Ureteral Activity during Increased Intravesical Pressure

By

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Ureteral activity during the intravesical infusion was examined by urometry and electro-ureterography in 12 normal persons and a patient with vesico-ureteral reflux. The urometrograms and electro-ureterograms in normal persons indicated that when the bladder was distended with physiologic saline solution, the ureteral peristalsis responded so as to overcome the increased intravesical pressure. In the case with vesico-ureteral reflux, the ureteral peristalsis was found to be preserved. The values measured on the urometrogram and electro-ureterogram were all within the range of normal ones, and the urine was transported smoothly from the renal pelvis to the bladder without the reflux, when the intravesical pressure was below 10 cm H₂O. When the intravesical pressure was raised up to 10 cm H₂O, the reflux appeared. Even in this ureter peristalsis responded so as to flow out the refluxed urine. These findings suggest that ureteral peristalsis, if it remains, works to repress the vesico-ureteral reflux as far as it can resist the increased intravesical pressure and that it works against the reflux, when it actually occurs.

How the ureter responds to bladder filling is an important problem to elucidate the etiologic mechanism of the vesico-ureteral reflux. But literature dealing with the problem is scanty, for there was no adequate examination method to grasp clinical feature of the ureteral function. Direct observation of the exposed ureter, cystoscopic examination of the ureteral orifices, radiographic examination, measurement of the intraureteral pressure (hydro-phorograph) and ureteral electromyography were employed for the purpose, but information obtained with these methods was not sufficient to clarify the ureteral function.

However, in 1957, Kiil¹ evaluated urometry in judging the functioning capacity of the ureter. On the other hand, physiologic significance of electro-ureterography was elucidated by the excellent work of Bozler.² Nevertheless, it was far from being applied clinically, for no reliable method for non-operative installation of the electrode was introduced, and its practical value was denied by Kiil himself. Recently, ureteral action potentials were successfully recorded in our department by inserting a special electrode-catheter through a cystoscope³.

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In the present study, the changes in ureteral peristalsis during intravesical infusion were observed by urometry and electro-ureterography.

METHODS AND MATERIALS

1. *Methods*

1) Preliminary experiment: In order to learn the influence on the ureteral function of the inserted urometric catheter or electromyographic catheter, indigocarmine excretion test was performed on 3 normal persons and a patient with vesico-ureteral reflux. The indigocarmine excretion from the ureteral orifice of the side under examination was observed cystoscopically before and during insertion of the catheter.

2) Urometry: Urometry was carried out by Kiil's method¹. In the present study, two F-5 polyethylene ureteral catheters were used; one of catheters was inserted into the ureter through a cystoscope and another into the bladder. The intraureteral pressure and intravesical pressure, which were conducted through these catheters, were recorded simultaneously with "Electronic Manometer", Mp-3, connected with "4-Channel Electrocardiograph", MC-42T (Nihonkoden Co. Ltd.).

3) Electro-ureterography: Electro-ureterography was performed by the previously reported method² using a "U-loop" collar bipolar electrode.

2. *Procedure*

Urometry and electro-ureterography were performed, while the bladder was infused with physiologic saline solution at a rate of 60 to 100 c.c./min. The urine flow was controlled to be 1 c.c./min by intravenous injection of the saline solution in order to keep out the influence of the change in urinary output.

In urometry, the intra-ureteral pressure was measured at intervals of 5 cm in the portion of the ureter between 20 cm and 5 cm from the ureteral orifice. The contraction interval was measured at 10 cm and intra-ureteral pressure was measured at 15 cm from the ureteral orifice which represents the upper portion of the ureter and at 5 cm which represents the lower portion. As urometry was recorded at a low speed, the contraction complexes formed a sharp spike. Accordingly, the duration was not expressed in figures.

Electro-ureterography was recorded at 10 cm from the ureteral orifice, for no significant difference was noted in discharge interval, amplitude, duration and propagation rate of the action potential measured between 20 cm and 5 cm.

3. *Materials*

The present examination was conducted on a total of 13 subjects: 12 adults of 20-50 years old who were urologically normal and a patient with tuberculosis of the solitary kidney in whom vesico-ureteral reflux was demonstrated.

