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FURTHER EXPERIMENTAL TREATMENT OF GONORRHŒA  
BY SALINE IRRIGATIONS.

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GONORRHŒA continues to present a problem of perplexity to all who are interested in the health of the Army, and it remains one of deep concern to those engaged in its treatment. The disease still maintains its well-known chronicity, cases may stay many months in hospital and we are still without any reliable therapeutic means whereby this period of inefficiency can be curtailed.

That the disease is more often than not a perfectly trivial and localized one only adds to the seriousness of the situation. Much has been attempted since the War, many forms of treatment have been tried, but we are still more or less in the same position as we were twenty years ago.

Those of us who have given thought to the subject ask what can be done to remedy this defect? The answer can only be sought through a consideration of the urethral mucous membrane and its relation to the habits of the gonococcus.

The mucosa is a very delicate tissue penetrated by numerous minute openings and the organism is one whose chief object appears to be that of hiding in some inaccessible recess. The picture of the fully established disease is that of a highly inflamed mucosa, often studded with numerous follicles containing gonococci.

How is such a condition to be treated? On general principles one

would suggest certain desiderata: (1) The removal of the gonococci by some simple method which will cause as little harm as possible to the urethra; (2) the prevention of follicles; (3) the building up of the patient's resistance.

Dealing first with (1) we have to consider the choice of irrigating fluid. We should naturally insist on the fluid being reasonably toxic to organisms and we should also most certainly insist on its being of such a nature that it is harmless to the highly inflamed mucosa of the urethra. Yet, what do we find in perusing a list of irrigating fluids which have been more or less standard treatment for the last twenty years? We find that they are nearly all very potent as antiseptics but at the same time very irritating. The application to a delicate and inflamed tissue of a concentrated and irritating solution cannot be defended on logical grounds. It would therefore appear desirable that our irrigating fluid should be non-irritating.

Dealing next with (2) we have to consider the prevention of follicles. It is considered that the astringent action of these powerful antiseptics tends first to narrow the minute openings of the various crypts and then finally to close them altogether and so actually produce the follicles which it should be our endeavour to prevent. If the crypts contain the causative organisms, as they usually do, we have reached the stage of trench warfare. The enemy has gone to earth and, secure in his well-constructed pill boxes, can defy for long periods our thrice daily bombardment of germ-killing chemicals. It would therefore appear advisable that our irrigating fluid should also be non-astringent.

Dealing lastly with (3) we should attempt to build up the patient's resistance and this can be done most effectively by vaccine therapy. This subject is referred to later.

Most workers having tried nearly everything else have returned to potassium permanganate as their standard form of irrigation. Such being the case all experimental treatment should be based on a comparison with this disinfectant, and the most rational procedure is to contrast two groups of cases, one on potassium permanganate as a control and the other on whatever we may wish to investigate.

What forms of irrigation are left after so many have been tried? This problem was the subject of consideration by the writer in 1927-28 in Rangoon and the possibility of employing saline as an irrigating fluid was investigated in a group of cases lasting over a period of eighteen months.

As reported in the *JOURNAL OF THE ROYAL ARMY MEDICAL CORPS* [1] and epitomized by the *British Medical Journal* [2], reasons were given for the selection of common salt for the purposes of research. It appeared probable that its effect on the disease might be similar to that of Wright's saline in the treatment of infected war wounds, i.e., leucocytes and lymph might be caused to flow from the deep parts of the mucosa into the urethral passage and so eliminate the gonococcus. At any rate it would be non-irritating and non-astringent.

## BURMA CASES.

The results obtained in a limited number of controlled cases showed a considerable advantage in favour of saline. In the two groups of thirty cases on potassium permanganate at 1 : 10,000 strength and thirty on saline at 1 per cent., an average saving in hospital days of 16·9 was shown for fresh infections, and 30·9 when relapse periods were included. The total figures for the thirty cases showed a saving of 926 hospital days.

After the publication of this report observation was continued for the remainder of the time the writer was in Burma and the subsequent cases brought the total up to fifty in each group. These additional twenty cases in each group reacted much in the same way as the first thirty and the total saving of hospital days was increased to 1,605.

These figures are shown in Table A, and it is pointed out that the first thirty in each column are not new cases, but are republished in order to make a complete survey.

