

URETERIC INTUSSUSCEPTION AS ANTI-REFLUX TECHNIQUE IN DILATED URETER IN DOGS

By

Morsy, A.A., * Seif, M.M.; **Shamaa, A.A. and ***Shalaby, A.A.

Urology Dept, Fac. of Med, Cairo University

*Surgery, anesthesiology and radiology Dept Fac. Vet. Med., Beni-Suef. **Surgery,
anesthesiology and radiology Dept Fac. Vet. Med., Cairo University

***Pathology Dept, Fac. Vet. Med., Beni-Suef.

ABSTRACT

Seven apparently healthy male adult mongrel dogs, were used in this study. The safety and efficacy of a ureteric intussusception in dilated ureter as anti-reflux technique was studied. The technique was evaluated using radiological and histopathological investigation. The results have shown the success of the technique as anti-reflux technique in dilated ureters.

INTRODUCTION

Vesicoureteral reflux (VUR) is a urologic condition in which there is a retrograde flow of urine from the bladder through the ureter back up to the kidney. The condition may be classified as primary or secondary phenomenon. Primary VUR occurs without detectable anatomic abnormalities of the vesicoureteral junction and often is transient during the patient growth. Secondary VUR has been related to bacterial urinary tract infection, congenital anomalies of the distal part of the urinary tract and neurogenic disorders of the urinary bladder (*Daniel et al 1984, and Ellsworth et al, 2000*).

Reflux by itself is not a serious clinical entity but it is potentially hazardous. uncomplicated reflux results in dilatation of ureteral lumen and hypertrophy of the ureteral smooth muscle, but if the urine is contaminated with bacteria, repeated episodes of pyelonephritis can occur (*Christie 1973*).

Great efforts were done by surgeons and many surgical techniques were performed in the management of vesico-ureteric reflux to overcome this perplexing problem. The result of the surgical management was accepted in low grades reflux, but unfortunately, the success was not satisfactory in refluxing dilated ureter, especially in cases of recurrent uretero-vesical surgery (*Aragona et al, 1997*).

Most surgical techniques described in the management of vesico-ureteric reflux depend on performing a new uretero-vesical junction, either intra- or extra-vesical, with long sub-mucosal tunnel and a good posterior detrusor support for the sub-mucosal ureter. So, it is difficult to be performed in dilated ureters and unhealthy bladders (*Michael and Alan, 1990*).

In 1957 *Grey et al* published a method described as ureter intussusception in which the vesicoureteral stricture that induce vesicoureteral reflux is replaced by ureteral intussusception nipple valve at the distal ureter to prevent vesicoureteral reflux. This technique could be used only for dilated ureter due to its technical difficulties. Only one case between four treated cases showed no Vesico-ureteric reflux for a short time.

A series of intussusception on non-dilated ureters in dogs with good results were achieved. A study performed by *Ruedi et al (1976)* showed that an invagination is technically possible and that reflux can be prevented in half the cases without significant obstruction of the urinary flow. Another study reported by *Moller et al, (1981)* who formed a valve in distal direction by means of invagination without opening the urinary tract in 15 undilated ureters in dog. After 3 months their function as an anti-reflux valve was checked. The result was good in 9 cases, a stenosis of the invagination appeared in 4 cases and no anti-reflux effect was existing owing to extussusception in 2 cases.)

The aim of this study is to assess the efficacy and safety of ureteric intussusception in dilated refluxing ureter as anti-reflux technique.

MATERIALS AND METHODS

1-Experimental animals

Seven apparently healthy adult mongrel dogs 5 males and 2 females were used in this study. Their ages ranged from 1 - 2 years and their weight from 15-25 kg. The animals were kept in separate kennels and put under observations and examination, one week before the experiment. The urinary system proved to be normal according to radiological examination.

