Title	REGENERATION OF THE BLADDER EPITHELIUM
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REGENERATION OF THE BLADDER EPITHELIUM

by

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It is a well known fact that the urinary epithelium has a remarkable regenerative ability. Is it not possible to construct a substitute bladder after the pelvic evisceration by utilizing this ability? For this purpose, the authors had to select a suitable tissue for bed on which the epithelium would develop. Bohne (1955) reported that the epithelium developed well on the connective tissue. Bohne (1957), Garret (1957), Tsuda and Narikawa (1958), however, found the hazardous point in the Bohne's method that the epithelium developed on the connective tissue was weak in resisting infection. What tissue is suitable for bed so that epithelium may regenerate and develop? The authors carried out a series of experiment on the theme. This report will describe the responce and behavior of the epithelium developed respectively on two kinds of tissue, granulation and muscle.

MATERIALS AND METHODS

In this experiment, 34 healthy mongrel dogs were used. They were divided into 2 groups by the operative technique.

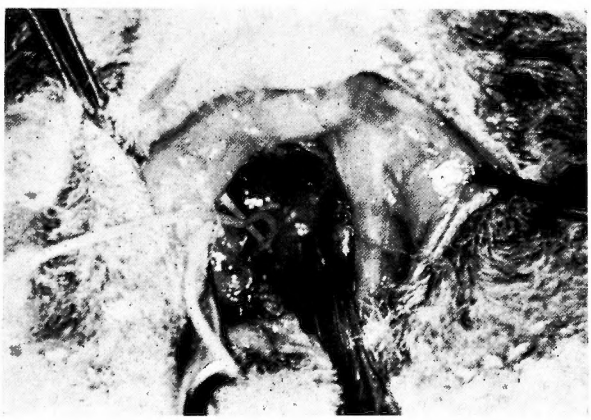


Fig. 1. A procedure of Group A. Postoperative view. A domeless bladder is placed in a perineal dead-space. Two ureteral catheters are noted.

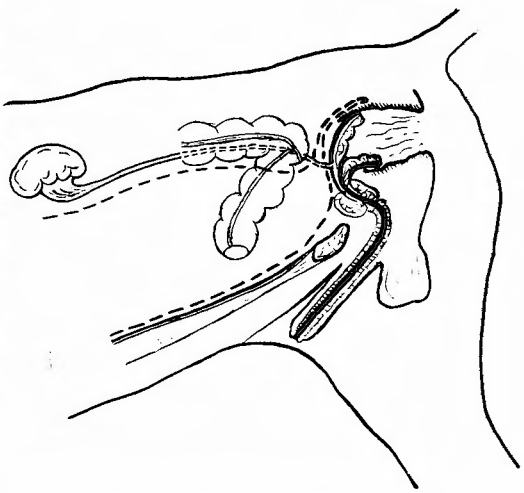


Fig. 2. A procedure of Group A. An illustrative sketch. An artificial anus is formed, and the terminal colon has been amputated. A domeless bladder is placed in a perineal dead-space.

Group A: Thirteen dogs were used in this group. They were anesthetized with Auropan-soda solution intravenously. The abdomen was opened and the dome of the bladder was removed surgically. Next, the terminal colon-sigmoideum, rectum and anus was amputated and removed by the abdominoperineal method. The stump of the bowel was exteriolized and fixed to the abdominal wall, as an artificial anus. The wall of the dead-space after the rectal amputation was covered with granulation. The residual bladder was reversed posteriorly and fixed on the granulation with fine silk. Then the abdomen was closed, the wound being left open in the perineum. Thus the bladder had been placed deep in the perineal wound. The ureters were left untouched and accordingly urine was temporarily collected in the bladder and then discharged through the perineal wound, not through the urethra (See, Figg. 1 & 2). Seven dogs in this group were incised on the perineum and a deep wound was formed at the prerectal region through the Douglas' space. The rectal amputation was not performed. The terminal colon remained free. Then the residual bladder was reversed posteriorly and fixed to the wall of the wound extraperitoneally which had been covered with the granulation. Urine was discharged through the wound (See, Fig. 3).

