

# Spread of Tuberculosis from the Urinary Bladder to the Male Genital Organs

## An Experimental Study

M. Duchek and B. Winblad

Departments of Urology and Pathology, University of Umeå, Umeå, Sweden

Received: June 12, 1973

**Summary.** In order to study the spread of tuberculous infection from the urinary bladder to the male genital organs, guinea pigs were inoculated with tubercle bacilli ( $H_{37}Rv$ ) into the bladder wall. Half of the animals were prepared by bilateral resection of the ductus deferens before inoculation. The infection spread to the prostate in most of the animals, and in more than half of them to the epididymis. In only one animal

was there spread to a seminal vesicle. - Spread occurred irrespective of whether the ductus deferens was intact, probably mainly by way of the lymphatics.

**Key words:** Genito-urinary tuberculosis, genital tuberculosis, male, experimental tuberculosis, spread of tuberculosis, lymphatic spread, experimental model - guinea pig

### Introduction

It is generally accepted that Mycobacterium tuberculosis can spread to the genital organs from the urinary tract both by the haematogenous route and directly by way of the ductus deferens. Clinical experience is that urinary tract tuberculosis often precedes infection of the genital organs in men (1, 2, 3, 4). Since both organ systems meet in the prostatic urethra, it has been generally assumed that infection from the urinary bladder and urethra invades the prostate, seminal vesicles and ducti deferentes by the intracanalicular route.

However, it is remarkable that most patients with urinary tract tuberculosis, with or without genital tuberculosis, show only minor changes in the urethra. Since reflux of infected urine to the prostate, seminal vesicle and ductus deferens only occurs under conditions of increased intraurethral pressure, we deemed it worth while to study other possible routes of spread of infection from the urinary tract to the genital organs. In this study we have used the same experimental model as was used in a previous study of the spread of tuberculosis within the male genital tract in the guinea pig (5).

### Material and Methods

**Experimental animals.** Tubercle bacilli were inoculated into the bladder wall in 18 sexually mature male guinea pigs. Half of the animals were prepared by bilateral resection of the ductus deferens before inoculation. The animals were individually caged with free access to food and water.

**Inoculum.** A 14-day-old culture of tubercle bacilli,  $H_{37}Rv$ , diluted with physiological saline to a concentration of 0.1 mg/ml and containing approximately 50 000 bacteria/ml, was used as inoculum.

**Operative procedure.** Mebumal sodium 2.5 mg/100 g body weight was administered intraperitoneally; supplementary ether anaesthesia was used on occasion. The abdomen was opened by a low midline incision and the testes, epididymes and seminal vesicles were exposed. In half of the animals both ducti deferentes were resected by a technique recently described (6). 0.05 ml of inoculum was injected into the bladder wall from a disposable syringe. The inoculation site was chosen so that the tip of the needle lay in the submucosa of the anterior part of the trigonum during injection. Before the needle was withdrawn, a cotton-tipped applicator stick soaked with Nobectan<sup>R</sup> Bofors was applied to the injection site and held in place for about one minute. When the in-

jection site had been thus sealed with a plastic film, the organs were replaced in the abdominal cavity and the scrotum. The abdominal wall was closed in two layers. The animals were killed after 4 weeks.

**Identification of tuberculous infection.** The tuberculous infection was evaluated by macroscopic inspection and microscopic examination of tissue specimens fixed in neutral formalin and embedded in paraffin. Histological sections were stained with haematoxylin-eosin and with a fluorescent stain (Auramine-rhodamine) for demonstration of tubercle bacilli (7).

The following organs were examined: testes, epididymes, ducti deferentes, seminal vesicles, prostate, urinary bladder, kidneys, spleen and iliac, renal and paraaortic lymph nodes.

The demonstration of tubercle bacilli in combination with characteristic morphological tissue changes was the criterion for characterizing an organ as tuberculous. Urine aspirated by direct puncture of the roof of the bladder at autopsy and blood taken from the heart were cultured on Löwenstein-Jensen's medium.

## Results

The results are shown in Tables 1 and 2.