RESULTS

1. *Effect of inlying catheter*

As seen in Table I, insertion of urometric or electro-ureterographic catheter brought about no recognizable change in the appearance, time duration and interval of the indigocarmine excretion. From the result, it seems that the ureteral function is scarcely affected by insertion of the catheter.

TABLE I. Influence of Inlying Catheter on the Indigocarmine Excretion Test

1) Before Insertion

Case	Appearance time Appearance		Duration	Interval
1	4 min	55 sec	1 sec	18 sec
2	6	07	2	12
3	6	35	2	13
4	8	54	3	28

2) During Insertion of Urometric Catheter

1	5 min	02 sec	1 sec	16 sec
2	6	35	2	13
3	6	40	1	17
4	8	20	2	27

3) During Insertion of Electro-ureterographic Catheter

1	5 min	02 sec	1 sec	12 sec
2	5	31	1	13
3	6	32	2	13
4	7	50	0.5	20

Cases 1-3 were normal persons

Case 4 was a patient with vesico-ureteral reflux.

2. *Urometrograms prior to the bladder infusion in the normal adults (Fig. 1)*

Interval of consecutive contraction complexes measured in 12 cases was 16.0 to 90.7 sec with an average of 31.6 sec, as shown in Table II. The resting pressure in these subjects was 1.5 to 13.0 cm H₂O with an average of 5.7 cm H₂O at 15 cm from the ureteral orifice and 0 to 18 cm H₂O with an average of 7.2 cm H₂O at 5 cm from the orifice (Table III). In 8 of 12 subjects, the resting pressure in the lower portion of the ureter was slightly higher than in the upper portion. The resting pressure showed no fluctuation when the bladder was empty. The contractile pressure ranged from 7.6 to 27 cm H₂O with an average of 13.4 cm H₂O at 15 cm from the ureteral orifice, and from 5.0 to 29.0 cm H₂O with an average of 17.0 cm H₂O at 5 cm from the orifice. As for the contractile pressure, no considerable difference was observed between the upper and lower portions of the ureter, as seen in Table III.

Fig. 1. Urometrogram prior to intravesical infusion.
Left normal ureter of a 21-year-old man.
The contraction interval was regular, although some difference is noted in each interval. The resting pressure and contractile pressure were nearly constant.

TABLE II. Interval of Contraction before and during
Intravesical Infusion

Case	Sex	Side	Before infusion (mean value)	At filling-up (minimum value)	Rate of decrease (%)
1	♂	right	28.3 sec	25.0 sec	11.7
2	♂	left	20.0	18.0	10.0
3	♂	left	16.0	4.0	75.0
4	♂	right	90.7	64.0	29.4
5	♂	right	66.7	44.0	34.0
6	♀	left	17.9	7.7	57.0
7	♂	left	22.8	13.0	36.0
8	♂	right	19.0	13.0	36.8
9	♀	left	17.8	18.0	Unchanged
10	♂	right	33.8	18.0	46.7
11	♀	right	25.0	15.0	40.0
12	♂	left	21.5	17.8	17.2
Average			31.6	21.5	32.0

3. Urometrograms during the intravesical infusion in the normal adults (Fig. 2)

When the bladder was distended to a state of repletion; that is, when the intravesical pressure was increased over 15 to 20 cm H₂O, the intervals of the contraction became shorter (Table II). This tendency persisted for some time even after a considerable amount of the solution had been discharged from the bladder. The rate of the decrease was from 10 to 75% of the original value with an average of 32%. The resting pressure increased markedly, following the increase in the intravesical pressure. The highest resting pressure in these cases was between 6.5 and 30.0 cm H₂O with an average of 15.4 cm H₂O at 15 cm from the ureteral orifice, and between 5.0 and 26.0 cm H₂O with an average of 13.8 cm H₂O at 5 cm from the orifice (Table III).

In proportion to the increase in resting pressure, the contractile pressure increased markedly in all the subjects and always exceeded the increased intravesical pressure.

The maximum contractile pressure was between 15.0 and 60.0 cm H₂O with an average of 26.1 cm H₂O at 15 cm from the ureteral orifice, and between 18.0 and 47.0 cm H₂O with an average of 30.7 cm H₂O at 5 cm from the orifice.

TABLE III. Intraureteral Pressure before and during Intravesical Infusion

a) Measured at 15 cm from the Ureteral Orifice

Case	Before infusion		At filling-up	
	Resting pressure (cmH ₂ O)	Contractile pressure (cmH ₂)	Resting pressure (cmH ₂ O)	Contractile pressure (cmH ₂ O)
1	4.0	9.0	9.0	17.0
2	13.0	19.0	20.0	28.0
3	8.0	10.0	19.0	23.0
4	4.0	27.0	12.0	31.0
5	5.0	8.0	8.0	15.0
6	2.5	15.5	15.0	25.0
7	4.5	9.5	6.5	20.0
8	1.5	7.6	11.0	30.0
9	3.0	9.7	30.0	60.0
10	5.0	9.0	12.5	15.5
11	6.0	22.0	18.0	18.0
12	12.0	20.0	24.0	31.0
Average	5.7	13.4	15.4	26.1

b) Measured at 5 cm from the Ureteral Orifice

1	6.0	15.2	15.0	25.0
2	6.0	15.3	9.0	24.0
3	4.0	8.0	11.0	47.0
4	13.0	19.5	22.0	36.0
5	7.5	17.5	18.0	29.0
6	10.0	29.0	10.0	41.0
7	0	5.0	9.0	22.0
8	2.5	9.3	14.0	29.0
9	8.0	21.6	5.0	33.0
10	6.0	22.0	18.0	18.0
11	5.0	13.0	9.0	32.8
12	18.0	28.0	26.0	32.0
Average	7.2	17.0	13.8	30.7

Fig. 2. Urometrogram during intravesical infusion.

Right normal ureter of a 35-year-old man.

When the intravesical pressure was raised, the intraureteral resting pressure increased almost in parallel to the intravesical pressure. When the resting pressure reached its maximum, the interval of contraction became shorter and the contraction pressure increased. The duration of a contraction also prolonged. This tendency was observed both in the upper and lower portions of the ureter, more markedly in the latter.

Tracing speed: 0.5/min

As seen in Fig. 2, the duration of a contraction complex prolonged markedly, when the intravesical pressure was raised.

4. *Electro-ureterograms prior to the bladder infusion in normal adults*

When the bladder was empty, discharge interval of the action potential measured in 12 subjects was 13.9 to 40.0 sec with an average of 21.3 sec (Table IV). The amplitude of the action potential was between 0.26 and 1.2 mV with an average of 0.58 mV (Table V). The discharge duration was between 0.20 and 1.05 sec with an average of 0.55 sec (Table VI). The propagation rate of the action potential was between 17.5 and 66.6 mm/sec with an average of 32.9 mm/sec, although it differed slightly in each complex (Table VII).

TABLE IV. Discharge Interval before and during Intravesical Infusion

Case	Before infusion (average value cm H ₂ O)	At filling-up (maximum value cm H ₂ O)	Rate of decrease (%)
1	31.6	13.5	57.2
2	14.4	5.4	62.5
3	13.9	5.3	61.9
4	34.1	18.0	47.2
5	40.0	7.6	81.0
6	17.8	7.7	56.7
7	17.1	4.1	76.0
8	19.4	10.4	46.4
9	17.7	14.0	20.9
10	14.2	14.1	0.7
11	20.7	18.0	13.0
12	14.7	6.4	56.5
Average	21.3	10.4	51.2

TABLE V. Amplitude of Action Potential before and during Intravesical Infusion

Case	Before infusion (mV)	At filling-up (mV)
1	0.47	0.52
2	1.59	0.85
3	1.2	0.73
4	0.26	0.26
5	0.29	0.27
6	0.51	0.47
7	0.67	0.53
8	0.60	0.49
9	0.72	0.73
10	0.65	0.54
11	0.54	0.53
12	0.46	0.4
Average	0.58	0.53

TABLE VI. Discharge Duration before and during Intravesical Infusion

Case	Prior to bladder infusion (min)	At filling-up (min)
1	0.57	0.50
2	0.25	0.30
3	0.93	1.15
4	0.50	0.40
5	0.33	0.45
6	0.50	0.70
7	0.75	0.80
8	0.20	0.40
9	0.78	1.05
10	1.05	1.10
11	0.40	0.45
12	0.34	0.34
Average	0.55	0.64

