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UPPER URINARY TRACT IN PATIENTS AFTER TRAUMATIC SPINAL CORD INJURY

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POST-MORTEM evaluations show repeatedly a high frequency of renal damage among patients who suffered spinal cord injuries. As a result, renal deficiency is assumed to be an important factor in determining the cause of these patients' death (Barber and Cross 1952; Dietrick and Russi, 1958; Bunts, 1959; Comarr, 1961; Pearce *et al.*, 1964; Talbot, 1966; Nyquist and Bors, 1967).

Functional renal studies, done to confirm the above-mentioned assumption, revealed varying degrees of renal insufficiency in chronic cases of spinal cord injuries (Morales, 1956; Pennisi *et al.*, 1959; Doggart *et al.*, 1963; Price *et al.*, 1966). This renal insufficiency was related to chronic pyelonephritis alone or associated with both pyelonephritis and amyloidosis (Dalton, 1965). Since both of the above processes are thought to be related to infections, anti-bacterial prevention and treatment should be sufficient to reduce renal failure. The picture which emerges from the above argument is that urinary tract infections lead to pyelonephritis which is sometimes associated with amyloidosis, resulting in renal deficiency and death.

The most problematical link in this causal chain is the concept of pyelonephritis. Chronic pyelonephritis is a morphological concept; according to current views, it is not necessary that the cause of the morphological changes, which are associated with this concept, be infection and therefore it is possible that there may be causes of renal deficiency other than infection (Kimmelstiel, 1964; Kalmanson *et al.*, 1965; Haveerstadt *et al.*, 1966; Freedman, 1967; Angell *et al.*, 1968). It is also possible that some of these anatomical changes occur without their being immediately expressed as renal insufficiency.

Early diagnosis of the pyelonephritic process is made especially difficult by both the lack of a unique distal cause of this process and the possibility that the anatomical changes which mark its onset do not always result in renal dysfunction. Since biopsy appears not to be a reliable method of diagnosis of this condition and is certainly not a recommended one in this type of patient, the best method to diagnose pyelonephritis should be radiological. According to Hodson (1959, 1967), intravenous pyelography reveals that pyelonephritis is the final state of a process which begins with pyelocaliectasis and progresses to the blunting of renal papillae, clubbing of the calyces and general narrowing of the renal substance. Smith (1962) confirmed part of this claim and Talbot (1966) recently stressed the importance of radiological diagnosis of pyelonephritis in patients with spinal cord injuries. If certain morphological changes are actually precursory to pyelonephritis, and if these changes can be detected by X-ray, then radiological diagnosis takes on a special significance.

The impression which emerged from our clinical work was that many cases of dilatation of upper urinary tract are revealed by X-ray examinations in patients with spinal cord injuries. This observation was made more frequently after we began to use large amounts of dye in keeping with the technique of continuous infusion of contrast material in intravenous pyelography (Whitesel and Heller, 1966). The following research was carried out to substantiate the above impression and to investigate its pathological significance.

RESEARCH POPULATION

In order to be included in this study, a patient had to have suffered a traumatic spinal cord injury and to have carried an indwelling catheter at the beginning of his treatment.

Fifty-three of 212 patients with a paraplegic or tetraplegic syndrome who were treated in this hospital during the last 10 years satisfied these criteria. One of the above 53, whose X-ray will be shown later, died 10 years after the beginning of treatment. Twelve other patients could not be reached in time for the following study. Our research group consisted of the 40 remaining patients. Of these, 37 were men and three women. The average age of the patients at the time of trauma was 30 years, with a range from 14 years to 59 years.

These patients had been rehabilitated in this hospital and examined periodically thereafter. They were hospitalised especially for the purpose of this study. On admission to the hospital for this study, they all underwent routine clinical and neurological examinations.