(Note : In each table the letter " F " denotes the presence of follicles and the letter " R " a relapse.)

## ALDERSHOT CASES.

Such were the results obtained in Burma. Would similar results be obtained elsewhere or was the success of this new treatment purely local, climatic or due to a particular strain of organism—in short, was there some factor which was not revealed ?

It was therefore a matter of interest to continue the investigation on arrival in England and find out whether the superiority of saline would be maintained under totally different conditions. Two series of investigations were therefore carried out at the Connaught Hospital, Aldershot, in 1932 to 1934.

It was originally intended to repeat the exact conditions of treatment which had prevailed in Burma, but certain factors had to be considered which led to two modifications.

The first was the strength of potassium permanganate. It was thought that 1 : 10,000 was perhaps rather too strong and that if it be as astringent as one supposes, it would be a fairer comparison to employ a weaker solution and so make it less astringent. It would probably narrow down the margin, in the event of saline again proving superior, but it would make it a more exacting test. The strength was accordingly reduced to 1 : 20,000.

The second factor which was different was the use in all cases of the Woolwich exotoxin vaccine which had not been available in Burma.

These have therefore been the only alterations made and the observations carried out in England have been on precisely the same lines as those in Burma.

It is emphasized that the Aldershot cases, like the preceding ones, were not selected, but consisted of the ordinary routine admissions placed alternately on potassium permanganate or saline.

TABLE A.—BURMA CASES.

(Length of stay in hospital in days.)

<i>Potassium Permanganate.</i>					<i>Saline.</i>				
Case No.	Fresh Days			Relapse Days	Case No.	Fresh Days			Relapse Days
1	83	F.	R.	119	1	30	F.		
2	80	F.	R.	155	2	62	F.		
3	64	F.			3	25			
4	44	F.			4	76	F.		
5	86	F.			5	31	F.		
6	83				6	56			
7	87	F.			7	61			
8	60	F.			8	59	F.		
9	52	F.			9	28			
10	29	F.			10	36	F.		
11	45	F.			11	15			
12	108	F.			12	91	F.		
13	79	F.			13	25	F.		
14	44				14	53			
15	76	F.			15	25			
16	23	F.	R.	14	16	24			
17	25	F.			17	42			
18	104	F.			18	20	F.		
19	74	F.	R.	28	19	17	F.	R.	13
20	33	F.	R.	74	20	19			
21	44	F.	R.	33	21	54	F.		
22	55	F.			22	47			
23	54	F.			23	22		R.	44
24	29		R.	33	24	29	F.		
25	29				25	45	F.		
26	33		R.	20	26	53			
27	85	F.			27	47	F.		
28	100	F.			28	118	F.		
29	16				29	58			
30	104	F.			30	53	F.		
31	104				31	30			
32	58	F.	R.	41	32	37	F.		
33	63	F.	R.	130	33	45			
34	60	F.	R.	65	34	43	F.	R.	51
35	56	F.	R.	66	35	50			
36	92				36	41			
37	39	F.	R.	22	37	41			
38	96	F.			38	160	F.		
39	58				39	24		R.	61
40	72	F.			40	56			
41	66				41	26			
42	59	F.			42	67			
43	61	F.			43	67	F.		
44	42		R.	24	44	40			
45	135	F.	R.	22	45	96	F.		
46	116				46	38			
47	83	F.			47	59	F.		
48	64				48	17			
49	65	F.	R.	18	49	61			
50	64				50	52			
	3,281	36	16	864		2,371	22	4	169
Average stay of fresh cases 65·6 days					Average stay of fresh cases 47·4 days				
Average stay of fresh cases plus relapse cases .. 82·9 days					Average stay of fresh cases plus relapse cases .. 50·8 days				
Total time to cure 50 cases 4,145 days					Total time to cure 50 cases 2,540 days				

TABLE B.—ALDERSHOT CASES (FIRST GROUP).

(Length of stay in hospital in days.)

