sides and backs, showed heaped masses of horny skin, broken here and there by cracks. At the points of the toes cornified matter projected for a quarter to half an inch, almost like horns. There was no exudation, and at one or two points where a portion of the mass had been detached the skin was pink, soft, and dry. In front of each knee there was a similar but less marked horny thickening in a well defined patch. There were also a few small patches of thickened epidermis on the left palm, but no rash of any kind elsewhere on the body. Her left knee was somewhat swollen, tender, and slightly reddened. Her left ankle was slightly swollen, but she made no complaint of pain. There was some general malaise.

I asked Dr. Eric Evans, in charge of the venereal disease clinic for women, to examine, and if necessary, treat her. Dr. Evans reported that on making a bimanual and other examination nothing abnormal was found, but that she had taken smears from the vagina, cervix, and urethra. On these Dr. Scholberg, pathologist to the Royal Infirmary, reported that gonococci were present in the films from the urethra and cervix, but not in that from the vagina. Dr. Evans then treated the case, giving trimine intramuscularly and rhubarb and soda mixture by the mouth.

By October 23rd the left knee was much improved, and the malaise relieved; there was still slight swelling of the left ankle. The urethra and cervix were treated with protargol, and contramine