SPECIFIC X-RAY EXAMINATION

Intravenous Pyelography. The I.V.P. technique, used in this study, is a modification of the technique commonly called Drip Infusion Pyelography. This technique was originally developed to overcome the problem of reduced renal function and urinary tract obstruction (Whitesel and Heller, 1964). It was found to have no more deleterious effect on kidney function and no greater incidence of toxic reactions than the low dosage standard intravenous pyelography (Gup *et al.*, 1966). A comparative study of 10 X-ray methods carried out in normals showed that a programme of Drip Infusion Pyelography which uses 1 ml. of contrast medium per pound weight of patient provides the highest percentage of excellent

results (Powel *et al.*, 1967). This technique was especially appropriate to our patient population since it aids in overcoming the problem of the unvoided contents of the bowels, which often reduces the clarity of X-rays in cases of paraplegia and tetraplegia.

Two ml. of a tri-iodinated contrast medium (Urographin 60 per cent., Scherring Lab.) per kilogram weight of patient was used. This was diluted in 300 ml. of glucose 5 per cent. or saline and infused for 10 minutes. No abdominal compression was performed at any time during the examination. Films were obtained 5, 10, 15, 30 and 45 minutes after infusion. These films were interpreted by comparing them with films previously obtained from the same patients.

The two phenomena to which particular attention was paid were the dilatation of the renal pelvis and the dilatation of the calyces. A team of three physicians who were not told the clinical history of the X-rayed patients examined and compared the X-rays. The pelvis was considered dilated when all three physicians agreed that a clear increase in width was evident on comparing the follow-up X-ray with one taken shortly after trauma. The calyces were considered dilated when all three physicians agreed there was flattening or clubbing and dilatation of several minor calyces which did not appear in the X-ray taken immediately after trauma. When there was dilatation of both the renal pelvis and the calyces, the patient was considered to have either unilateral or bilateral pyelocaliectasis.

The thickness of the renal parenchyma of each kidney was measured in millimetres by taking the smallest distance from the calyx to the renal border (Hodson, 1959).

The shape of the kidney border was also observed for indirect evidence of kidney shrinkage. An irregular border was considered a sign of kidney shrinkage.

Size of kidney was not taken into consideration because, in our circumstances, it could not be measured reliably (Friedenberg *et al.*, 1965).

Cystourethrography. This examination was carried out according to the method described in a paper read at the Fifteenth Annual Spinal Cord Injury Conference in 1966 (Najenson *et al.*, 1966). It was performed to detect vesico-ureteral reflux.

SPECIFIC LABORATORY EXAMINATIONS

Kidney Functions Tests. Two tests of kidney function were performed. The first was an endogenous creatinine clearance test. This test is an accepted clinical method of determining the glomerulo-filtration rate and it has been used in many clinical studies (Tobias *et al.*, 1962; Doggart *et al.*, 1966). The particular variation of this test used in this study measures alkaline creatinine picrate (Jaffé Reaction) with adsorption into Lloyd's reagent (Pilsun and Bovis, 1957). These rates were correlated with patient's body surface. Values below 70 ml. per minute were considered pathological.

The second test was a urine concentration test which is used to determine distal tubular transport (Campbell, 1965). Any specific gravity below 1018 was considered pathological.

Electrolyte Examinations. The blood level and urinary excretion of chloride sodium and potassium were determined after a strict diet. This examination was carried out to uncover advanced cases of renal insufficiency and to exclude cases of renal damage due only to electrolyte disturbance. The sodium and potassium

in the blood and urine were determined using the Baird Atomic Flame Photometer. Chloride level was measured by the mercuric nitrate method of Shales and Shales (1941).

Bacteriological Examination. Three specimens of urine were obtained after strict aseptic precautions and examined for qualitative and quantitative evaluation. Specimens which contained bacteria growing at a rate of 100,000 per ml. of urine were considered pathological (Sonnenwirth, 1963).

All patients were put under a strict special diet for five days with a determined quantity of 2100 calories which included 80 g. of protein, 1500 ml. of fluids, 1 g. of salt and 3 g. of potassium per day. At the end of the fourth day of the diet, endogenous creatinine clearance was estimated from 24 hours' collection of urine and analysis of fasting blood. From the same specimen, electrolytes in blood and urine were determined. At the end of the fifth day, the patients were put under a strict diet of dry food for 12 to 16 hours after which specific gravity of urine was determined.