2-Surgical intervention:

The animals were prepared for aseptic surgery as usual. They were premedicated with atropine sulfate in a dose of 0.04mg/kg subcutaneous and promazine HCl in a dose of 2-3mg/kg intra-muscular. Anaesthesia was induced and maintained by intravenous injection of sodium thiopental in a dose of 20-30mg/kg. 2.5%.

a-Surgical induction of dilated ureter:

All dogs were subjected to left unilateral ureteral obstruction. A left prepubic paramedian laparotomy incision was made in males and median laparotomy in females (5 - 7 cm long) just cranial to the pubic symphysis. The left ureter exposed and ligated using vicryl 2/0 distally close to the wall of the bladder for induction of dilated ureter (Fig.1). The abdominal muscles were closed in layers with interrupted 0 vicryl sutures, and skin closed with interrupted 0 silk sutures. Penicillin/streptomycin were injected intra-muscular for three days in a dose of 10000 IU/kg and 10 mg /kg respectively.

b-Construction of ureteric intussusception:

After one week ,the dogs were relaparatomised as mentioned before. The dilated left ureter dissected from its mesentery for 5 cm above the bladder, and cut close to the wall of the bladder. A longitudinal ureterotomy 2cm in length was done on the ventral surface of the dissected part of the lower ureter. The inner surface of the ureter was grasped by a Babcock clamp 2 cm above the cephalic angle of the ureterotomy and pulled caudally with gentle and continuous traction to make intussusception in the ureter. The length of the intussusception was about 1.5cm. The exposed stripe of the muscularis of the invaginated ureter on one side sewn together with 2 interrupted sutures vicryl 3/0 in a longitudinal manner . The 2 walls of the base of intussusception fixed together with 4 to 5 interrupted 3/0 vicryl sutures all around its circumference to secure the intussusception and prevent extussusception (Fig.2&3). A ureteric catheter size (3) was left in the ureter and passed through the bladder and urethra to the outside. the ureteric catheter left in situ fore seven days then removed by gentle pulling to outside the body. The ureterotomy was closed with watertight interrupted 3/0 vicryl sutures. The anti-reflux mechanism of the ureteral valve was tested by retrograde infusion of normal saline through the ureter (Fig 4). A simple ureterovesical re-implantation was performed. the ureter pulled into the bladder and an end to side mucosa to mucosa anastomosis was done with interrupted sutures 3/0 vicryl. The outer surface of the ureter was fixed to the outer surface of the bladder with 4 to 5 interrupted sutures 2/0 vicryl. The abdominal incision was closed in routine manner.

3-Radiographic examination:

Either Plain x-ray of urinary tract, ascending cystography and intravenous pyelography were performed to approve the induction of ureteral dilatation and for evaluation the performance of ureteral anti-reflux valve. Radiographs are taken with the animals in supine position and the right and left lateral projections. The contrast medium used in all examinations was sodium diatrizoate (76 % concentration) diluted to about 20%.

This was prepared by adding the contents of a 20 ml ampoule of the contrast material to 50 ml sterile saline. Radiographs were taken at potential of 65Kvp, 25 mAs and 100cm ffs.

a) Plain x-ray of urinary tract (P.U.T.):

It was performed to show soft tissue shadow of the kidney in the urinary tract

b) Retrograde Ascending urethro-cystography technique :

Retrograde cystography involves the insertion of a catheter into the bladder through, after a preliminary radiograph of the abdomen has been obtained; the bladder is filled with a radiopaque solution. The instillation was accomplished through a 6 ch. Folley's Catheter. Using infusion set connected to the bottle contain the diluted dye, the bladder was filled slowly, usually 50 – 60 cc sufficient. The catheter was then closed by clamp. Ambulation was allowed and after the lapse of 15 – 30 minutes, x-ray film taken.

c) Excretory urography (I.V.U.):

Radiographic films were taken at 5, 15 and 20 minutes after completion of the injection of contrast material. The technique was performed before the surgical interference and at intervals of one, 2, 4 and 6 weeks postoperatively to control function of the kidney and anti-reflux effect of the valve by normograde and ascending cystogram.

d) After euthanasia, the kidney ureter and bladder were taken and made ascending cystogram with contrast substance for detection the function of the valve.