TABLE VII. Propagation Rate of Action Potential before and during Intravesical Infusion

Case	Before infusion	At filling-up	Rate of decrease
1	26.3	23.8	9.5
2	66.6	38.5	42.1
3	—	—	—
4	26.3	21.7	17.5
5	43.5	31.3	28.0
6	32.3	38.6	11.5
7	22.7	19.2	18.7
8	18.7	27.8	Increased
9	26.5	23.5	11.3
10	49.2	49.2	Unchanged
11	17.5	17.0	2.9
12	33.3	20.0	39.3
Average	32.9	27.3	19.9

5. *Electro-ureterograms during the intravesical infusion (Fig. 3)*

When the bladder was filled up, the discharge interval of the ureteral action potential shortened markedly in all the cases, as seen in Fig. 3, although the shortening rate differed slightly from case to case. The average shortening rate was 51.2 % of the original value (Table IV). The amplitude of the action potential remained almost unchanged throughout the intravesical infusion (Table V). When the discharge interval shortened, the discharge duration prolonged slightly. The prolonged discharge duration ranged from 0.30 to 1.15 sec with an average of 0.64 sec (Table VI). In parallel to the shortening of the discharge interval, the propagation rate at filling-up was 17.0 to 49.2 mm/sec (Table VII). The average decrease was 19.9% of the original value.

Prior to infusion

At filling-up

Fig. 3. Electro-ureterogram during intravesical infusion.
Left ureter of a 42-year-old man.

When the bladder was empty, the action potential measured was 34.8 sec in discharge interval, 0.80 mV in amplitude, 0.8 sec in discharge duration and 40.4 mm/sec in propagation rate. When the bladder was filled up, the interval diminished to 10.8 sec and the propagation rate delayed to 12.1 mm/sec. The amplitude remained almost unchanged, being 0.86 mV.

E.U.G. through a cystoscope using a collar bipolar electrode.

Interpolar distance: 2 cm.

Tracing speed: 10 cm/sec.

Amplitude: 1 mV=15 mm.

Fig. 4. Cystogram of a patient with renal tuberculosis.
Vesico-ureteral reflux is observed in the left ureter.

Fig. 5. Urometrogram of the patient shown in Fig. 4.

Upper tracing is the recording of the intravesical pressure and the lower tracing is that of the intraureteral pressure.

The interval of contraction ranged from 9 to 20 sec with an average of 12 sec throughout the length of the ureter, when the bladder was empty. The resting pressure was between 3 and 6 cm H₂O. When the bladder was filled up, the resting pressure increased as high as 29 cm H₂O, coinciding with the intravesical pressure and the contraction pressure increased as high as 43 cm H₂O.

Fig. 6. Electro-ureterogram of the same patient.

When the bladder was empty, measurements of the action potential were 30.0 sec in discharge interval, 1.7 sec in discharge duration, 25 mm/sec in propagation rate and 1.3 mV in amplitude. When the bladder was filled up, the discharge interval shortened to 22.0 sec and the discharge duration prolonged up to 1.7 sec. The propagation rate diminished to 20 mm/sec. The amplitude remained unchanged.

6. Urometrograms and electro-ureterograms in a patient with vesico-ureteral reflux

The patient underwent right nephrectomy for renal tuberculosis some years previously. The cystoscopic examination revealed that the vesical mucosa was nearly normal with a slight trabeculation.

The capacity of the bladder was about 200 c.c., a little lower than normal. The left ureteral orifice was small and of round and depressed shape and no contraction movement was observed there. When cystography was performed with more than 100 c.c. of the contrast medium, that is, when intravesical pressure became over 10 cm H₂O, vesico-ureteral reflux appeared (Fig. 4).

1) *Urometrogram*: In this ureter, pressure fluctuation which was characteristic of the ureteral peristalsis, was still preserved (Fig. 5). As shown in Fig. 5, the interval of contraction complexes, the intraureteral resting pressure and contractile pressure were all within the range of the values obtained in normal persons when the bladder was empty. When the intravesical pressure was raised, the same ureteral response was observed as in the normal subjects, except for the resting pressure. The resting pressure fluctuated coincidentally with the intravesical pressure.

2) *Electro-ureterogram*: The electro-ureterograms obtained with an electrode placed at 10 cm from the ureteral orifice are shown in Fig. 6. The ureteral electromyogram in this patient shows the same features as in the normal persons, when the bladder was either empty or filled up, but discharge duration was more prolonged in this case than in the normal subjects.

DISCUSSION

As to the ureteral response to the increased intravesical pressure, there was some disagreement among the investigators. This might be due to difference in species of experimental animals, methods of observation and experimental conditions. Pflaumer⁴ reported that the contraction movement of the ureteral orifices became more frequent, when the bladder was distended. Similar results were reported by Graves and Davidoff,⁵ who worked with exposed rabbit ureter. On the contrary, Narath⁶ was of the opinion that frequency of ureteral contractions was reduced during bladder filling. From the urometric observation, Kiil¹ reported that frequency of ureteral contractions increased when the bladder was rapidly distended. He noted further that intraureteral resting pressure increased and the duration of contraction became longer. This reaction, he pointed out, was of the same type as those encountered when the urine flow exceeded the emptying capacity of the tract. Consequently, he concluded that the reaction was not due to the vesico-ureteral reflux but to the storage of urine in the ureter. Further, Scott and De Luca⁷ stated that when the intravesical pressure was slightly raised, the contractile pressure of a normal canine ureter exceeded the intravesical pressure with greater frequency of the contraction. However, the resting pressure remained constant. When the intravesical pressure was raised higher, the resting pressure also increased and the contraction pressure increased more. In the present experiments, the frequency of contraction increased when the intravesical pressure was raised by the intravesical infusion. Almost in parallel to the

increase, the resting and contractile pressure increased and the duration of the contraction prolonged. The results of the present study coincided with those reported by Kiil, and by Scott and De Luca. Further, electro-ureterography gave the results similar to those obtained by urometry: When the intravesical pressure was increased, the discharge interval of an action potential shortened markedly, discharge duration prolonged slightly, and the propagation rate lowered. Since indigocarmine excretion persists during the bladder filling, the above-mentioned change in ureteral activity observed by urometry and electro-ureterography may be regarded as a reaction to overcome the increased intravesical pressure.

As to vesico-ureteral reflux, many attempts have been made to elucidate the phenomenon from the anatomical standpoint, but there are still only a few reports dealing with the role of the ureteral function in the phenomenon. Although Tinckler⁸ laid a stress on the valve action in the vesico-ureteral juncture, he was of the opinion that the ureteral peristalsis itself could react against the reflux, when the valve action was insufficient. In the experiments in dogs, Scott and De Luca⁷ observed that the ureter, in which the vesico-ureteral reflux occurred, did not respond to bladder filling by an increase in contraction amplitude. When the intravesical pressure was raised up to the level of the resting pressure, the reflux, they say, occurred with disappearance of the contraction complexes. The resting pressure itself increased, taking the same pressure level as the intravesical pressure. Davis and Zimskind⁹ reported the result of urometry performed in 2 cases in which vesico-ureteral reflux was observed. In one of the cases the resting pressure increased mildly, following an abrupt rise of intravesical pressure and in the other case a rise in intravesical pressure was followed by a simultaneous rise in resting pressure. In none of these cases, the peristaltic movements were observed.

In the present study, a patient with vesico-ureteral reflux due to tuberculous involvement of the uretero-vesical juncture was examined. When the intravesical pressure was below 10 cm H₂O, urometric and electro-ureterographic findings were within the range of the normal values and vesico-ureteral reflux did not occur. Accordingly, it may be thought that the urine was smoothly transported from the renal pelvis to the bladder by ureteral peristalsis. When the bladder was filled up, the same ureteral reaction was observed as in the normal persons. The fact that the increase in the resting pressure was simultaneous with that of the intravesical pressure, seems to mean that the vesico-ureteral reflux occurred in the ureter. However, in this case the contractile pressure increased higher and discharge interval of action potential lasted longer than in the normal persons. Judging from the ureteral reaction observed in normal persons, these changes in ureteral activity can be considered as the ureteral reaction to flow out the refluxed urine again into the bladder. From these facts it is concluded that vesico-ureteral reflux does not occur as far as ureteral peristalsis, if it is

preserved, can overcome the increased intravesical pressure and that the ureteral peristalsis works against the reflux when it actually occurs.

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