RESULTS

Kidney X-ray Evaluation. Table I shows that 12 patients from our research population were found to have pyelocaliectasis. There were six unilateral and six bilateral cases. Figure 1 is an example of mild bilateral pyelocaliectasis and Figure 2 is an example of severe pyelocaliectasis. Table II indicates that the mean width of the renal parenchyma of those patients suffering from pyelocaliectasis was shorter than those without this condition. The borders of the kidneys of 39 patients were smooth. The borders of the one remaining patient were irregular, and besides suffering from bilateral pyelocaliectasis this patient showed signs of permanent bacteriuria and renal insufficiency.

Demographic and Clinical Concomitant Factors. There does not appear to be a difference in age between the patients with pyelocaliectasis and those without this condition. The average age at the time of trauma of those suffering from pyelocaliectasis was 31 years with a range from 14 to 51 years and the average age at the time of trauma of all the patients was 30 years with a range from 14 to 59 years.

Table III reveals that there is no relationship between the level of the spinal cord lesion and pyelocaliectasis. The positive relationship between spasticity and pyelocaliectasis indicated by Table IV seems to be quite small. A more appreciable relationship emerges from the data presented in Table V which shows a positive association between the number of years after trauma and pyelocaliectasis. Table VI indicates that there is also a positive relationship between the extent of paralysis and pyelocaliectasis. Ten patients out of 12 who were totally paralysed four years after trauma showed signs of pyelocaliectasis.

Concomitant Pathological Findings. A large percentage of patients who underwent transurethral resection were from the group which exhibited X-ray signs of pyelocaliectasis as shown in Table VII. This indicates that patients with pyelocaliectasis tend to suffer from bladder outflow obstruction which results in retention of urine. As a result of the present follow-up study, the possibility of carrying out a transurethral resection on additional members of the group with pyelocaliectasis is being discussed. Figure 3 demonstrates that the introduction of an indwelling catheter for an extended period of time helps to overcome the urinary tract obstruction and, thereby, decreases markedly the dilatation of the upper urinary tract.

TABLE I
Pyelocaliectasis

Unilateral	6 cases*
Bilateral	6 cases
Total	12 cases

* One case after nephrectomy.

TABLE II
Thickness of Renal Parenchyma*

	Mean width
Without dilatation (27 patients—54 kidneys)	23 mm. (17-30)
With pyelocaliectasis† (11 patients—17 kidneys)	18 mm. (10-25)

* Two cases after nephrectomy—1 with pyelocaliectasis and 1 without—were excluded.

† Out of the 11 patients, 6 had bilateral and 5 unilateral dilatation.

TABLE III
Level of Lesion

	No dilatation	Pyelocaliectasis	Total
Tetraplegia	4 (67%)	2 (33%)	4
Paraplegia	24 (70%)	10 (30%)	34
Total	28	12	40

TABLE IV
Type of Paralysis

	No dilatation	Pyelocaliectasis	Total
Spastic	14 (61%)	9 (39%)	23
Flaccid	14 (82%)	3 (18%)	17
	28	12	40

TABLE V
Years after Trauma

	No dilatation	Pyelocaliectasis	Total
4 years and more	10 (48%)	11 (52%)	21
Less than 4 years	18 (95%)	1 (5%)	19
	28	12	40

Of the patients whose present or past cystourethrographies pointed to reflux, a large number showed signs of pyelocaliectasis, as can be seen from Table VIII.

Although all members of the research population at one time or another during the rehabilitation period had bacteriuria, at the time of their dismissal from the hospital they were all free of this condition. Table IX indicates that there

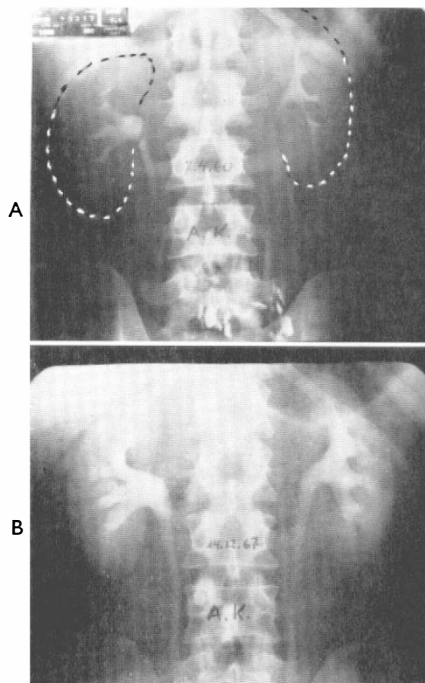


FIG. 1

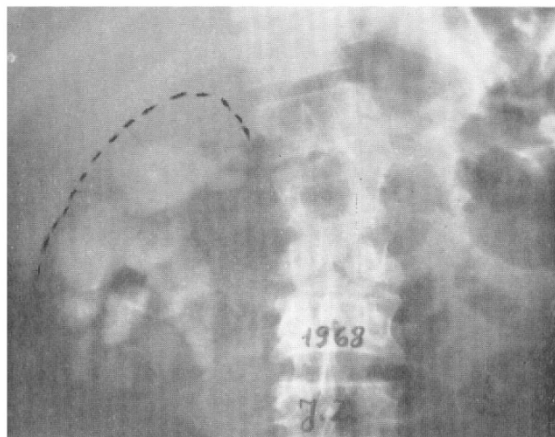


FIG. 2

Fig. 1—Example of mild bilateral pyelocaliectasis. (A) I.V.P. of 23-year-old patient (A.K.) with complete spastic paraplegia, due to fracture of T_5 and T_6 , taken shortly after trauma, showing normal pelvis and calices. (B) I.V.P. of same patient, taken 7 years later, during which time no intervention on his urinary tract was performed, although urinary rest was always around 100 ml. and acute urinary infections were detected several times. At the time of I.V.P. there was normal renal function. The I.V.P. shows flattening and dilatation of calices and relative dilatation of pelvis.

Fig. 2—Example of severe pyelocaliectasis. I.V.P. of 42-year-old patient (J.Z.) with complete spastic paraplegia due to fracture of T_{12} , taken 16 years after trauma, during which time he underwent left nephrectomy due to nephrolithiasis and suffered several urinary tract infections. In 1961 dilatation of upper urinary tract was noticed. In 1964 hypertension was detected. Since 1966 creatinine clearance has been reduced and specific gravity of urine, during concentration test, has been low. The I.V.P. shows severe dilatation of pelvis and calices and extreme reduction of thickness of renal parenchyma.

was a higher percentage of re-contamination in the group presenting signs of pyelocaliectasis than in the group with no such signs. At the time of the follow-up study only two members of the former group were carrying an indwelling catheter.

All four patients with clinical signs of renal insufficiency were from the group with pyelocaliectasis, as shown in Table X. The renal deficiency of two of these patients was revealed by the endogenous creatinine clearance test, whereas the renal insufficiency of one other patient showed up only in the urine concentration test. Both these tests were pathological for the fourth patient.

The electrolytes examination did not indicate any pathology.

TABLE VI
Extent of Paralysis

	No dilatation	Pyelocaliectasis	Total
Complete	12 (52%)	11 (48%)	23
Incomplete	16 (94%)	1 (6%)	17
	28	12	40

TABLE VII
Patients who underwent Transureteral Resection

	No dilatation	Pyelocaliectasis	Total
T.U.R.	5 (38%)	8 (62%)	13
No T.U.R.*	20 (83%)	4 (17%)	24
	25	12	37

* Women not included.

TABLE VIII
Patients who were found to have Vesico-ureteral Reflux

	No dilatation	Pyelocaliectasis	Total
With V.U.R.	2 (33%)	4 (67%)	6
No V.U.R.	26 (76%)	8 (24%)	34
	28	12	40

TABLE IX
Bacteriuria at Time of Check-up

	No dilatation	Pyelocaliectasis	Total
Bacteriuria	6 (46%)	7 (54%)	13
No bacteriuria	22 (81%)	5 (19%)	27
	28	12	40

TABLE X
Renal Insufficiency*

	No dilatation	Pyelocaliectasis	Total
Renal insufficiency	0 (0%)	4 (100%)	4
Normal	27 (77%)	8 (23%)	35
	27	12	39

* One case with severe cardiac insufficiency excluded.

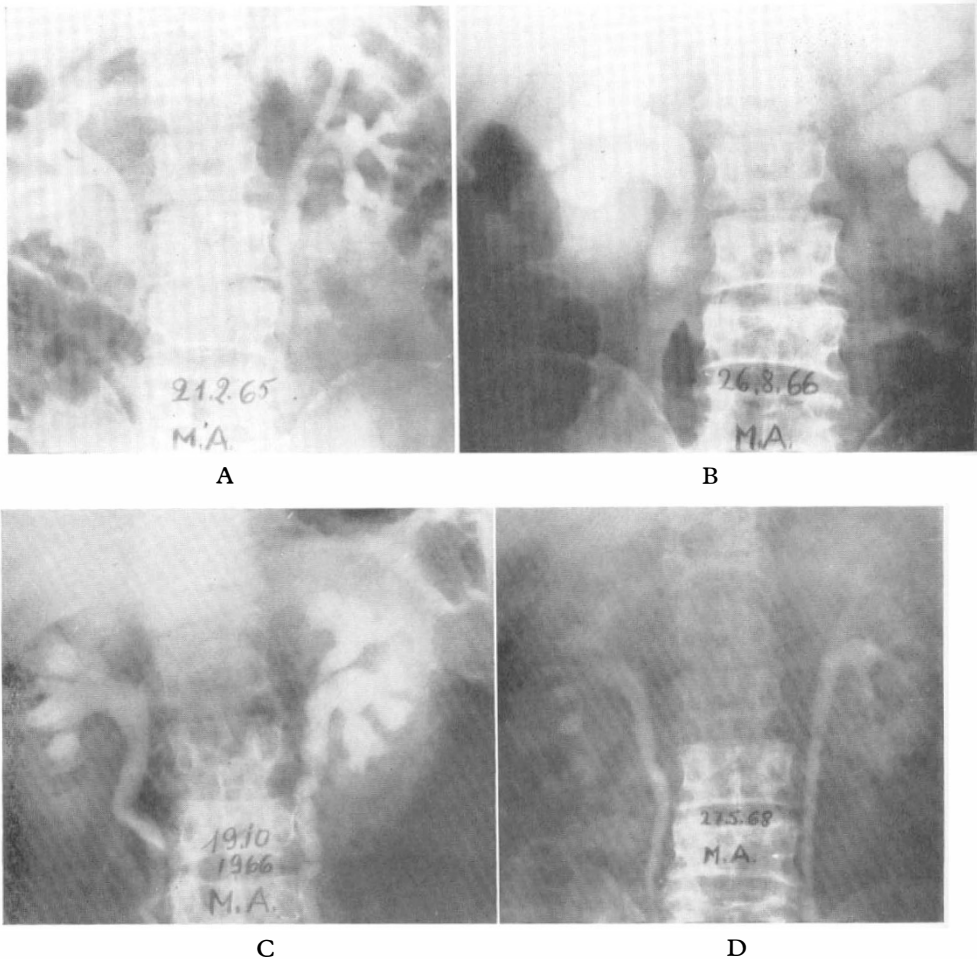


FIG. 3

Reduction of dilatation of upper urinary tract after overcoming functional retention of urine. (A) I.V.P. of a 36-year-old patient (N.A.) with flaccid paraplegia, due to fracture of vertebrae T₁₂-L₁, taken in 1965, one year after trauma, showing flattening of calices in right kidney. (B) I.V.P. of same patient, taken in August 1966. This periodical check-up revealed urinary tract infection and high urinary rest. The I.V.P. shows severe dilatation of upper urinary tract. (C) I.V.P. of same patient, taken in October 1966, after carrying an indwelling catheter for 7 weeks, shows reduction of dilatation. (D) I.V.P. of same patient, with indwelling catheter, shows an even greater reduction of dilatation.

DISCUSSION

This study investigated the significance of pyelocaliectasis when this state is considered as a purely X-ray morphological concept. Pyelocaliectasis, which was defined as dilatation of the renal pelvis and flattening or clubbing and dilatation of several minor calyces, was the criterion for the presence of this morphological state. Twelve patients from among 40 paraplegics and tetraplegics whose disability

had a traumatic origin were found to exhibit the radiological signs of pyelocaliectasis when Drip Infusion Pyelography was used to obtain clear pictures of their upper urinary tracts. These cases of pyelocaliectasis were accompanied by narrowing of the renal parenchyma. Irregularity of the kidneys which is generally thought to be a later sign of pyelonephritis pathology was found only in one of these 12 cases. This particular patient also suffered from permanent bacteriuria and renal insufficiency. Figure 4 is an X-ray of the patient who died before this study was begun. This X-ray shows irregularity of kidney border associated with pyelocaliectasis. Before death, this patient exhibited renal deficiency. A post-mortem revealed pyelonephritis and moderate amyloidosis in the kidney. There is, therefore, reason to assume that pyelocaliectasis is a radiological sign which points to renal pathology.

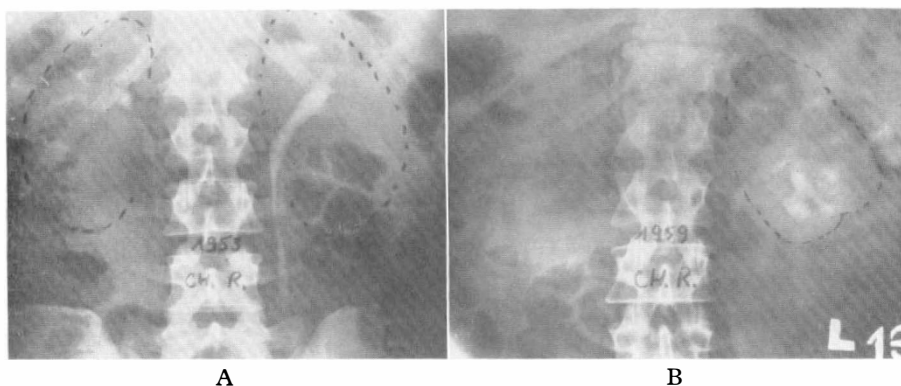


FIG. 4

Pyelocaliectasis in a patient whose P.M. showed severe renal damage. (A) I.V.P. of a 31-year-old patient (Ch.R.) with complete spastic paraplegia due to fracture of vertebra T₁₂, taken one year after trauma. The I.V.P. shows no dilatation of the upper urinary tract. (B) I.V.P. of same patient, taken 6 years later, during which time he underwent right nephrectomy due to nephrolithiasis. At the time of I.V.P., the patient suffered urinary infection and hypertension. The I.V.P. shows pyelocaliectasis and narrowing of the renal parenchyma. His general condition then became worse and renal deficiency was found in an increasing degree. The patient died in 1962. The P.M. revealed pyelonephritis and moderate amyloidosis.

The general incidence of cases of pyelocaliectasis among patients whose paraplegia or tetraplegia is of traumatic origin would be quite difficult to determine. Pyelocaliectasis has been studied by different researchers under such labels as hydronephrosis and dilatation of the upper urinary tract. These researchers arrived at estimates of the incidence of this condition which varied from the low of 14.5 per cent. to a high of 42 per cent. Morales (1956) reports that 14.5 per cent. of the paraplegics whom he examined were suffering from hydronephrosis. Ross (1963) found that more than one-third of the paraplegics in his experience showed this condition. Irvine (1959) and Damanski (1963) in independent studies stated that as many as 42 per cent. of the paraplegics whom they investigated had dilatation of the upper urinary tract. Thirty per cent. of our study's research population exhibited signs of pyelocaliectasis. