A LECTURE

ON

THE CLINICAL SIGNIFICANCE OF THE SIMPLE
SOLITARY ULCER OF THE URINARY
BLADDER.¹

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OUR knowledge of the clinical history of non-malignant ulceration of the bladder, other than that due to tuberculosis, is meagre and inaccurate. Our ignorance is perhaps excusable, for the diagnosis and prognosis of such simple lesions of the mucous membrane in precystoscopic times were beset with difficulty. Even the finger of an experienced operator could not detect an ulcer unless it had eaten deeply or was lime-encrusted, while the medical practitioner was so haunted by the teaching that chronic ulceration of the bladder was tantamount to tuberculosis, that he expected all such vesical trouble would extend to the kidney and end fatally. Eight years of careful and routine cystoscopy have shown me that the entire subject of non-malignant ulceration of the bladder needs recasting. I am convinced that many simple forms of ulceration are met with, which are wrongly diagnosed as tuberculous, and as wrongly considered incurable. I venture to record my own experience on the subject, and propose dealing first with the very simplest form of all forms of chronic vesical ulceration—the solitary ulcer.

THE "SOLITARY" ULCER OF THE BLADDER.

A well-nourished man, aged 20, came under my notice in 1888 with intermittent attacks of profuse hæmaturia and constant penile pain. He never had had sexual connection. With the cystoscope I saw on the posterior wall behind the interureteral bar, a small ulcer the size of a shilling. It had an upraised, gelatinous edge, and a blood-stained, sloughy base. Its aspect reminded me of the scar of a bullet on a target. I was not allowed to operate, but he has since then reported his progress to me every year. During the last two years all his symptoms have disappeared. I presume that the ulcer in this case has healed, but I do not lay any stress on the surmise, as I have not recystoscoped the patient. I merely mention the case as having been the first to come under my notice, and draw my attention to the disease.

Since then I have been able to examine and re-examine various patients of both sexes with a similar form of vesical ulcer. Most of them, however, have been young men at or about the age of 20. They have had no venereal history. The onset has been sudden, consisting chiefly in slightly increased frequency of micturition. Blood has subsequently appeared, and the hæmaturia has been intermittent; but the marked feature has been a constant pain at one part of the penile urethra. In some this has been greatly increased by exercise, or by jolting or overholding water. Some walk about guarding their penis with their hand, to prevent it being shaken or jarred. I have even known men cut away the pocket of their trousers to enable them to carry the penis in their hand. Now, although the pain is a marked symptom, it is not pathognomonic. Other salient features exist, and these combine to make up a clinical picture, which, I believe, can be readily recognised and the diagnosis made without the aid of the cystoscope.

The life-history of the "solitary" ulcer may be divided into three stages. The first, of very variable duration, is before the advent of cystitis. It is most important to recognise the disease in this stage, for in it the surgeon may interfere to the best advantage. The following three cases will serve to illustrate the advancing grades of severity of the first stage.

CASE I.—W. B., aged 20. No venereal history or sexual intercourse; no family history of phthisis. Three or four months before seeing me he was seized suddenly with a burning pain in the urethra, at the peno-

scrotal angle. The pain was only there during micturition. A fortnight later blood appeared mixed with the urine. Since then bright hæmaturia (with clots) has occurred once or twice a week. Sometimes the blood was mixed with the urine, sometimes it was passed pure at the end of the stream. Exercise had no effect on the pain or the blood. He had no marked frequency of urination, for he could hold water for four hours. Urine, specific gravity 1022, acid, containing a microscopic amount of pus. No evidence of tuberculosis anywhere.

Cystoscopy.—Situated to the inside of the right ureteral orifice, low down on the posterior wall and partly overlaying the trigone (Fig. 1) was

Fig. 1.—Bladder laid open to show trigone. Shaded area represents ulcer.

a film of greyish-white material (phosphatic muco-pus?). The centre was eroded, forming a superficial red-edged ulcer. The rest of the mucous membrane of the bladder was in faultless health, and the capacity of the viscus was normal.

This case represents the ulcer in an early part of the first stage. The pain was not constant, the frequency was not marked, the ulcer was not deep.

CASE II.—F. G., a robust-looking lad of 20, without venereal history or family history of phthisis. Ten months before seeing me he noticed blood in his urine, and simultaneously he had to pass his water more often than usual, rising once at night. At the end of six months the bleeding ceased. Pain in the glans penis after micturition was now suffered from, and the vesical irritability increased. Urine, specific gravity, 1015; pus $\frac{1}{8}$, acid. I cystoscoped and saw a small ulcer in the usual area on the posterior wall low down, near the base of the trigone. No evidence of tubercle anywhere. I suggested to the medical attendant that the bladder should be washed out with nitrate of silver (gr. j ad 3viij). Two years after I was again asked by his medical man to examine this patient, as he was still suffering. I learnt the following interesting history. For two years the patient had daily washed out his own bladder with nitrate of silver solution (gr. $\frac{1}{2}$ ad 3j), half an ounce of which was always left in the bladder. This relieved him. If he did not wash out he used to get terrible pain in the penis and frequency of micturition. He could not stand up when the pain was present, and much walking increased its severity. Directly he injected the solution the pain left him, and he was free from it for twenty-four hours. The ease he obtained was greater if he lay on his back when he injected. He could by this means hold water for three hours in the day, and did not rise at night. He could retain 15 ounces. If he missed injecting a day, all his troubles returned. Testes normal, prostate normal. Urine, 1030, a little pus, and a little bladder epithelium present in it.

Second Cystoscopy.—Prostate swollen. Part of the trigone and all the urethral orifice was covered with a black film, not shining like a silvered surface, but a dead black. Obviously this was argyria of the epithelial layer. A little roughness with the edge of the prism of the cystoscope detached a flake of this film, and the subjacent reddened mucous membrane became exposed. The rest of the bladder was quite unaffected by the silver. It was dull, but moderately healthy in every part, except at the inner side of the right ureter. Here, on the posterior wall, low down, was an ulcer covered with a white layer of phosphate of lime and mucus (Fig. 2). Its edge was not bloodstained. It struck me that the nitrate of silver had "electroplated" the surface of the ulcer and protected the exposed nerve from the action of the urine. Pain and micturition reflex were therefore relieved. A perineal cystotomy was performed, the ulcer briskly rubbed, and the bladder drained for six weeks. At the end of the second week all pain had ceased.

CASE III.—A fine looking man, aged 26, was sent me, with a history that for seven years he had suffered from violent attacks of hæmaturia, with excruciating pain in the penis and frequency of micturition. The colour of the urine varied. Sometimes it was arterial in character, and sometimes it was very dark. The pain in the penis was constant, but was felt most acutely on any jar or jolt being received. The frequency of micturition was every ten minutes, but a rectal suppository of morphine permitted

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Fig. 2.—Bladder laid open to show trigone. Shaded area represents position of ulcer.

him to retain urine for three or four hours. Urine 1020, acid. Cystoscopy revealed a deep crateriform ulcer, situated on the inner side of the left ureteral orifice (Fig. 3). Its edges were gelatinous, everted and blood-stained. * Perineal section was performed, and the ulcer scraped. He has now remained well for eight years.

Fig. 3.—Bladder laid open to show trigone. Shaded area represents ulcer.

These three cases illustrate only the first stage of the life-history of the "solitary" ulcer. In them cystitis had not become a marked feature, for in each the urine was still acid, the specific gravity was still high, and pus was not present in any quantity. The length of the first stage is very variable. In Case III it had already lasted seven years.

Second Stage.—The stage of cystitis. In common with all forms of chronic ulceration or necrosis of the vesical mucous membrane, the "solitary" ulcer shows a marked tendency to become encrusted with phosphate of lime upon the super-vention of cystitis. From the date of the commencement of this deposit the character of the symptoms alter. The phosphatic crust becomes heaped up like a limpet shell, which it resembles visually. From time to time pieces break off, and are passed with more or less suffering, or they are retained and increase in size until they form definite calculi. I crushed one in 1890, nearly an ounce in weight. As the

fretted bladder becomes more and more inflamed by the irritation of these rough crusts, so the grade of the cystitis increases in severity. The inflammatory exudation traverses the muscle layers (interstitial cystitis), and first shackles their free extension, and later on, when the infiltration becomes absorbed or contracted, reduces the capacity of the viscus.

STALACTITE AND STALAGMITE ULCERS.

In some bladders, especially the female organ, there is a tendency during the second stage to form "contact" ulcers. A corresponding limpet-like, lime-encrusted ulcer forms on the anterior wall just above the urethral orifice. There is here in the female bladder (Fig. 4) a distinct ledge, and if

Fig. 4.—Vertical section of bladder and uterus. The shaded area on anterior wall of the bladder represents the encrusted "contact" ulcer.

this position be neglected and left unscraped, the patient will not be cured. This second ulcer is often due, I believe, to the actual abrasion of the anterior wall against the basal calcareous collection, as the bladder empties. Once formed it becomes very quickly coated with lime deposit. In cystoscopy, these ulcers resemble in appearance the stalagmite and stalactite collections seen in limestone districts.

Third Stage.—In this stage the mucous membrane has become more or less destroyed, but the areas affected have skinned over. The bladder is a mere inelastic bag capable of holding an ounce or so. The patient is troubled with extreme frequency of micturition or suffers from incontinence. Although I have met with such cases, I suspect that this stage is rarely reached and that the ascending pyelitic changes which affect the ureters and the kidney generally terminate the sufferings of the patient towards the end of the second stage.

Diagnosis.—A careful inquiry into the onset symptoms is of the highest importance. If repeated, causeless, sharp hæmaturias, with increased frequency of micturition and urethral pain, be complained of by a young adult of either sex, without venereal history or evidence of stone or tubercle, we have in all probability to deal with ulceration of the bladder. Is it primary tuberculosis of the bladder or a simple solitary ulcer? Maternal phthisis, extreme vesical irritability at night, and pale neutral murky urine of 1010 specific gravity point to tuberculosis. On the other hand, constant penile pain, clear good-coloured urine of specific gravity 1020, and an undisturbed night indicate the possibility of the solitary ulcer being present. This latter suspicion is strengthened if morphine or a nitrate of silver wash subdues the frequency of micturition. Of course, a glance with the cystoscope is sufficient in the early stages to arrive at a correct diagnosis. In the solitary ulcer the sheen of the rest of the bladder is perfect and the capacity is normal. In tubercle the posterior wall is seen patched with areas of vivid red, and peeling from them are the white flakes of necrotic tissue, whilst the capacity of the bladder is reduced at the very outset.

Prognosis and Treatment of the Solitary Ulcer.—The prognosis of the solitary ulcer is excellent. I have seen them even heal spontaneously. One case especially impressed me.

J. H., aged 19, without venereal history, was seized in January, 1893, whilst making water, with so violent a pain at the peno-scrotal angle that he almost fell. Well marked symptoms of solitary ulcer followed. He consulted me in November, 1893, and I found him still in the first stage. I examined him three times with the cystoscope. The ulcer,

which was situated on the posterior wall in the median line, showed no disposition to heal. In March, 1894, he became infected with syphilis, and was placed upon mercury. To my surprise the bladder symptoms gradually diminished, the penile pain from which he had suffered so long disappeared, the urine cleared, and in October, 1894, I noted that he was cured of his bladder ailment. I examined him with the cystoscope last week (April, 1896). On the posterior wall of the bladder, low down, was a florid, gelatinous, keloid-like scar. Radiating from its puckered centre and diverging like a star were prominent thin-edged ridges. Obviously the scar tissue in contracting had drawn into folds the loose mucous membrane. The rest of the bladder was in perfect health, 12 ounces capacity.

The best form of treatment in the first stage is sandal oil, followed by maltine and cod oil, small doses of mercury at night, liberal diet, and fresh air. Should the ulcer prove obstinate, curettage will have to be performed.

Treatment in the Second Stage.—I know of no reliable medicine when once the ulcer has become encrusted with lime phosphate (second stage). Vesical washes are better. Lactic acid from 1 per cent. or nitrate of silver or acids are of use, but they are very trying and uncertain. The best way is to thoroughly scrape the surface of the ulcer. In men this must be done perineally or suprapubically. In women, who seem to be particularly prone to this form of ulcer, curetting is easy enough. A 28 (Fr. gauge) speculum is introduced in the Trendelenburg position, and the ulcer scraped every other day under electric light. It is surprising how rapidly cases in the earlier stages improve after this treatment. I have known a fortnight a sufficient time to cure an ulcer of months' duration. But when the case is advanced much patience and perseverance is necessary. One lady, who was sent me by Dr. James Tuxford, of Boston, in October, 1891, was almost entering the third stage when first I saw her. Her bladder only retained one ounce of urine and that with difficulty. Her sufferings were extreme. She had a lime-encrusted ulcer in the usual position on the posterior wall, and a "contact" ulcer on the anterior wall (Fig. 4). I scraped these ulcers, with and without the electric light, fifteen times, and I am glad to say she was able after six months' treatment to hold water for three hours in the day and longer at night, and is now without pain or discomfort. When I last examined her with the cystoscope the ulcers had healed.

Fallacy.—It must be distinctly understood that the solitary simple ulcer repays active curettage, but tuberculous ulceration resents such a proceeding. I fear surgeons often do more harm than good by interfering with the tuberculous bladder. I suspect that the very favourable reports which have appeared from time to time in the press of cure of tuberculous ulcer of the bladder after curettage and drainage have, in some instances at least, been attacks upon the simple solitary ulcer which so nearly resembles the tuberculous in its symptoms, but which differs from it so markedly in its prognosis.

THE CAUSE OF MALARIA.

Extract from an Address delivered at the Grant Medical College, Bombay, April 4th, 1896.

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[AFTER some preliminary remarks, the lecturer showed a case of recurring malarial fever, with enlarged spleen, in whose blood Laveran's bodies were found. Criticising the figures of these bodies, which have appeared in English medical journals and in other works, he characterised them as "fanciful pictures;" some of them being "drawn from the imagination, others," he said, "especially the rosette form, are caricatures of vacuoles and disintegrating blood cells." Others he considered as being "probably crenating red cells." "It is not surprising," he continued, "that the theories of malarious fever, founded upon the assumption that Laveran's bodies are animal parasites living in the blood are fantastic and fine spun." After a brief sketch of some of the more salient features of the modern doctrine of malarial disease, Dr. Lawrie proceeded, in the following words, to give his own views as to the nature of Laveran's bodies:—]

Healthy blood contains two kinds of cells, the red and the white. The red cells convey gases to and fro between the lungs and the tissues. Their functions are urgent and al-

important, and admit of no interruption or relaxation. Hence, among other marvellous qualities, they possess an elasticity which is absolutely perfect; nothing stops their career, and they dash through the narrowest channels, round the sharpest corners, and past obstacles of any and every kind without the smallest check or hindrance. The mobility, energy, and outward activity of the red cell give it the stamp of what Drummond calls "maleness;" it is an organism principally concerned with nutrition. The white cells are very different from the red; when fully developed they appear to me to be filled with granules, which are minute living protoplasmic cells, and many of them contain large clear spaces, hitherto regarded as nuclei, which must, in my opinion, either be fertilising or nutrient areas; most likely they hold reserves of protoplasm. I throw it out as a hint to the profession that they supply the blood and all the tissues each with the particular kind of protoplasm and young protoplasmic cells suitable for its own special requirements. They incorporate in their own being the two main activities of all living things, nutrition and reproduction, and their internal activity or passivity, and the fact that they teem with young cells and granules, indicates that they are the female, in the sense of being the maternal cells of the blood. The white cells are never in a hurry like the red; they loiter about in the capillary system, and stick to the walls of vessels and pass through them, shedding their contents either in the blood or in the tissues. The white cells have special movements of their own, which consist of varied activities of their protoplasm. These cause the cell itself to change its shape and position, and they produce intracellular movements of the granular contents, which are seen sometimes moving slowly, and at others actively "swarming" with the identical movement described by Laveran in connection with his malaria bodies as that of the "disturbance of boiling water."

The white cells of the blood further have the power of throwing out pseudopod processes which, if thread-like or filamentous, are called cilia or flagella, and these protoplasmic offshoots can be detached, and lead for a time an independent existence. The ordinary forces of the circulation, the heart and the elasticity of the vessels, are not sufficient to account for the whole of the movement of the blood in the capillaries, and it seems, therefore, highly probable that both the intracellular circulation called "swarming" and the evolution of "pseudopoda," which is a primitive force of the circulation, are what Pettigrew long ago described as those occult forces which regularly assist in the peculiar circulation of the blood cells and of the blood plasma in the capillary system.

A most important point, bearing on the origin of Laveran's bodies, is the source from which the blood cells are derived. They are largely manufactured or elaborated in the spleen or liver. In man the red cell is not nucleated but in the human embryo it is nucleated, and it is also nucleated in the frog, and in the frog the nucleus is clearly the intracorporeal stage of the white cell.

No. 1 is a photograph of a red and white cell of frog's blood, copied from Landois and Stirling's book, and it is evident that the white cell is identical with the nucleus of the red. I was led to make an examination of the blood of the frog by an accident. In accordance with letter No. 3,278 from the Government of India Foreign Department to the Resident at Hyderabad, covering a paper by Dr. Patrick Manson on the Nature and Significance of the Crescentic and Flagellated Organisms in Malarial Blood, the medical officers serving under the orders of the Resident at Hyderabad were directed to make observations on the "organisms of malaria, and were specially enjoined to pay particular attention to the life history of the parasite." At the time this letter was received in my office we had been working for several months at the microscopic appearances of the blood in malaria, and it appeared to me that before Laveran's bodies could be properly assumed to be parasites they must be shown to have an independent existence outside the human body, and that a likely *habitat* for them, if they had such an existence, would be the body or the blood of frogs, frogs being known to flourish where malaria abounds. The examination of the blood and of the liver and spleen of frogs was undertaken while the animals were alive (anæsthetised). In the blood and in the