<i>Potassium Permanganate.</i>				<i>Saline.</i>			
Case No.	Fresh Days		Relapse Days	Case No.	Fresh Days		Relapse Days
1	56	F.		1	54		
2	56			2	63		
3	54	R. R.	70 69	3	35	F.	
4	74	F.		4	44	R.	29
5	104	F.		5	37		
6	61	R.	33	6	37		
7	59	F.		7	34		
8	46	F.		8	75	F.	
9	23			9	73		
10	53	F.		10	52		
11	54	F. R.	60	11	47	F.	
12	39			12	101	F.	
13	59	F.		13	35		
14	51	R.	11	14	36		
15	40			15	53	F.	
16	22	F.		16	29		
17	151	F. R.	74	17	28		
18	78	F.		18	29		
19	64			19	45		
20	47			20	133	F.	
21	28			21	31		
22	40			22	29		
23	27			23	37	F. R.	40
24	50	F.		24	38		
25	30			25	106	F.	
26	66	F.		26	10		
27	84			27	49		
28	149	F.		28	60		
29	28			29	96	F.	
30	43	F.		30	94		
31	20	F.		31	35		
32	28			32	72		
33	30	F.		33	48		
34	66	F.		34	71	F	
35	34			35	25		
36	83	F.		36	73		
37	63	F.		37	41		
38	50	F.		38	23		
39	63	F.		39	85	F.	
40	24	F.		40	54	R.	38
41	50	F.		41	31	F.	
42	53	F.		42	32		
43	36			43	57		
44	97	F.		44	67	F.	
45	46	F.		45	77	F.	
46	39			46	21	F.	
47	105	F.		47	48		
48	70	F.		48	53		
49	26			49	36	F.	
50	50	F.		50	89		
	2,769	30 6	317		2,628	16 3	107
Average stay of fresh cases			55.3 days	Average stay of fresh cases			52.5 days
Average stay of fresh cases plus relapsed cases			61.7 days	Average stay of fresh cases plus relapse cases			54.7 days
Total time to cure 50 cases			3,086 days	Total time to cure 50 cases			2,735 days

TABLE C.—ALDERSHOT CASES (SECOND GROUP).

(Length of stay in hospital in days.)

<i>Potassium Permanganate.</i>				<i>Saline.</i>			
Case No.	Fresh days		Relapse days	Case No.	Fresh days		Relapse days
1	71			1	65	F.	
2	51	F.		2	138	F.	
3	53			3	39	F.	
4	32	R.	42	4	54		
5	60	F.		5	20		
6	37	R.	13	6	59		
7	23	F.		7	25	F.	
8	34	R.	46	8	37		
9	51	F.		9	38		
10	42			10	13		
11	30	R.	28	11	26		
12	139	F.		12	66		
13	104	F.		13	54	F.	
14	127	F.		14	46		
15	61	F. R.	73	15	46		
16	40			16	57		
17	34			17	56	R.	23
18	42	F.		18	85		
19	77			19	47		
20	80	F.		20	51		
21	22			21	59		
22	45	F. R. R.	56 29	22	65	F.	
23	42			23	67		
24	32			24	114		
25	60	F.		25	42	F.	
26	45	F.		26	27	R.	26
27	123	F. R.	111	27	34	F. R.	20
28	26	F.		28	63	F.	
29	95			29	56	F.	
30	92	F.		30	88		
31	50	F. R.	50	31	42	F. R.	29
32	107			32	74		
33	65	F.		33	34	F.	
34	64	F.		34	32		
35	43	F.		35	48		
36	116	F.		36	23	R.	18
37	76			37	74	R.	14
38	17			38	54		
39	60			39	18		
40	56	F.		40	31		
41	53			41	44		
42	42	F.		42	11		
43	46	F. R.	216	43	100	F.	
44	101	F.		44	46		
45	85			45	54		
46	47			46	87		
47	42	F.		47	69	F.	
48	40			48	67		
49	40			49	98	F.	
50	39			50	41		
	2,964	26 10	664		2,684	15 6	130
Average stay of fresh cases			59·3 days	Average stay of fresh cases			53·7 days
Average stay of fresh cases plus relapse cases			72·5 days	Average stay of fresh cases plus relapse cases			56·3 days
Total time to cure 50 cases			3,628 days	Total time to cure 50 cases			2,814 days

As is inevitable in a military hospital a number of patients do not go right through the whole of their treatment at one centre. They may have commenced treatment while on leave, they may be ordered abroad in the trooping season before they are cured, or they may be discharged to the Army Reserve. Such cases were not included. All those under review received the whole of their treatment and surveillance at the Connaught Hospital.

The first series of cases was commenced in February, 1932, and was completed in August, 1933, and is summarized in Table B.

