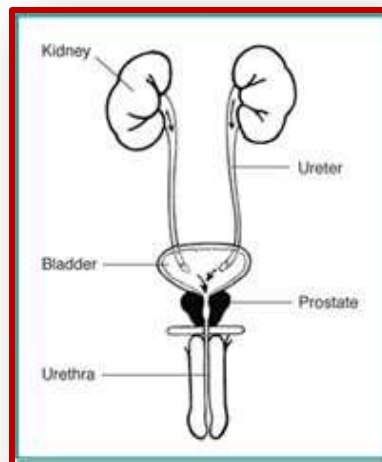


Vesicoureteral reflux & congenital abnormalities of the urological tract

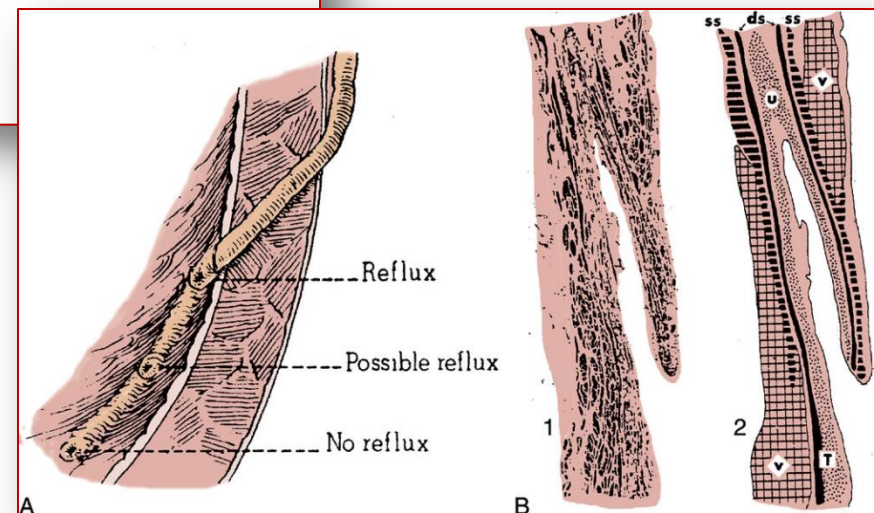
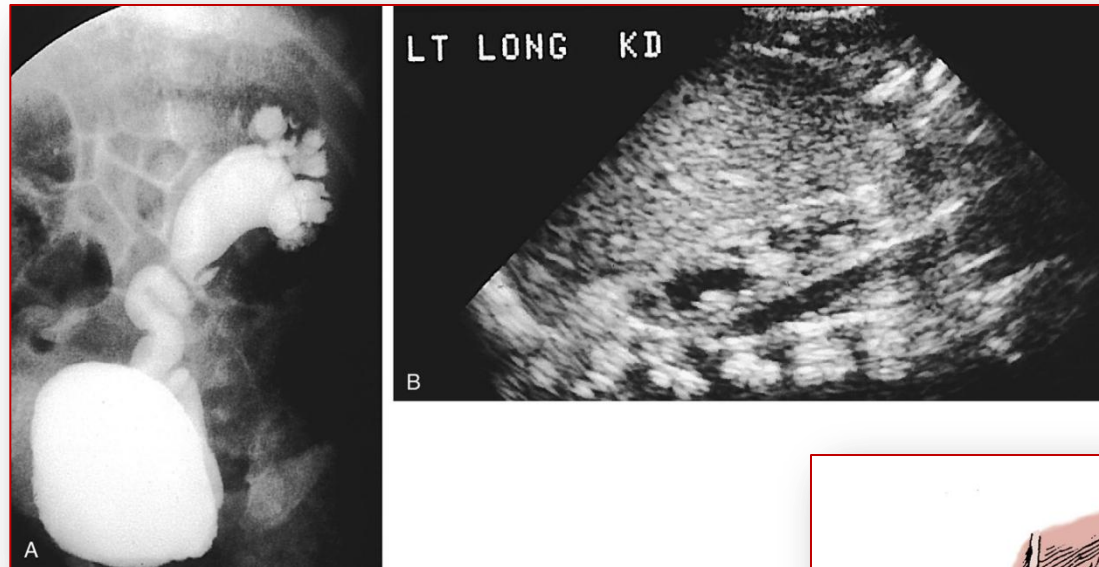
Introduction

Urology is a field that covers the surgical management of diseases of urological tract and the male external genitalia. The urological tract consists of the upper tracts which are the kidneys and ureters, the middle urological tract which is the bladder and lower urinary tract which is the urethra distally to the bladder neck, and the male includes the prostate.