4-Histopathological investigation:

The animals were euthanatized for histopathological study at six weeks after ureteral intussusception. Tissue samples were collected from ureters of all dogs. A longitudinal sections from the operated ureters were carried out. Tissue specimens were fixed in Formalin 10%, dehydrated, cleared and embedded in paraffin. Sections of 5-6 microns were stained with hematoxylin and eosin according to *Bancroft and Stevens (1996)*.

RESULTS

A) Surgical outcome :

There was no post-operative leakage, wound infection or surgical complications in all patients. The reflux was overcome by intussusception in 5 animals. In 2 cases, the reflux was still present due to extussusception .

B) Radiographic findings:

Urographic examination of the animals pre-surgery revealed that both kidneys were bean shaped with smooth and regular margins. The medial border of both kidneys appeared straight with a depression in its center, the hilus. The hilus leads to the renal sinus that enclosed the renal pelvis that become clearly evident when filled with the contrast materials. The renal pelvis was demonstrated as a radiopaque crescent in the radiolucently appearing kidney sinus. It was narrowed toward the both poles of the kidney. On the medullary margin of the pelvis there were 10-12 pelvic recesses or diverticulae, which were indented by the renal papillae (Figure 5).

One week after ligation the Intravenous pyelography revealed unilateral increase in the size of the kidney of the ligated ureter without opacification of the renal pelvis and ureter (Fig.6). Four to six weeks after ureteral reconstruction, the kidney begin to regain its size and function and appeared approximately normal. Also It showed a patent ureter and absence of leakage from the ureterotomy (Fig. 7&8).

Follow-up ascending cystogram performed at 2, 4 and 6 weeks post-operative showed no dye above the intussusception in 5 cases (71.4 %) (Fig.9), and reflux in 2 cases (28.6 %). The later two cases showed hydro-nephrosis and the ureter was dilated down to the lower end (Fig.10).

c) Histopathological findings

Grossly, both kidneys were of the same size and color. On cut section, the renal pelvis of the involved kidney was slightly distended. The ligated ureters showed minimal hydroureter distal to intussuscepted ureteral valve.

Histopathological examination of the operated ureter revealed that, The basal layer of the transitional epithelium was intact and no desquamation or exfoliation were observed along the length of the operated portion of the ureter. In one case, the mucosa which consisted of a transitional epithelium, (Fig. 11) showed hyperplastic proliferate activity (Fig. 12). In the ureteral lumens, at the site of operation, the mucosa was protruded forming a fold-like lesion (Fig. 13). In the hyperplastic tissue intraepithelial vacuolation were observed (Fig.14).

At the proximal end, remnants of suture materials were observed (Fig. 15) surrounded by mild leukocytic infiltration mainly neutrophiles (Fig. 16). The submucosal connective tissue, both at the proximal and distal ends of suturing showed no inflammatory reaction with no hemorrhages or edema. The surrounding muscle layer showed mild hypertrophy. The lumen of the ureter was patent and free from exudates. In one case, apart

from the pathway of the ureter in the distal portion there was massive leukocytic infiltration.

DISCUSSION

Vesico-ureteral reflux is one of the most common problems encountered by urologists. It is also one of the most perplexing. Although the surgical solutions to reflux have withstood scrutiny for years, the success was not optimal and efforts were spent to overcome this problem. The presence of reflux places the kidney at risk to deleterious effects from urinary tract infections and increased intra-renal pressure resulting from high intra-vesical pressure during filling and voiding phases of micturition. So, judicious operative intervention is required to correct vesico-ureteral reflux in those patients with severe derangement of the uretero-vesical junction or intractable recurrent urinary tract infection.