The second series began in August, 1933, and ended in February, 1934, and is summarized in Table C.

#### *First Group (Table B).*

The fifty cases in this group showed an advantage in favour of saline but the difference was not so marked as in the Burma ones.

#### *Comparison with Burma Cases.*

(1) Saline cases : 5·1 days longer for fresh infections ; 3·9 days longer for fresh infections plus relapse.

(2) Potassium permanganate : 10·3 days less for fresh infections ; 21·2 days less for fresh infections plus relapse.

The advantage of saline over potassium permanganate was, however, maintained in each category, and in total time to cure a saving of 351 hospital days was shown. Compared with the corresponding Burma figure of 1,605 it might at first sight appear disappointing, but it was, however, still in favour of saline by a fairly wide margin and further the weaker strength of the potassium permanganate had to be taken into account.

Follicles in the potassium permanganate cases were 30, and in the saline 16. Similarly the relapses in the former were greater by 6 to 3. An interesting feature in the saline group was the relative shortness of the relapses, 35·7 days to 52·8 on potassium permanganate.

The chief points are summarized as follows :—

Saving in hospital days for fresh infections..	..	..	141
Saving in hospital days for relapses	..	..	210
			351
Total saving in hospital days	..	..	351
Number of follicle cases fewer on saline	..	..	14
Number of relapses fewer on saline	..	..	3

#### *Second Group (Table C).*

Here a slight modification was made in the saline. An interesting article by Major H. G. Winter, R.A.M.C., entitled "Notes on the Management of Venereal Diseases," published last year in the JOURNAL OF THE ROYAL ARMY MEDICAL CORPS [3] contained a reference to saline which he advocated for some of the more chronic cases. He also recommended the trial of an alkalinized saline.

In view of the well-known fact that gonococci tend to die in an alkaline medium this appeared to be a very reasonable suggestion and this group of fifty cases was accordingly placed on saline 1 per cent + sodium bicarbonate 1 per cent.

*Comparison with Burma Cases.*

(1) Saline cases: 6·3 days longer for fresh infections; 5·5 days longer for fresh infections plus relapse.

(2) Potassium permanganate: 6·3 days less for fresh infection; 10·4 days less for fresh infections plus relapse.

The margin was again narrowed but saline maintained its superiority over potassium permanganate in all categories. The total saving in hospital days was 814. Follicles in the potassium permanganate cases were 26 and in the saline 15. The relapses in the former were 10 compared with 6 in saline. The average for relapse periods in hospital was again markedly less in the saline cases where only 21·7 days are shown against the 66·4 for potassium permanganate.

The chief points are summarized as follows:—

Saving in hospital days for fresh infections.. ..	280
Saving in hospital days for relapses .. ..	534
Total saving in hospital days ..	814
Number of follicle cases fewer on saline .. ..	11
Number of relapses fewer on saline .. ..	4

*Comparison between the two Saline Groups.*

The question whether the addition of an alkali had made any difference is answered as follows:—

*Alkalinized Saline.*—1·2 days longer for fresh infections; 1·6 days longer for fresh infections plus relapse; 79 more days to cure the 50 cases; 3 more cases of relapse; 1 less follicle case.

It is thus seen that the advantage rests with the pure saline but only by a narrow margin.

## COMPLICATIONS.

In the first 30 of the Burma cases, as reported in the previous article, there were 7 complications on potassium permanganate and 8 on saline. In the remaining 20 no special complications occurred, except the one referred to below under the heading "Notes on the Saline."

In the Aldershot cases complications occurred as shown in Table D. This demonstrates a slight advantage in the saline cases.

It includes all complications, however mild they might be, and with the exception of a severe prostatitis following potassium permanganate treatment in the first group no case was of outstanding severity.

TABLE D.

	Potassium permanganate	Saline
(1) <i>First Group.</i>		
Arthritis .. ..	3	2
Prostatitis .. ..	5	8
Epididymitis .. ..	7	4
(2) <i>Second Group.</i>		
Arthritis .. ..	2	4
Prostatitis .. ..	3	1
Epididymitis .. ..	5	1
	25	20

## SPECIAL FEATURES OF THE SALINE CASES.

The details so far given relate to the final results of treatment, but it is a matter of some interest to consider certain features during the actual course of treatment.

The first point is the rate of disappearance of the gonococci from the smears and whether it is more rapid in one form of treatment than in the other. A perusal of the Aldershot records shows that on an average the organisms disappear from the potassium permanganate cases at 15·5 days and from the saline at 14·5. Whilst there is nothing very conclusive in this it does, however, show that saline is no less effective in killing off the gonococci than is potassium permanganate; in fact it appears to be slightly more so, a point about which there was naturally considerable doubt at the outset of the investigations.

The next feature is one which should be particularly emphasized. This concerns the rate of decrease of the discharge. In saline one employs a drug with lymphogogic powers, fluid being drawn out of the deep tissues into the urethra, and so the discharge is more profuse. Potassium permanganate, on the other hand, tends to dry up the urethral mucous membrane. The difference is therefore one which would be expected, viz., for a certain period the discharge under saline treatment is far more profuse. This period is a variable one lasting from a week to about a month, but the discharge gradually decreases as the case improves. This phenomenon, in the writer's opinion, accounts very largely for the difference in results obtained by other workers who often discontinued saline as it did not appear to be doing any good. Had such cases been kept on this treatment the chances are that they would have cleared up in a comparatively short time.

A third feature is observed towards the final stages. The discharge gradually becomes smaller and smaller, the smears cease to show pus cells and the patient reports merely a "stickiness" in the mornings. This tends to persist for some little time and is apparently a continuance of the draining effect of the saline. The smears contain epithelial cells and perhaps some debris.

Here one is confronted with the problem of when to discharge such a case from hospital. The practice in these investigations has been to deal with them on precisely the same lines as the potassium permanganate cases and to wait till the case is completely dry for four days before proceeding with the test for cure. This has probably increased the length of stay in hospital of the saline cases and may have added several days to the average figures, but it has been felt desirable to play for safety.

There is therefore some possibility that a number of these cases have really cleared up some time before being allowed to leave hospital. At any rate they would appear to be more likely to be "cured" than those on potassium permanganate, and this is borne out by their fewer relapses and the shorter stay in hospital when they do relapse.

A further question remains to be asked, but owing to the average age of our Army patients is a difficult one to answer. It is this: what are the comparative chances of stricture in these two groups? The answer, however, appears to be in the form of another question: which is the more likely case to develop stricture, the one treated with a simple bland non-irritating fluid or the one with a concentrated, astringent and irritating chemical?

#### NOTES ON THE SALINE.

Except for the last twenty cases in the Burma figures the strength at which saline has been employed has been one per cent. In these later Burma cases it was raised to two per cent, but this did not appear to be of any particular advantage. Three per cent proved liable to cause discomfort and a five per cent used accidentally on one occasion produced a severe but temporary œdema of the penis.

At one per cent strength the solution is slightly hypertonic and although Sir Almroth Wright advocated five per cent for full lymphogogic action there seems little doubt that at the strength employed in these investigations it is definitely capable of producing a flow of lymph. This is shown by the more profuse discharge in the intermediate stages and the final "stickiness." The one per cent strength encourages the production of Nature's own antiseptic, viz. the leucocytes, and this would appear to be the explanation of the results.

#### THE USE OF VACCINES.

As explained above the Burma cases were not treated with the Woolwich exotoxin vaccine as it was not available in that country. A few cases were treated with stock vaccine, but only if they developed complications.

In the two groups of Aldershot cases exotoxin was used as a routine for all patients both on saline and on the control. The injections were given weekly and were only discontinued if the case did not appear to be progressing. A change was then made to stock gonococcal vaccine and often an improvement occurred. Similarly it has been noticed, but not quite to the same extent, that a change back to exotoxin is followed by improved results.

The exotoxin vaccine appears to be good for a number of cases, but by no means all. The stock vaccine is of undoubted value in complications such as epididymitis and arthritis.

The future treatment of gonorrhœa, whatever our irrigating fluid, seems to demand some form of assistance to the patient's immunity, which is exceedingly variable and at times apparently non-existent.

#### NOTES ON TREATMENT.

Irrigations have been carried out in all cases by the posterior method in order to afford thorough lavage to the entire urethra. They have been given three times daily.

No special forms of treatment apart from the irrigations have been employed, and the management of these cases has been largely on orthodox lines.