Table 1. Epithelial development on granulation tissue

Group	Number	Sex	Weight (kg)	Duration (Days)	External ureterostomy	External colostomy	Epithelial development	Cicatric shrinkage of the bladder-stump	Findings in the perineal wound	Cause of death
A	1	F	10.0	3	Yes	Yes	No	No	Filled with coagulated blood	Death from surgery
	2	M	9.0	5	Yes	Yes	No	Slight	Pus retention large in quantity; Insufficient suture	Peritonitis due to infection
	3	F	8.5	8	No	Yes	Slight	Moderate	Bladder-stump adhered closely to the granulation base	Pyelitis due to infection
	4	F	11.5	4	No	Yes	Moderate	No	Washy matter stagnated	Peritonitis due to infection
	5	F	8.5	5	No	Yes	No	Slight	Covered up with peel	Peritonitis due to perforation
	6	F	10.5	10	Yes	Yes	Moderate	Moderate	Bladder-stump adhered closely to the base	Pyonephrosis due to ascending infection
	7	F	8.5	3	Yes	No	No	No	Bladder-stump separated; No contamination	Death from surgery
	8	F	11.0	3	Yes	No	Slight	Slight	Partial insufficient suturing	Peritonitis due to perforation
	9	M	10.0	21	No	No	Slight	Severe	Bladder-stump adhered	Pyonephrosis due to ascending infection
	10	F	9.5	17	Yes	No	Slight	Severe	Marked contamination	Pyonephrosis due to ascending infection
	11	M	8.0	4	No	No	No	No	Pus retention, large in quantity; Bladder-stump separated	Peritonitis due to insufficient peritonealization
	12	M	12.5	6	No	No	Slight	Slight	Partial insufficient suturing	Peritonitis due to insufficient peritonealization
	13	F	9.0	7	No	No	Slight	Severe	Partial insufficient suturing	Peritonitis due to insufficient peritonealization

Table 2. Epithelial development on muscle

Group	Number	Sex	Weight (kg)	Duration (Days)	External ureterostomy	Epithelial development	Cicatric shrinkage	Change of the bladder capacity: Just after operation	Change of the bladder capacity: At autopsy	Cause of death	Complications	Remarks
B	14	M	12.0	50	Yes	Perfect	Slight	7	11	Sacrificing	Hydronephrosis due to obstruction on the r. ureteral orifice; Submucosal ossification	
	15	F	9.0	11	Yes	No	Slight	7	6	Peritonitis due to insufficient peritonealization	Pyelitis	
	16	F	10.5	2	Yes	No	Slight	6	5	Death from surgery		
	17	F	11.0	13	Yes	Moderate	No	8	8	Pyonephrosis due to ascending infection	Obstruction of the l. ureteral orifice	
	18	M	9.0	12	Yes	Moderate	No	5	7	Sacrificing	Neglisible ascending infection; Calcification on both ureteral orifices	
	19	F	8.5	3	Yes	No	No	6	4	Peritonitis due to insufficient peritonealization		
	20	M	10.0	10	Yes	Moderate	No	8	10	Pyonepherosis due to ascending infection		
	21	M	13.0	8	Yes	Slight	Moderate	8	8	Uremia from ureteral stenosis		
	22	M	12.0	18	No	No	Moderate	9	10	Phlegmone of abdominal wall due to urinary infection	Urinary leakage in abdominal wall	
	23	M	11.5	75	No	Perfect	No	9	30	Sacrificing	Submucosal ossification	
	24	F	9.0	19	No	Perfect	No	7	15	Sacrificing	Hematuria	
	25	M	10.0	8	No	No	No	8	10	Death from surgery		
	26	M	13.0	26	No	No	Severe	9	12	Peritonitis due to perforation	Urinary leakage in the abdominal cavity; Hydroureter	
	27	F	14.5	85	No	Perfect	No	6	35	Sacrificing	Submucosal ossification	
	28	M	9.0	20	No	Moderate	No	10	16	Sacrificing	Hydronephrosis	
	29	F	8.0	14	No	Moderate	Slight	7	7	Sacrificing		
	30	M	17.0	315	No	Perfect ?	No ?	8		Surviving		
	31	M	14.0	32	No	Perfect ?	No ?	9		Surviving	Pollakysuria	Escaped
	32	M	11.5	18	No	Perfect	Slight	8	14	Sacrificing	Inperfect incontinence	
	33	F	12.0	60	No	Perfect	No	5	22	Sacrificing	Pollakysuria submucosal ossification	Cystformation in muscle
	34	M	10.0	41	No	Perfect	Slight	7	18	Sacrificing	Hydronephrosis	

Group B: Twenty one dogs were used in this group. The dome of the bladder was resected. The rand of the residual bladder was sutured to the posterior sheath of abdominal rectus muscle. The defect of the bladder was capped with the muscle. Urinary discharge was through the normal way (See, Figg. 4 & 5). External ureterostomies were performed upon eight dogs in this group, thus the bladder being separated from the urinary passage (See, Fig. 6).

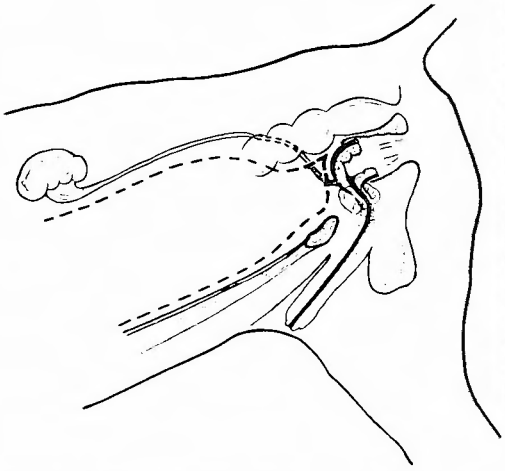


Fig. 3. A procedure of Group A. An illustrative sketch. A domeless bladder is placed in a prerectal space. Anus and ureters are free from surgery. Urine is discharged from the perineal wound.

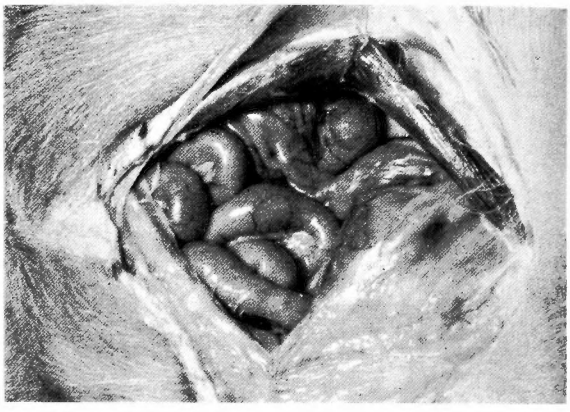


Fig. 4. A procedure of Group B. Findings by relaparotomy. Inside of the rectus muscle, an uroepithelial cyst is formed. Urine is discharged from normal way.

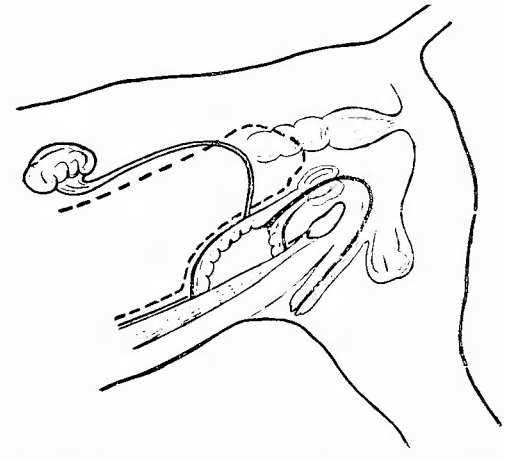


Fig. 5. A procedure of Group B. An illustrative sketch. A domeless bladder is capped with rectus muscle. Ureters have no surgery. Urine is discharged from normal way.

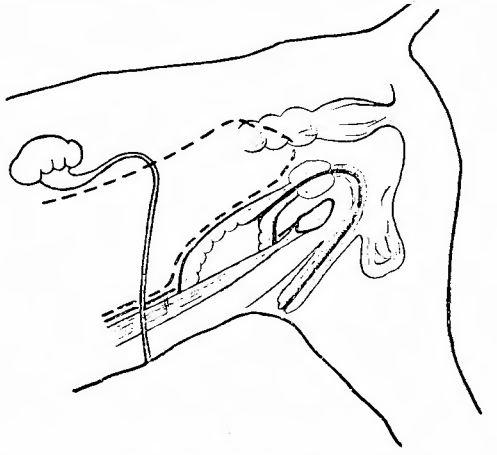
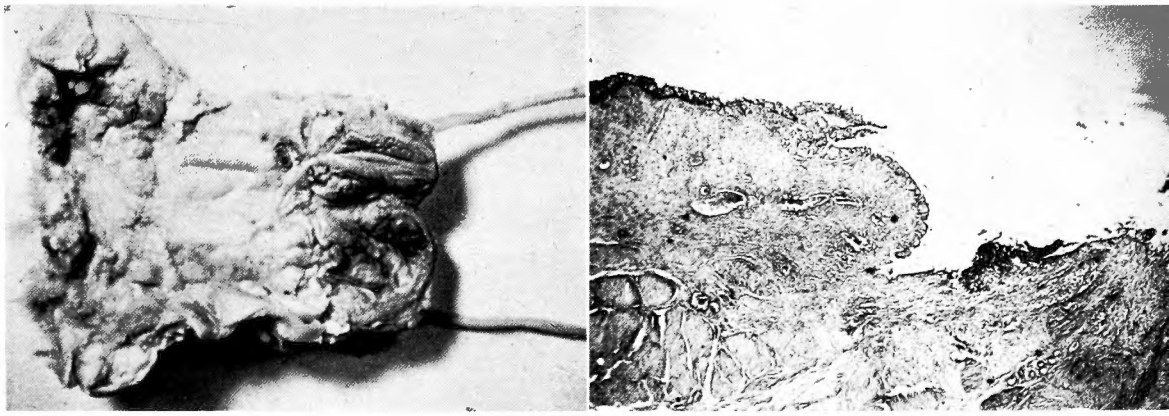


Fig. 6. A procedure of Group B. An illustrative sketch. A domeless bladder is capped with rectus muscle. Ureterostomies are performed.



Figg. 7 & 8. Macroscopic and microscopic findings of a case of Group A. Postoperative 21 days. Note undeveloped uroepithelium on the granulation.

Fig. 9

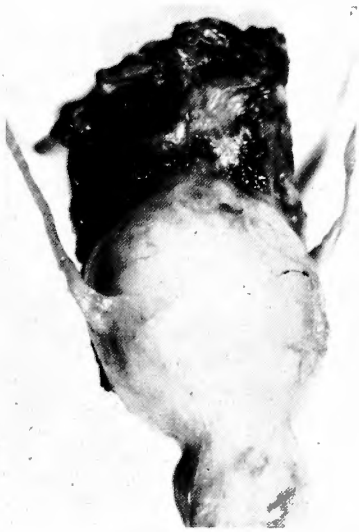


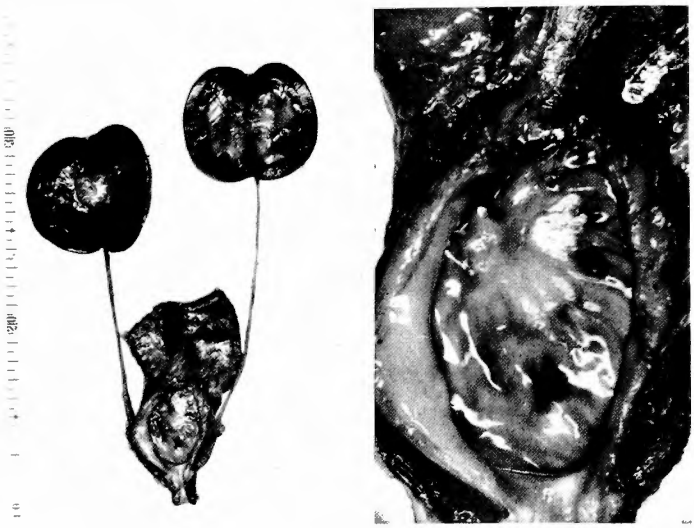
Fig. 10

Figg. 9, 10 & 11. Macroscopic findings of a muscle-capped bladder. Postoperative 75 days. The artificial bladder can collect urine sufficiently.