The animals gained weight and none died of miliary tuberculosis. In all animals tuberculous granulation tissue and tubercle bacilli were found at the site of inoculation, that is, in the anterior part of the trigonum and in the anterior wall of the

Table 1. Spread of tuberculous infection in the male genital system

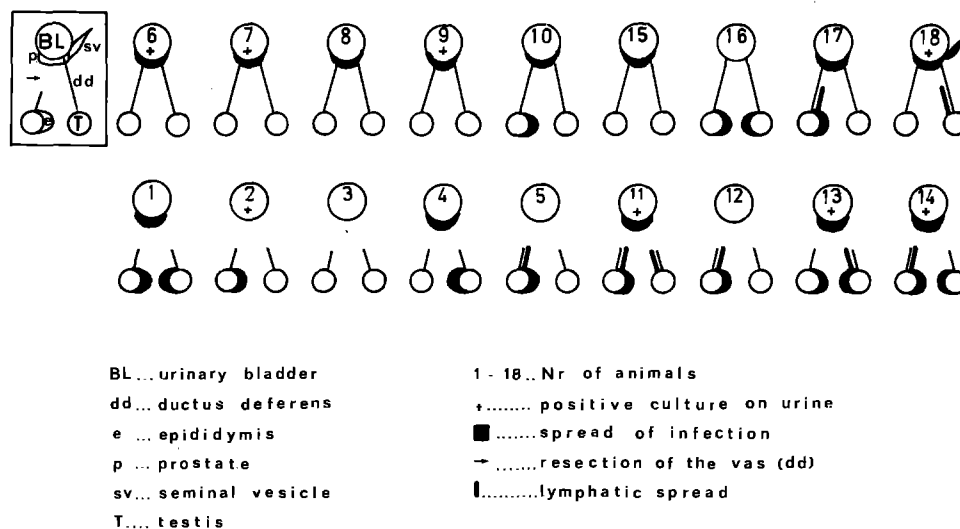


Table 2. Tuberculous changes in the genital tract of male guinea pigs following inoculation into the urinary bladder wall. Review of results

	Number of animals	LE	LSV	P	B1	RSV	RE	U	B
Intact vas	9	1	1	8	9	0	3	4	0
Resection of vas	9	4	0	5	9	0	7	4	0

L... left

U... L-J culture on urine

R... right

B... L-J culture on blood

□... indicates the site  
of inoculation

Other symbols see table 1

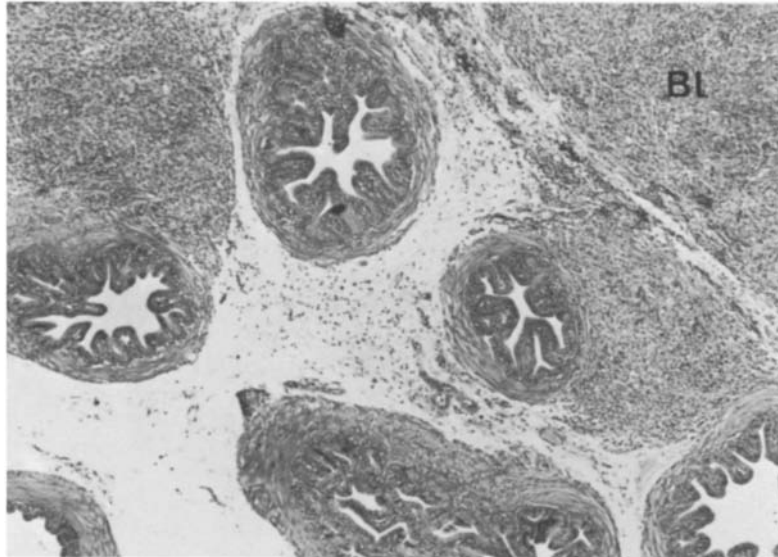


Fig. 1. Section from prostate with continuous spread of tuberculous granulation tissue from the bladder (B1), surrounding the secretory ducts. Htx. -eosin x 50



Fig. 2. Section from urinary bladder wall at the site of injection. Granulation tissue (G) beneath the epithelium (E) and granulomas in the perivesical tissue (probably in lymph vessels) (L). Htx. - eosin x 30

bladder. The tuberculous granulomas were mainly located in the submucosa and in the muscle layers. In some animals they were seen to penetrate the epithelium. Cultures of urine on Löwenstein-Jensen's medium were positive in 8 animals.

The prostates were macroscopically oedematous and in 12 of them interstitial epithelioid cell granulomas containing tubercle bacilli were seen. These changes usually represented continuous spread (Fig. 1), but there was sometimes evidence of lymphatic spread (Fig. 2). The seminal vesicles were free from infection in all animals but one.

The iliac lymph nodes were enlarged and contained confluent granulomas rich in tubercle bacilli. Although the changes in the renal and para-aortic lymph nodes were somewhat less pronounced, microscopic examination clearly indicated that these nodes were also infected.

The scrotal genitalia were macroscopically normal in appearance, except in one animal in which there was torsion of the right testis (animal 11). Microscopic examination showed that 11 animals (8 with resection of the ductus, 3 non-resected) had tuberculous epididymitis of interstitial type; in 4 of them the infection was bilateral. There were no tuberculous changes in the testes.

In 9 animals cross-sections of the scrotal part of the ductus deferens and surrounding tissue revealed inflammatory granulomatous areas containing tubercle bacilli in the loose periductal tissue, often in the lymph spaces. Inflammatory changes in the ductus deferens were not seen in any of the animals.

The spleen was enlarged and showed nonspecific inflammatory changes in about half of the animals. A few spleens, however, contained scattered tubercles. Few tubercle bacilli were present. In 4 animals no tubercle bacilli were demonstrable in the spleen. A few bacilli were found in 4 kidneys, but there was no tissue reaction around these organisms. Blood cultures were negative in all animals.

### Discussion

Since genital tuberculosis in men is usually secondary to tuberculosis in the urinary tract, an attempt was made to produce an experimental urinary tract tuberculosis in animals resembling that in man. However, the kidneys of the guinea pig are highly resistant to tuberculous infection (8). Nor does the injection of tubercle bacilli into the lumen of an intact urinary bladder lead to infection. To ensure infection it is necessary to either ligate the urethra and/or damage the bladder wall (9, 10). Ligation of the urethra simulates stricture of the urethra in man and has similar consequences: a marked increase of pressure in the urinary passages and secondary urethroseminal reflux.

In most patients, however, there are only minor changes in the urethra when the infection spreads to the genitalia. We therefore chose an experimental model retaining normal micturition, and injected tubercle bacilli directly into the bladder wall.

Although tuberculous changes in the human bladder are most marked in the bladder base, we wished to avoid direct infection of the prostate and therefore performed the inoculation just above the bladder neck.

The time of observation in these studies was, of course, much shorter than the prolonged natural course of the disease in man. However, a short observation time facilitates analysis of the routes of spread since the picture is not confused by generalized disease.

In our material tuberculous infection always occurred at the site of inoculation. There is a close relationship between the trigonum and the prostate which is reflected in their common lymphatic drainage. Therefore it was not surprising that most of the prostates were infected and that the disease had spread to the prostate both continuously and by way of the lymphatic spaces.

There was spread to the epididymis in all but one of the animals in which the ductus deferens had been resected. In only 3 of the animals with intact ducti had infection reached the epididymis. The inflammation was of interstitial type in all cases. In sections taken distal to the site of resection there were no tuberculous changes in the ductus deferens. However, tuberculous granulation tissue was present around the vessels and in the lymphatic spaces in the surrounding tissues.

Not even in the 8 animals for which urine cultures were positive on Löwenstein-Jensen's medium were there signs of intracanalicular tuberculosis in the ductus deferens or in the epididymis.

As in earlier studies, lymph vessels showing inflammatory changes were seen to connect the urinary bladder and the prostate with the iliac nodes. The inflammatory changes were much more marked in the iliac nodes than in the paraaortic or renal nodes. These findings, in combination with the negative blood cultures and the moderate changes in the spleen, indicate that the predominant route of spread of tuberculosis is to the regional lymph nodes, followed by generalized infection at a later stage.

It is of interest that tuberculous epididymitis was present even in animals in which there were no signs of tuberculosis of the prostate. This suggests that spread may occur directly to the scrotal organs from the bladder at an early stage when the pelvic genitalia are not infected.

### References

1. Chevassu, M.: Tuberculose rénale des tuberculeux génitaux mâles. Congr. franç. d'urol. 35, 630 (1935)
2. Borthwick, W. M.: Tuberculosis of the male genital tract. Glasg. med. J. 144, 173 (1945)
3. Joller, A.: Die urinogene tuberkulöse Prostatitis. Acta davos. 8, (No. 3, 4) 1 (1949)
4. Ljunggren, E.: Pathogenesis and pathology of genital tuberculosis in the male. Handbuch der Urologie IX/2, 32. Berlin, Göttingen: Springer 1959
5. Duchek, M., Winblad, B.: Experimental male genital tuberculosis - the possibility of lymphatic spread. To be published in Urological Research (1973)
6. Duchek, M., Winblad, B.: An experimental Method for studying the Spread of Genital Tuberculosis. Urological Research 1, 32 (1973)
7. Winblad, B., Duchek, M.: Comparison between microscopical methods and cultivation for demonstration of tubercle bacilli in experimental tuberculous infection. To be published in Acta path. microbiol. scand
8. Birkhäuser, H.: Die Resistenz des Meer-schweinchens gegen Tuberkulose. Schweiz. Z. allg. Path. 13, 455 (1950)
9. Cayla: De la tuberculisation des organes génito-urinaires. Thèse de Paris (1887). Quoted by Hansen
10. Hansen, P. M.: Recherches expérimentales sur la tuberculose génitourinaire, surtout sur la tuberculose du rein. Ann. Mal. Org. gén. - urin. 21, 31 (1903)

Miloš Duchek, M. D.  
Dept. of Urology  
University of Umeå  
S-90185 Umeå  
Sweden