The one possible departure from orthodoxy has been in the passage of sounds. It was originally taught that sounds should be reserved for the later stages and that they should on no account be used before the acute stage was over. It was, however, very obvious that by this time follicles would be fully established.

The principal object of treatment by sounds is to massage the urethra and remove mechanically the organisms and pus cells which are lying in the crypts, perhaps the most important detail of accessory treatment. If this can be done successfully follicles may be prevented.

It therefore appears logical to commence sounds at an earlier time than was formerly advised, and to do so, if possible, before there is a chance of follicle formation.

Originally the custom was to wait for a fortnight. Follicles were, however, present at this period. The period was accordingly reduced to a week, and again follicles were frequently found. It became, therefore, the practice in these cases to pass sounds as early as five days from the commencement of the disease. This method has undoubtedly prevented the formation of many follicles.

It might be urged that this is much too early and that great discomfort or pain might be caused. With the average soldier this is by no means the case, and if due care be taken and the manipulation be of the gentlest kind no discomfort is experienced and no harm is done. Clutton's sounds have been used in all cases, and the size selected has been one which is smaller than that which will ultimately be used. There seems little doubt that if massage on sounds could be used sufficiently early and frequently the problem of follicle formation would be largely solved.

A further point of interest is the length of time the cases are put to bed and given milk diet. In the second group of Aldershot cases the usual period of a fortnight was reduced to seven days. It seems desirable to keep up the patient's general health and resistance as much as possible, and there is little doubt that a full fortnight on milk diet tends to lower it unduly. One's personal conclusion is that a week is sufficient time for bed and milk diet, and that the cases tend to do better once they are up and walking about and taking a full ordinary diet.

The remainder of the treatment having been mostly on stereotyped lines there is little to be said except to refer to the thrice daily administration of an alkaline mixture; barley water was given three times daily as well, and prostatic massage at weekly intervals. Kollmann's anterior dilator was also used as a routine.

Lastly, the Test for Cure may be summarized: Case four days dry; stop treatment; then prostatic massage; provocative vaccine; instillation of silver nitrate and two bottles of beer for two days. If still dry the case is then discharged to full duty with his unit.

## SUMMARY OF ALL CASES.

The results of the experimental treatment for all cases are summarized in Table E. It will be noted that in each category the advantage rests with saline, in some categories very markedly so; for example, the number of relapses and follicles, and particularly in the total saving of hospital days, which reaches the figure of 2,770.

TABLE E.—SUMMARY OF ALL CASES ON EXPERIMENTAL TREATMENT.

	Potassium permanganate	Saline
(1) Total cases .. .. .	150	150
(2) Total days for fresh infections .. .. .	9,014	7,683
(3) Total days for relapses .. .. .	1,845	406
(4) Total for fresh cases plus relapses .. .. .	10,859	8,089
(5) Average days for fresh cases .. .. .	60	51·2
(6) Average days for relapses .. .. .	57·6	31·2
(7) Average days for fresh cases plus relapses .. .. .	72·39	53·8
(8) Number of relapses .. .. .	32	13
(9) Number of cases with follicles .. .. .	91	53
(10) Number of cases with complications .. .. .	32	29
Total saving of hospital days = 2,770.		

## CONCLUSIONS.

In commencing these series of investigations the object was to compare two forms of treatment. The intention was neither to condemn potassium permanganate nor to favour saline. Each contrasted group of cases has received identical treatment in all other respects, and the aim throughout has been to exercise strict impartiality.

In the employment of saline no claim is made for the discovery of a new "cure" for gonorrhœa. The length of stay in hospital is too great to permit of any such suggestion.

What however is claimed, as a result of four years' investigation covering such diverse conditions as Burma and England, is that saline is a preferable alternative to the strong antiseptic of traditional teaching.

Its advantages are shown by: (1) The shorter periods spent in hospital for both fresh cases and relapse conditions; (2) the fewer number of relapses; (3) the fewer cases with follicles; (4) the total saving of hospital days.

It is considered that once the freely discharging period is over the cases clear up more quickly than on potassium permanganate.

It is finally suggested that the future treatment of gonorrhœa should depend on: (1) A bland and harmless irrigating fluid which will drain the deep tissues of the urethra; (2) early and systematic massage on sounds; (3) artificial assistance to the patient's natural immunity in the form of vaccine therapy.

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