Many procedures were performed to correct the incompetent uretero-vesical junction but, unfortunately, the success was not optimal and still, the surgical correction of reflux is a problem especially in those who have had previous uretero-vesical surgery and those with refluxing dilated ureters. In such cases, technical operative difficulties were the most frequent reason for continued reflux due to failure to create an adequate length of sub-mucosal tunnel. All operative techniques described in the management of reflux depend on performing a new uretero-vesical junction either intra-vesical or extra-vesical with long submucosal tunnel supported with good posterior detrusor support for the sub-mucosal ureter. So, it is more difficult in dilated refluxing ureters than in non dilated refluxing ureters and it may need modeling or tailoring of the dilated lower part of it (*Fujisawa et al ,2000 ,Shioji et al, 2002 , Fumi et al 2004 and Benjamin et al 2006*).

Most megaureters that require surgical correction due to obstruction will also require some form of revision to reduce their diameters and ensure successful ureteroneocystostomy. Most urologist agree that total ureteral reconstructions are rarely necessary for even the most tortuous and dilated megaureters. revising the distal segment provides the solution for nearly every system. Surgical correction should accomplish three goals regardless of the techniques preferred by the surgeon. They are (1) excision of the abnormal distal ureteral segment that has caused the obstruction; (2) reimplantation of the affected ureter with the appropriate submucosal tunnel length- to-ureteral lumen width ratio (four or five to one)necessary to prevent reflux; and (3) remodeling of the affected ureter to a width that allows that desired reimplantion ratio to be achieved (*Michael and Alan,1990*).

Intussusception of an intestinal segment as anti-reflux technique is used in urinary intestinal diversion and it is successful in preventing reflux (Kock *et al*, 1982; Skinner *et al*, 1989). Accordingly, the idea of making ureteric intussusception in dilated ureters as anti-reflux valve, especially in recurrent patients with strictured ureters accompanied with bilharzial bladder wall came to our mind.

Vesico-ureteric reflux can be prevented by a ureteric nipple alone, provided the nipple is at least 1.5 cm long. This eliminates the need for an oblique ureteric entry or a submucosal tunnel in the re-implantation of a ureter into the bladder. Longer nipples may be used although they may lead to difficulties with catheterization. Reduction in the length of the nipple frequently occurs later. They conclude accordingly a relation between nipple length to internal dimension of at least 2:1 (Urquhart-Hay *et al*, 1977).

Failure of Grey *et al.*, (1957) regarding ureteral intussusception can be concluded because the author gave no technical details. In contrast the results of Ruedi *et al.*, (1976) correlated well with our results including the effect of intussusception on the flow of urine. They controlled with by contra-lateral nephrectomy and regular estimation of urea and creatine in serum, methods that were partially comparable to X-ray. Moller, *et al.*, (1981) tried on ureteric intussusception in dogs in non dilated ureters. He performed the ureteric invagination externally in closed ureter without slitting it opened. In 9 cases out of 15 (60%) the reflux was prevented, in 4 cases there was stenosis and in 2 cases there was reflux.

The voiding cystourethrogram remain the gold standard for the detection and grading of vesicoureteral reflux. It may be concluded that the voiding cystourethrogram is more predictive of cessation of vesicoureteric reflux than endoscopic examination (Mark, 1985).

Reflux may be suspected from the appearance of the kidneys and ureters on intravenous urography. In particular, a dilated lower ureter, a ureter visible for its entire length, ureteral or pelvic striations from redundant mucosa, hydro-nephrosis, calyceal distortion, and renal scarring may be clues to the presence of vesicoureteral reflux or its existence in the past. A normal intravenous urography does not rule out reflux. However, retrograde cystography remains the most sensitive and accurate study to detect or exclude reflux (Bisset *et al* 1987 and Lavine *et al* 2001).

To evaluate the performance of ureteral antireflux valve retrograde cystography is performed prior to intravenous

pyelography in order to avoid confusion about the source of contrast material in the upper tracts. Follow-up by intra-venous contrast substance and ascending cystography for six weeks post-operatively revealed that the valve was competent in 71% of cases and there was no stenosis, sloughing or leakage in the valve technique. These results was better than results of *Moller et al,(1981)* where 9/15 dogs (60%) had competent valve, 26.7% had stenosis of the intussusception and 13.3% showed reflux.

Early in its use detussusception of the nipple was recognized as a common complication, Dislocation in 2 cases of our materials recognized by invagination that was fixed by sutures lead to the conclusion that 4 stitches were not sufficient for fixation. Only one of the dogs, which showed extussusception of the nipple valve, demonstrated the reflux (*Tsukamoto, 1996 and Friedman et al ,1992*).

It is safe and efficient to eliminate postoperative VUR in most patients who had a simple ureteral reimplantation for reflux (*Lavine et al,2001*).It was concluded that anti-reflux procedures offered no advantage over non-anti-reflux ureteric re-implantation in adults (*Stefanovic et al 1991 and Kiyokawa et al,1999*) this was in agreement with the present results.

The cause of massive leukocytic infiltration Apart from the pathway of the ureter in the distal portion was explained by *Malek et al (1983)* who reported that the ureteral re-implantation decreased the incidence of pyelonephritis ,but had no influence on lower tract infections.

Fortunately, the dilatory response of the upper ureter itself dose not seem to be an irreversible one for most obstructed megaureter .muscular hypertrophy and hyperplasia with maintenance of muscle cellular integrity usually occur after alleviation of distal obstruction, functional recovery of the affected ureter can be predicted in most instances (*Michael and Alan,1990*).This agreed with our results.

The advantages of this technique over the other ureteral remodeling techniques, includes; ease of performance, no need for extended ureteral stenting, reduction of the functional ureteral lumen at the site of valve without disruption of the ureteral integrity, preservation of the ureteral intrinsic vasculature, and no need for submucosal tunnel ureterocystostomy reimplantation.

REFERENCES

- Aragona F, D'Urso L, Scremin E, et al (1997): Polytetrafluoroethylene giant granuloma and adenopathy: Long term complications following subureteral polytetrafluoroethylene injection for the treatment of vesicoureteral reflux in children. *J.Urol.,158:1539*

- Bancroft, J.D. and Stevens, A. (1996): Theory and Practice of Histological Technique. Churchill liveingstone, New York.
- Benjamin I.C., Karim, J.H., Leonard, N.Z., and John, A.L. (2006) The Use of Bowel for Ureteral Replacement for Complex Ureteral Reconstruction *The Journal of Urology, Volume 175, Issue 1, Pages 179-183*
- Bisset GS, Strife JL and Dunbar JS (1987): Urography and voiding cystourethrography: Findings in girls with urinary tract infection. *A.J.R., 148:479, 1987.*
- Christie B.A. (1973) Vesicoureteral reflux in dogs *J.A.V.M.A., vol.162, no.9*
- Daniel A.F., Gary R.J., Carl A.O., and Michael J. T. (1984): Maximum distention retrograd urethrocytography in healthy male dogs : occurrence of vesicoureteral reflux. *Am J. Vet. Res., vol 45, No.5*
- Ellsworth PI, Cendron M, McCullough MF (2000): Surgical management of vesicoureteral reflux. *AORN J. 2000 Mar;71(3):498-505, 508-13; quiz 517-20, 523-4.*
- Friedman RM, Flashner SC, King LR (1992): Effectiveness of a handsewn nipple valve for reflux prevention in bladder reconstruction. *J Urol. Feb;147(2):441-3.*
- Fujisawa M., Isotani S, Ishimura T, Yamanaka K., Arakawa S and Kamidono S (2000): A novel antireflux uretero-ileal anastomosis for urinary diversion: an experimental study *BJU International Volume 86 Page 1064 - December 2000*
- Fumi M., Akira T. and Kenji S. (2004): Effect of ureteral reimplantation on prevention of urinary tract infection and renal growth in infants with primary vesicoureteral reflux *International Journal of Urology Volume 11 Page 1065*
- Grey DN, Flynn P, and Goodween EW. (1957); Experimental methods of ureteroneocystostomy: experiences with the ureteral intussusception to produce a nipple or valve. *J Urol. Feb;77(2):154-63*
- Kiyokawa H, Igawa Y, Muraishi O, Tamai C, Nishizawa O. (1999): Simple anti-reflux uretero-ileal anastomosis: an experimental study in dogs. *J Urol. Sep;162(3 Pt 1):902-4.*
- Kock NG, Nilson AE, Norlen LJ and Philipson BM (1982): Urinary diversion via a continent ileal reservoir: clinical results in 12 patients. *J. Urol., 128:469.*
- Lavine MA, Siddiq FM, Cahn DJ, Caesar RE, Koyle MA, Caldamone AA (2001): Vesicoureteral reflux after ureteroneocystostomy: indications for postoperative voiding cystography. *Tech Urol. 2001 Mar;7(1):50-4.*
- Malek ,R.S., Svensson, J.P., and Torres, V.E. (1983): Vesicoureteral reflux in the adult: III Surgical correction : Risks and benefits *J. urol., 130:882-886.*
- Mark F B (1985): The management of vesicouretric reflux *Urologic clinic of north America- Vol.12, No.1*
- Michael, A.K. and Alan, B.R. (1990): Management of the dilated obstructed ureter. *Urologic clinics of North America- vol.17, NO.2.*
- Moller A, Schneider HJ. (1981): Ureteral intussusception - a practicable anti-reflux method *Z Exp Chir. 1981;14(3):118-23*
- Ruedi P, Geroulanos S, Leisinger HJ. (1976): Prevention of reflux by a ureteric intussusception valve: a preliminary study on dogs. *Eur Urol.;2(6):289-92.*
- Shioji Y, Muraishi O, Nishizawa S, Tokue A. (2002): De-serosalized muscle layer covering method for antireflux ureteroileostomy: a new operative technique and pressure study with ureterometry at the ureteroileal anastomotic site in dogs. *J Urol. 2002 Jul;168(1):285-8.*
- Skinner DG, Lieskovsky G and Boyd S (1989): Continent urinary diversion *J. Urol., 141:1323.*
- Stefanovic KB, Bukurov NS, Marinkovic JM. (1991): Non-antireflux versus antireflux ureteroneocystostomy in adults. *Br J Urol. Mar;67(3):263-6.*
- Tsukamoto T. (1996): Non-refluxing ileal ureter replacement using intussuscepted nipple valve--an experimental study in dogs. *Hinyokika Kyo. J Apr;42(4):289-94*
- Urquhart-Hay D, McIlwaine J, and Stephenson CB. (1977): The use of a ureteric nipple alone for reflux prevention *Br J Urol. Oct;49(5):375-7.*

LEGENDS

U= Ureter V= Valve C= Catheter B= Bladder
PU= Proximal ureter DU= Distal ureter
RK= Right kidney LK= Left kidney
RU= Right ureter LU= Left ureter

Fig (1): Dilated ureter before intussusception (U)

Fig (2): Intussuscepted ureter forming a nipple valve.

Fig (3): External fixation of the valve.

Fig (4): Testing of the anti-reflux mechanism of ureteral valve

Fig (5): Excretory ventrodorsal urogram showing normal two kidneys, and ureters before surgery.

Fig (6): Excretory ventrodorsal urogram showing hydronephrotic kidney after one week of ureteral ligation

Fig (7): Excretory ventrodorsal urogram showing kidney after four weeks of relief of ureteral ligation

Fig (8): Excretory ventrodorsal urogram showing kidney after six weeks of relief of ureteral ligation

Fig (9): Post-operative ascending Cystogram .

Fig (10): Ascending Cystogram in extussuscepted ureter.

Fig (11): Showed normal ureteral mucosa (H&E X)

Fig (12): Showed hyperplasia and of the transitional epithelial mucosa (H&E X)

Fig (13): Showed intraepithelial vacuolation of the mucosa. (H&E X)

Fig (14): Showed protrusion of a fold-like lesion in the uretral lumen. (H&E X)

Fig (15): Showed remnants of suturing materials with a minimal leuckoctic infiltration (H&E X)

Fig (16): Showed mild leuckocytic infiltration (H&E X)



Figure (11)

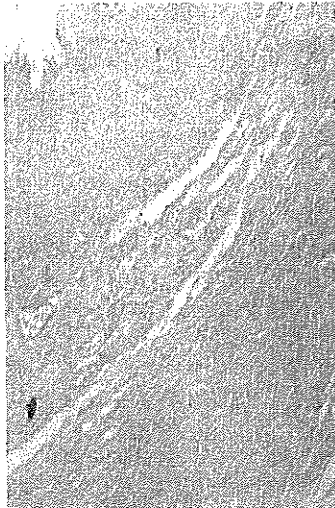


Figure (12)



Figure (13)

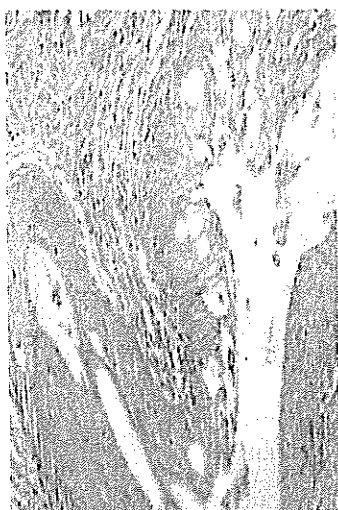


Figure (14)



Figure (15)

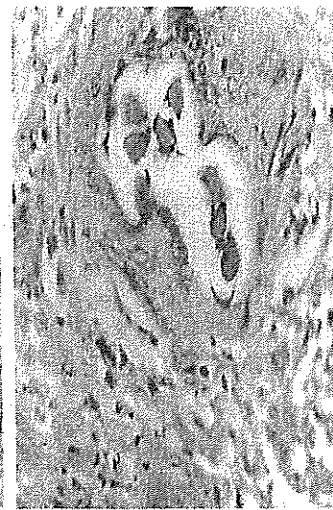


Figure (16)

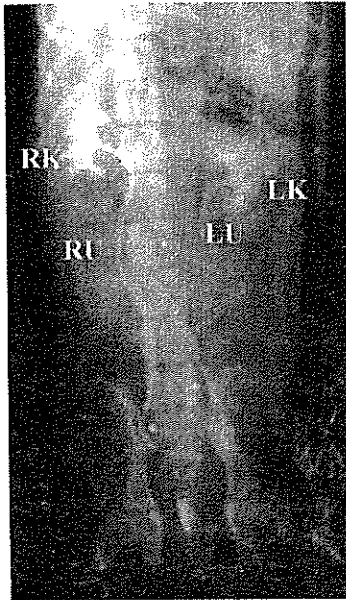


Figure (5)

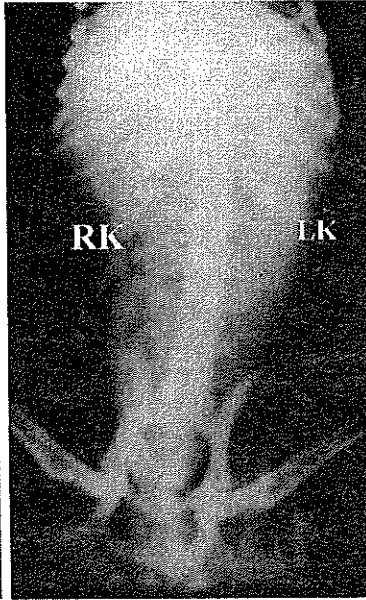


Figure (6)

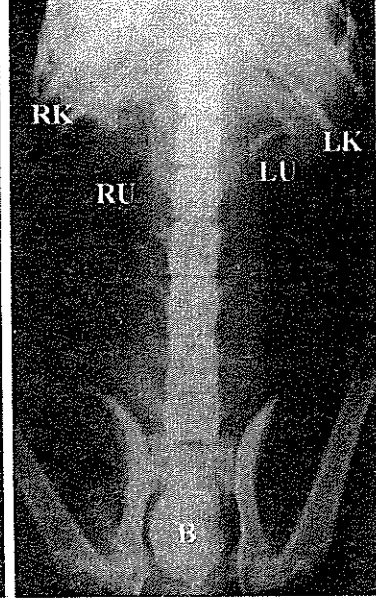


Figure (7)

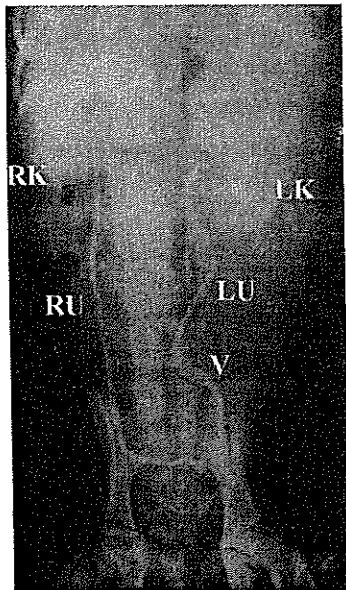


Figure (8)

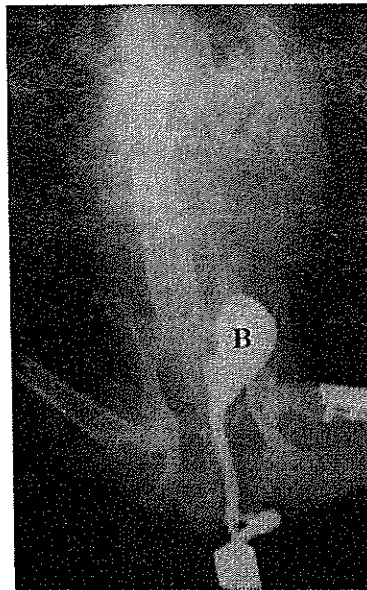


Figure (9)

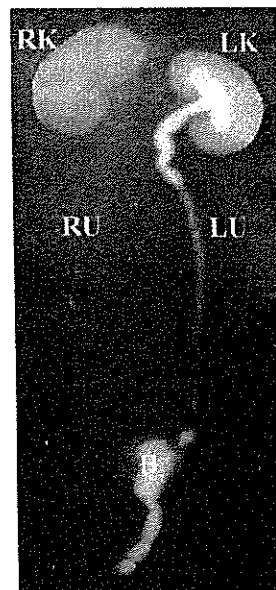


Figure (10)



Figure (1)

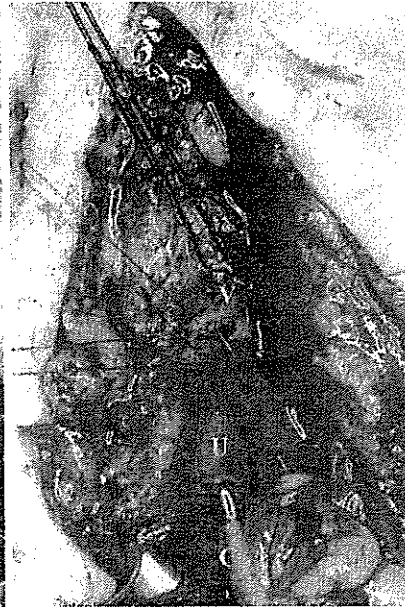


Figure (2)

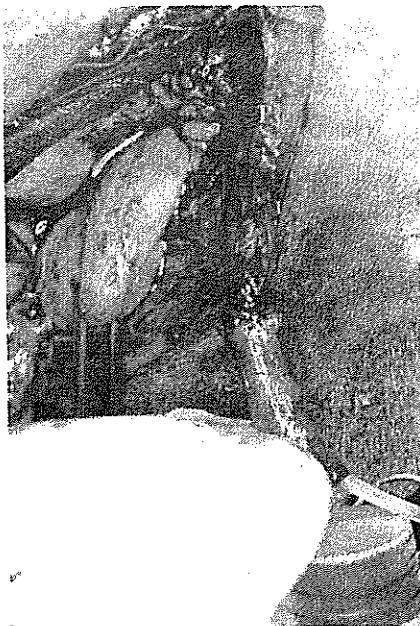


Figure (3)



Figure (4)