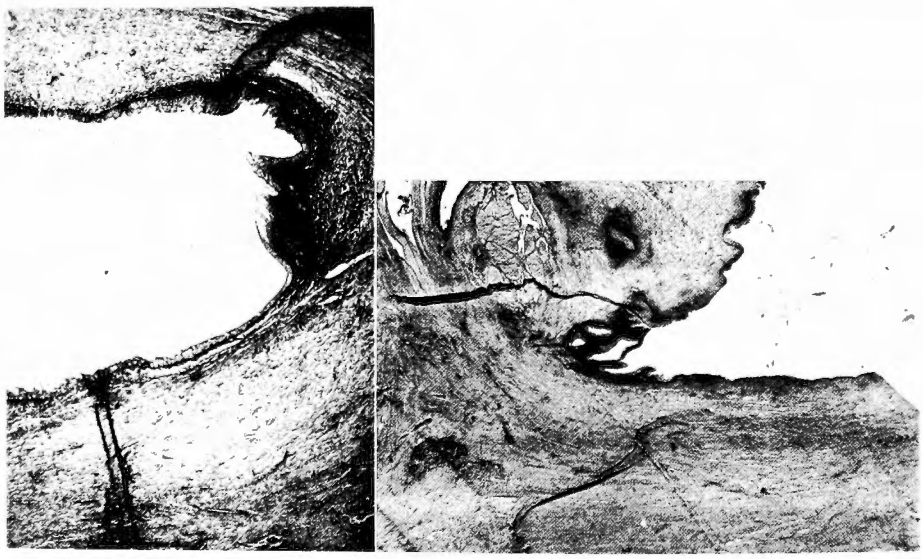
Every animal upon which the above mentioned procedure had been performed was carefully maintained for a period of 10 months and then examined by urograms, cystograms and cystometrograms. After they were dead or sacrificed, the entire bladder with its surrounding tissue was removed and sectioned.

RESULTS

The results are shown in Table 1 and 2. Animals in Group A had marked



Figg. 12 & 13. Macroscopic findings of a muscle-capped bladder. Postoperative 85 days. Note the remarkable development of the uroepithelium on the muscle.



Figg. 14 & 15. Microscopic findings of a muscle-capped bladder. Postoperative 85 days. Note the remarkable development of the uroepithelium on the muscle.

contamination by urine and feces, and many of them died from peritonitis or pyelitis. Furthermore, the development of their bladder epithelium was generally poor and in most cases the contact between the epithelium and the bed was lost (See, Figg. 7 & 8).

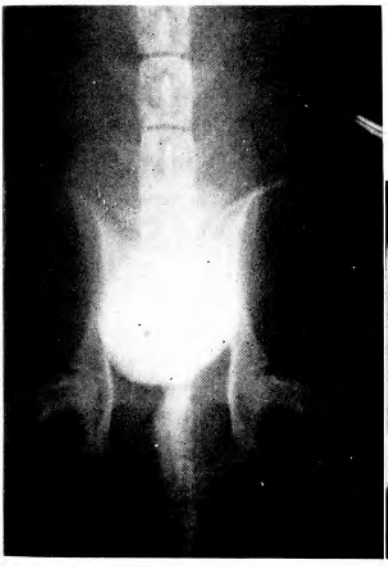


Fig. 16

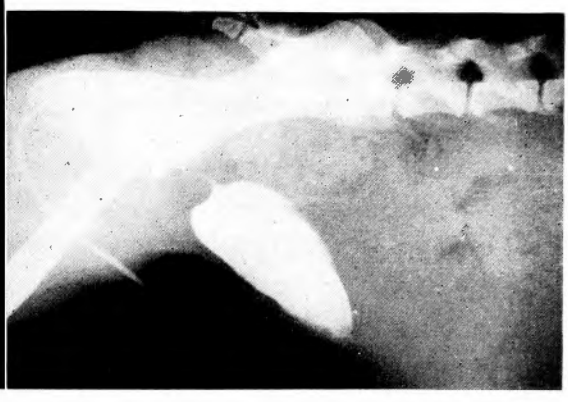
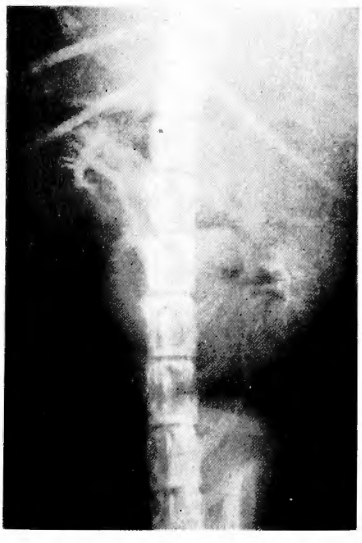


Fig. 17



Figg. 16, 17 & 18. Cystograms and excretory urogram in a muscle-capped bladder. Kidneys are not injuried. Note a giant urinary collector in rectus muscle.

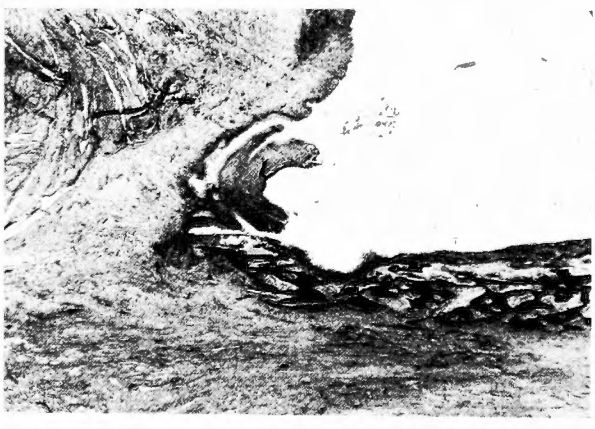


Fig. 19. Note the extraskeletal ossification in subepithelial layer. Postoperative 75 days. The uroepithelium develops smoothly.

Animals with external ureterostomy in Group B usually licked and bit the external fistulal orifice, which brought about the ascending infection and the disturbance of urinary passage, and finally, uremia. Accordingly, there were few sur-

vivals in these animals. The behavior of the bladder epithelium, however, was favorable for applying this method clinically.

Animals without external ureterostomy in Group B had an uneventful postoperative course. Urine was discharged regularly through the normal urethra. Infection did not affect the intraperitoneal cavity or the pelvis of the kidney. The bladder epithelium developed smoothly on the muscle. It needed two weeks to cover the defected area with the epithelium completely. There was no difference between newly formed and original bladder epithelium. Section showed that the epithelium had attached firmly on the rectus muscle. Cystograms showed no leakage of urine through the junction between the bladder and muscle, and showed contraction of the bladder wall. The capacity of the bladder appeared to have been increased by urinary collection. In the submucosal layer of newly formed mucosa, extraskeletal bone-formation was noted (See, Figg. 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 & 20).

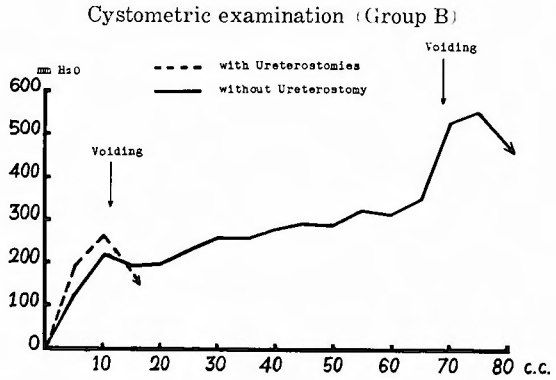


Fig. 20. Cystometric examination of a case of Group B. The curve shows normal way.

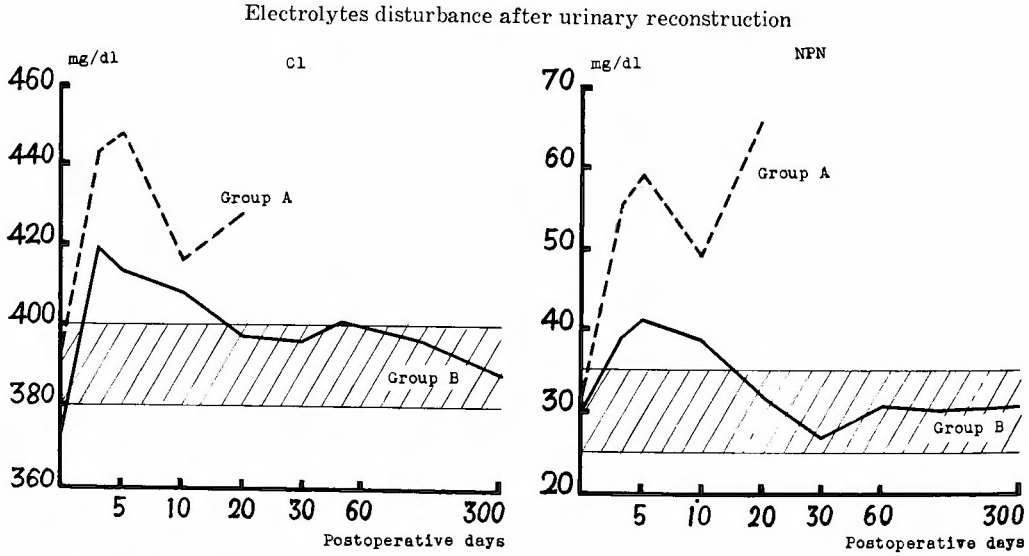


Fig. 21. Blood chemical pattern of both Groups. A case of Group B has a normal pattern.

DISCUSSION

The bladder epithelium could develop poorly on granulation tissue. It shows that the dead-space after the pelvic evisceration cannot be vesiculized into a kind of artificial bladder. It is, however, a notable finding that the bladder epithelium could develop favorably on muscle tissue.

It is the authors' hopeful expectation to have the epithelium develop and regenerate on the seromuscular graft of the intestine, which is possesed of a muscle layer, and the results acquired in this experiment seems to suggest its possibility. The seromuscular graft with the transitional epithelium will be used for an excellent artificial bladder. The bladder, thus made, will not reabsorb the elements of urine (See, Fig. 21). SHOEMAKER (1955) devised a technique utilizing an inverted seromuscular graft for the purpose of preventing the urinary reabsorption. The authors' idea may have the same effect and the more rational basis.

And then, the epithelium, when buried in the muscle, will form a cyst, which will work as a practical urinary collector when ureterostomy is performed upon it. This is also what the authors' results suggest.

These ideas may be used on the facts that there is a affinity between muscle and epithelium.

The teenhique the authors took in this experiment may not be applied to the practical case because the human bladder dose not move pendulumly. The authors feel, however, a great satisfaction in reporting their findings that epithelium can smoothly develop on muscle, and that it involves many problems valuable for the future development of this field.

CONCLUSION

1. The bladder epithelium regenerates and develops smoothly on a muscle tissue, and on the contrary, it shrinks on a granulation tissue.

2. The fact that there is some affinity between muscle and transitional epithelium will propose many ideas for urinary surgery.

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和文抄録

膀胱上皮の再生に関する研究

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（原稿受付 昭和33年12月19日）

人為膀胱には尿路上皮が必要である．私達は，尿路上皮そのものゝもつ再生能力を利用して人為膀胱をつくろうと試みた．ところが，再生という現象は，外科学において新しい分野に属し，多くの未開拓の疑問を含んでいた．その中でも，尿路上皮を移植するのに，如何なる組織を移植床とすれば，効果的に生着し，再生発展するかを決定しなければならなかつた．当教室の津田は，結合織を移植床とした研究を発表したのにつゞいて，我々は，肉芽ならびに筋肉を移植床とした場合の尿路上皮の態度について研究した．

その実験の結果，肉芽は，尿路上皮の移植床としては不適当であり，筋肉は完全に適合していることがわかつた．

筋肉内或は筋肉上を尿路上皮は好んで再生進展するという新しい事実は，尿路外科学に多くの独創的発想をもたらしうるので，注目に値する．