Vesicoureteral reflux

Vesicoureteral reflux (VUR) represents the retrograde flow of urine from the bladder to the upper urinary tract.



This is a condition that has been long known to man already in the first century AD Galen referred to the valve mechanism between the ureters and the bladder as a unidirectional flow. This was also shown in sketches made by da Vinci in the middle ages. It was however only in the 20th century that it was realized that it is not nearly a anatomical curiosity but that vesicoureteral reflux could be associated with diseases.



Vesicoureteral reflux can often be asymptomatic, but in specific and certain instances the backflow of the urine into the kidneys can cause pyelonephritic scarring, urinary tract infections and progressive kidney disease and deterioration. It is a nebulous condition and all the answers to it's riddle are not known but as it is such a common condition, often found in children with urinary tract infections, it is an important disease entity to take note of.

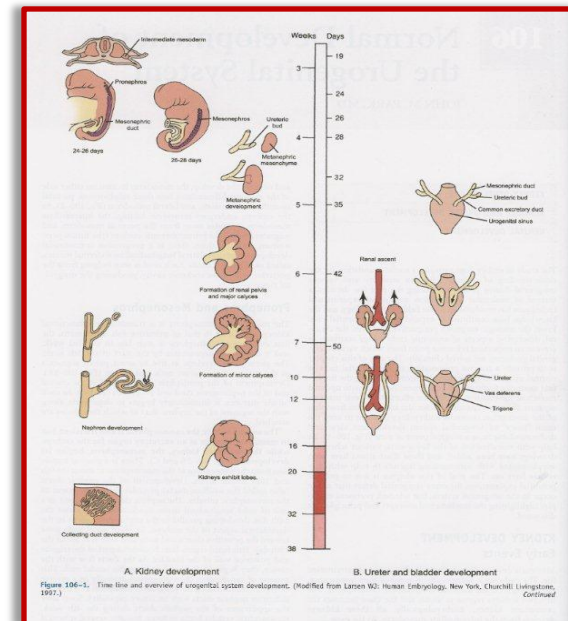
***A urinary tract infection* implies an infection of the upper and middle tract of the urinary system, i.e. *actively dividing bacterial organisms in the urological tract above the internal sphincter of the bladder.* That is why it is important to document this infection by a properly collected urine specimen, i.e. a Midstream, catheter specimen or suprapubic aspiration.**

Vesicoureteral reflux is an important associated condition with urinary tract infections especially in children and up to 70% of infants with UTI can have reflux. Reflux is more common in male infants with UTI's (approximately 75%), but in older children the majority of reflux cases, up to 85%, are in females. It is much more common in caucasians, and black infants have a 10 times lower incidence of reflux.

There is a genetic association, and the children of patient's with reflux themselves have a higher incidence with an autosomal dominant pattern of inheritance. Probably many genes are involved but the clinical evidence is undisputed.

Embriology

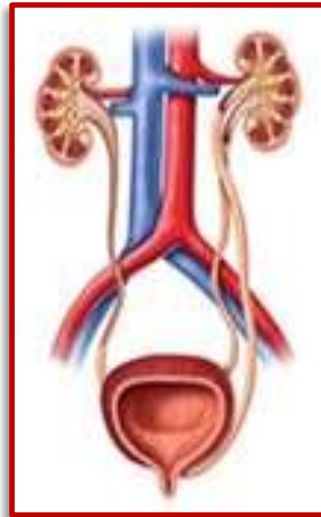
At 4 weeks gestation an outpouching arises from the distal mesonephric duct. This is the ureteric bud and it interacts with a primitive mesenchyme that is the metanephric blastema. This interaction results with the ureteric buds branch and developing into the calyces, renal pelvis and ureter. The metanephric blastema is induced to form all elements of the nephron including the collecting duct and the distal convoluted tube, loop of Henle, proximal convoluted tubuli and the glomerulus.



The segment of the mesonephric duct distal to the ureteric bud is the common excretory duct. The rest of the mesonephric duct proximal to the bud develops into the epididymis, vas deferens, seminal vesicals and the prostate in the male and into epoophoron, oophoron and Gartner's duct in the female.

It is important to realize that the common excretory duct is absorbed into the developing bladder and first enters the bladder in the distal position and then migrates cranially. Due to this cranial migration it is obvious that if the ureteric bud arises too distally on the mesonephric duct it will migrate to an abnormal cranial and lateral position while if it arises too proximal it does not migrate all the way into its correct position in the bladder and can end up too distally.

The cranial and lateral position causes an abnormal functioning valve resulting in vesicoureteral reflux. The distal placement of the ureteric bud with incomplete migration into the bladder forms an ectopic ureter which can end up in the male prostate or seminal vesicals, and in the female in the Fallopian tube, uterus or upper vagina.



That is also the explanation why if there is a duplicated ureteric system, the upper pole is usually the ectopic ureter, while the lower pole ureter is a refluxing ureter ending in the bladder.

Etiology of vesicoureteral reflux

- 1. *Primary reflux*** is a congenital condition as explained above where the valve mechanism of the ureter bladder junction is defective. In this case the ureter is often laterally displaced, and the submucosal tunnel that is needed to promote the unidirectional flow and one way valve mechanism is deficient.

- 2. *Secondary reflux*** is a condition where the valve mechanism is probably not deficient, but due to different other conditions of the middle and lower urinary tract, the valve mechanism has been rendered inefficient.

The common mnemonic for these conditions is **N.O.T.I.C.E**, a bit of a misnomer that is known to all urologists and implies the following :

- 1. Neurogenic bladder** – where a high pressure bladder could cause the reflux.
- 2. Obstruction** – distal obstruction, in an infant commonly posterior urethral valves.
- 3. Trauma** – surgical trauma to the ureter that renders the valve mechanism inefficient.
- 4. Infection** – infection with oedema of the mucosa can shorten the submucosal tunnel and causes a temporary reflux.
- 5. Congenital Ectopic** – even an ectopic ureter can sometimes reflux due to the position into the bladder and is for clinical reasons a different entity.

The association between reflux and infection

This can not be easily explained. The distal urethra normally has organisms, and it is so that an uncircumcised boy has a tenfold increase in bacterial colonization and local immune mechanisms might play a roll to prevent the bacteria to spread into the proximal urethra and bladder. In the “normal situation” the minimal invasion of bacteria is probably controlled by local immune mechanisms and the excretion of urine at a high flow through the bladder and urethra. When there is reflux the tendency of these bacteria to take a foothold into the ureters and upper tract is higher, and this migration of bacteria probably explains the resulting higher incidence of infection. Reflux is thus not necessarily a general cause of UTI's, but seems to promote the incidence and the prevalance of pyelonephritis or kidney infection.

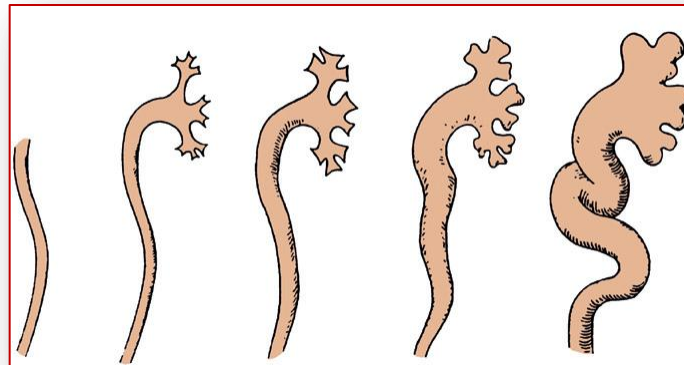
Diagnosis of reflux

The gold standard of reflux diagnosis is a radiological investigation called a urinary cystogram. In this test, contrast is inserted by a radiologist into the bladder, the bladder is passively filled to capacity and then the child is asked to urinate or in the infant waiting for spontaneous urination. This backflow of contrast into the ureters is observed under a x-ray screen, and this is used to grade reflux into 5 grades.



- * **Grade I** : Into a non-dilated ureter.
- * **Grade II** : Into the pelvis and calyces without dilatation.
- * **Grade III** : Mild to moderate dilatation of the ureter, renal pelvis and calyces with minimal blunting of the four moderate urethral tortuosity and dilatation of the pelvis and the calyces.
- * **Grade IV** : Gross dilatation of the ureter, pelvis and calyces, loss of papillary impression and urethral tortuosity.

It is often difficult to be absolute certain about the grading and reflux is often described as Grade I to II, IV to V etc.



Diagnosis of reflux in a child

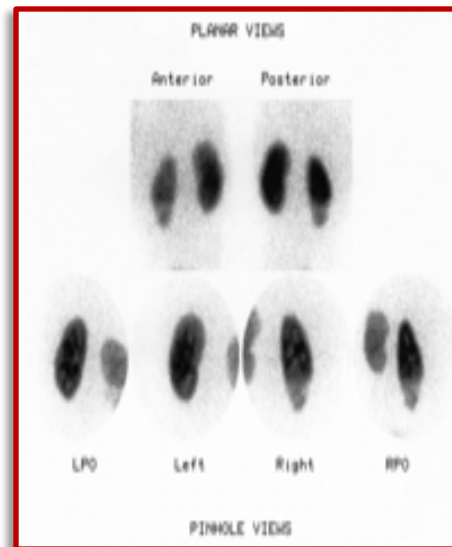
1. In the child with fever a properly collected urine sample must be examined and sent for culture. If the culture is positive a documented urinary tract infection has been diagnosed, and vesicoureteral reflux must often be excluded.

2. Special investigations

- **Renal ultrasound – this is non-invasive, and the clinician must be astute as minimal grades of hydronephrosis can give away low grade reflux.**
- **Urinary cystogram**
- **Radio-isotope study – this also obviates the use of a catheter, but is not anatomically as descriptive as the x-ray tests. The isotope of choice is Mag-3.**

Cystoscopy is not indicated in the investigation of reflux, and is reserved for examination and final assessment at the final stages of surgical reflux management.

- **DMSA renogram – this is a form of radio-isotope study where the isotope is mainly concentrated in the glomerulae and cortex of the kidney. This is very sensitive to scarring, and is the gold standard to diagnose and follow up scarring of the kidneys that can be associated with vesicoureteral reflux and reflux nephropathy.**



Reflux nephropathy

This is a poorly understood entity and probably has to do with maldevelopment of the kidney tissue itself due to the induction that took place caused by the abnormal ureteric bud positioning. In essence urine is refluxed into the papillary component of the kidney itself, and caused progressive damage in a kidney that was probably genetically predisposed to deterioration. It has been noticed that renal papillae with a concave architecture is more prone to damage than the pyramid or convex type and may play a role in the ultimate kidney deterioration.

There is however evidence that management of reflux and especially avoiding reflux in association with urinary tract infections, can prevent or delay the progressive damage of reflux nephropathy, and it is probably the main emphasis behind early and timely management of the reflux in ureters.

Management of reflux

Infection must be controlled by the appropriate antibiotic treatment.

All secondary conditions (N.O.T.I.C.E.**) must be excluded and treated before definitive surgery to the vesicoureteral junction can be contemplated. This implies that posterior urethral valves must first be treated, a neurogenic bladder with high pressures must be treated and the bladder pressures must be brought down to acceptable levels before management of reflux is considered, and in severe bladder conditions free drainage of the system must be done before definitive treatment of the reflux can be considered. One of these forms of permanent drainage of the bladder in a child is called a vesicostomy where the bladder is opened to the anterior abdominal wall and allows free drainage without increases in bladder pressure.**

Conservative management

It is important that reflux probably only causes severe damage to the upper tract before the age of 5 years and that mild degrees of reflux without infection is most probably not dangerous. Conservative management can either be treatment of acute urinary tract infections as they occur, or for many years have been the use of a long term urinary antiseptic, i.e. Nitrofurantoin, Cotrimoxazole or Trimethoprim. The reasoning behind this is that non-infective reflux has minimal effect on the upper tract and as there is spontaneous resolution in a notable number of cases, it can be used in the patient that is easily controlled.

The success of management

Reflux has a tendency to resolve with age and the lower the degree of reflux the higher the incidence of spontaneous resolution. It is therefore not uncommon to follow a patient up until there are specific indications for surgery.

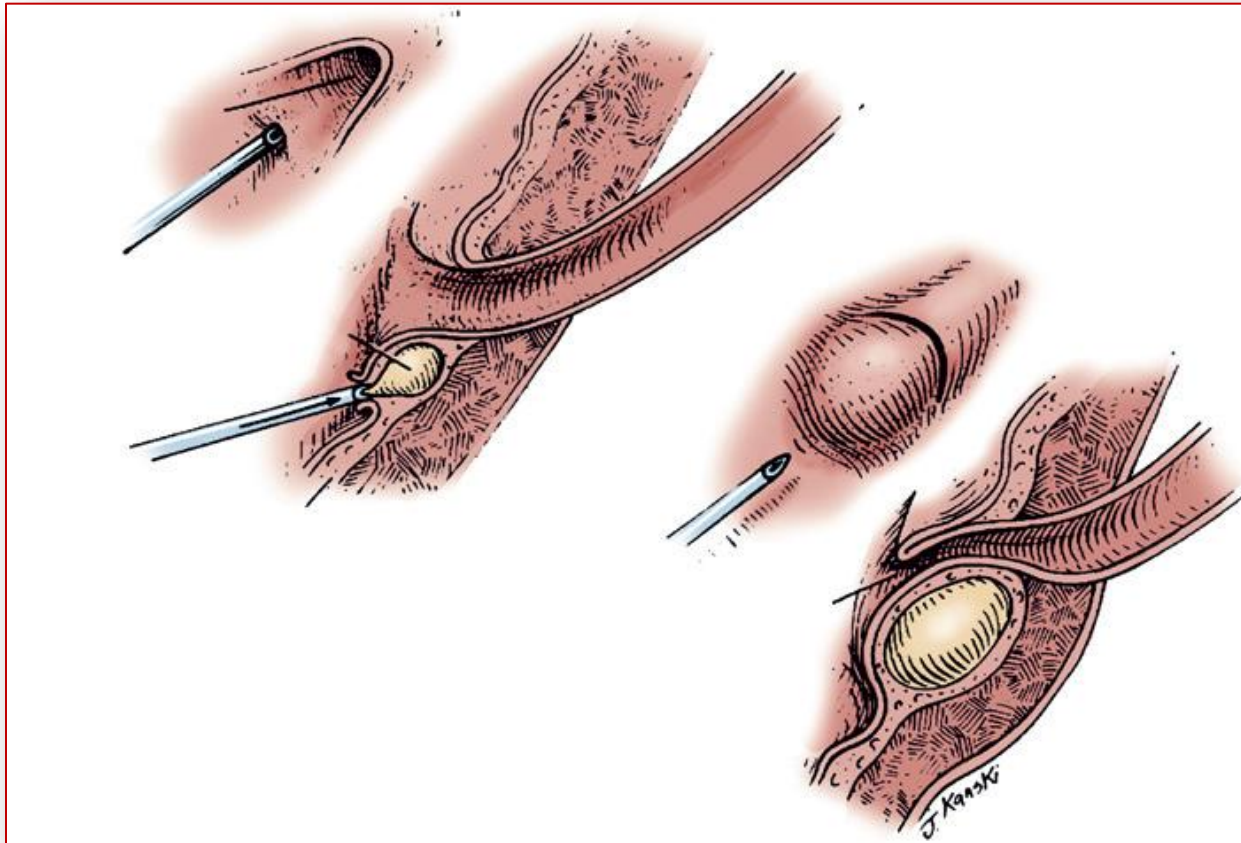
Surgical management

The indications for surgery in reflux are the following :

- * Breakthrough infection despite proper antibiotic treatment and prophylaxis.**
- * Severe abnormalities associated with reflux i.e. a ureter opening into a diverticulum of the bladder.**
- * Higher grade reflux III to V with proven kidney deterioration.**

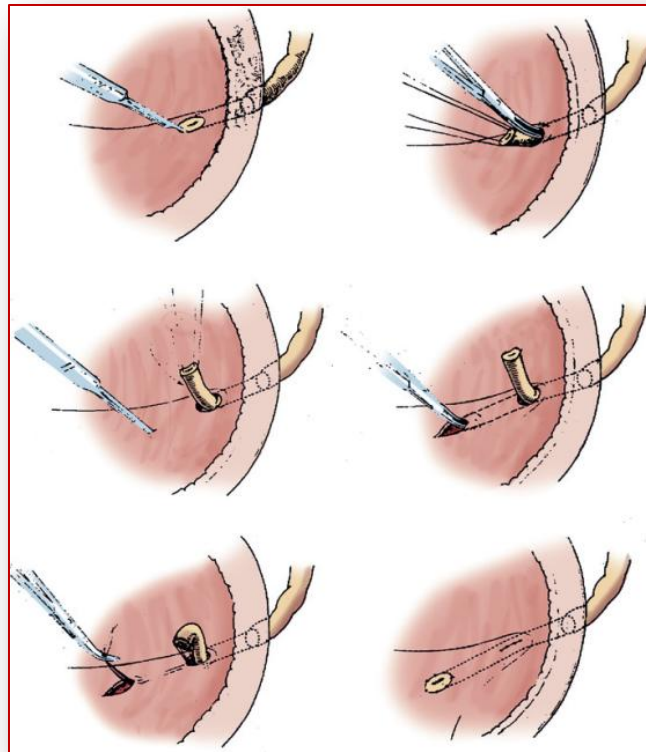
Endoscopic management

With this a cystoscope is used and a bulking agent is injected to lengthen the intra-vesical part of the ureter.



Open surgery

In this way, which can be done either laparoscopically with formal surgery, the principle is to lengthen the tunnel and the submucosal part of the ureter. This can be done through a purely intra-vesical or a combined intra- and extra-vesical or a totally extra-vesical method, but the end result is a longer submucosal tunnel.



Complications of surgery

- * Obstruction of the ureter**
- * Persistent reflux**
- * Persistent urinary tract infections, then often associated with bladder dysfunction.**

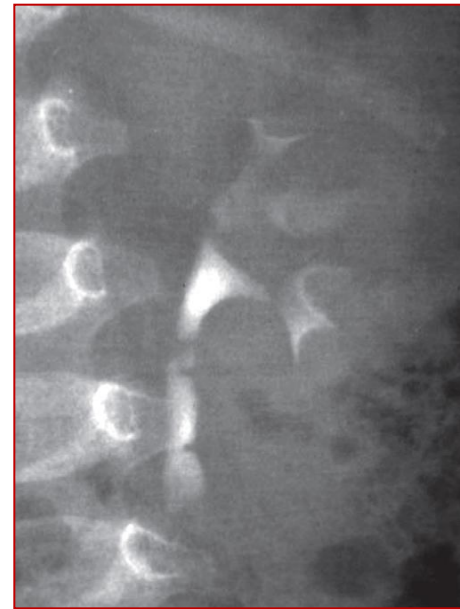
Associated bladder disturbances

It is imperative to understand that when associated with reflux there are other reasons for urinary tract infections. The overactive or unstable bladder is often associated with reflux and if UTI's persists after the successful management of reflux, the etiology is usually bladder dysfunction and this must be evaluated and managed as a separate entity.

Congenital anatomical abnormalities

Pelvi-ureteric junction obstruction

This is a congenital condition that also has to do with abnormalities in the development of the ureteral bud and the induction of the kidney and is probably embryologically associated with reflux.



In this condition there is an adynamic segment between the pelvis of the kidney and the ureter with a hydronephrotic or distended kidney, where the distal ureter is normal.

This can be associated as a secondary condition to vesicoureteral reflux, and with growths, Grade IV to V reflux, it is not uncommon to have a large distended ureter with obstruction at the PUJ junction and a condition called a secondary PUJ obstruction.

This is the most common reason for hydronephrosis in the infant, and it's an important differential diagnosis for a flank mass in a child.

Investigation

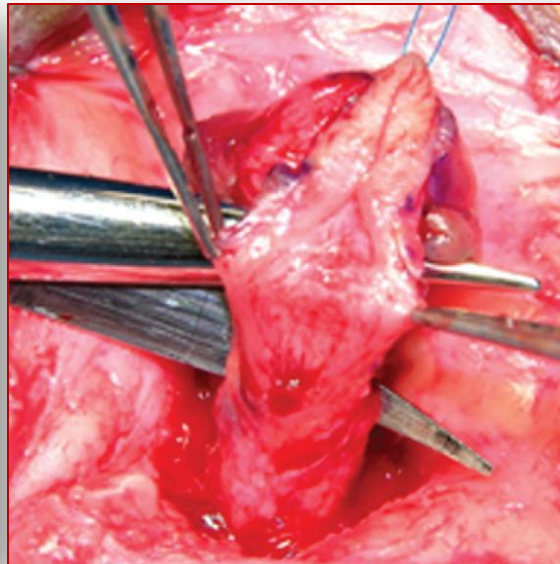
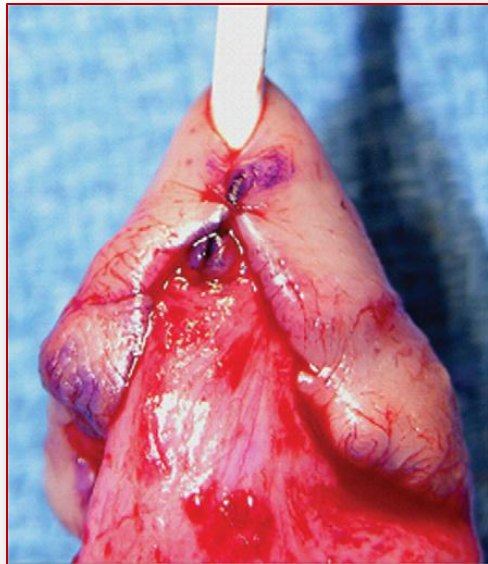
A diuretic renogram is the mainstay of the clinical diagnosis after an ultrasound has confirmed the hydronephrosis, and an obstructive flow pattern is often helpful in the management. The degree of obstruction is often difficult to make with certain as there are many grey areas and also there are distended non-obstructive ureters.

Hypospadias

Hypospadias is a congenital disorder where the tubularization of the urethra did not occur normally.

The triad of a hypospadias is the following :

- * A ventrally displaced urethral meatus**
- * A ventral chordee or curvature of the penis**
- * A dorsal skin hood**



Important facts regarding a hypospadias is the following :

- 1. Don't do a circumcision on the abnormal foreskin. This is important as it is often a request from the parents, but the foreskin is needed for the subsequent repair of the condition.**
- 2. To get a functional penis, the chordee must be repaired and the penis straightened.**
- 3. Urethral reconstruction is fraught with complications as the tissue used for the repair of the urethra is not the normal spongy tissue the patient should've been born with, but skin or other tissue that has to be taken in position. A successful hypospadias repair however is possible in the majority of patients, but this surgery should be reserved for people with a special interest in this condition.**

Exstrophy of the bladder

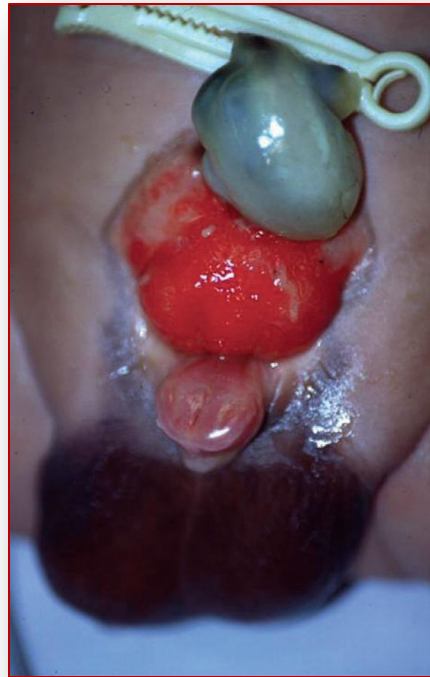
In this condition the mesoderm ingrowth of the anterior abdominal wall was abnormal. This devastating congenital condition is a situation where the anterior abdominal wall is not closed, and on looking at the patient you look at the inside of the posterior bladder wall with the ureters sitting on the anterior abdominal wall.

This must be repaired in the first few days after birth, and important points for the attending obstetrician are the following :

- Cover the bladder with a plastic or non-stick dressing**
- Refer the patient to a specialist centre ASAP**

Repair consists of the following :

- * Closure of the bladder and the bladder neck in the initial stages**
- * Converting the epispadic penis into a hypospadia, for future repair**
- * Repair of the external genitalia as well as the bladder neck**



Epispadia

This is part of the exstrophy complex, and is a mild degree of this disorder. This is a condition as a spectrum of a total incontinent patient, to just a distal misplaced urethra.

Compared to hypospadias, epispadia has :

- * A dorsally displaced urethra**
- * A dorsal penile chordee**
- * A ventral skin hood**

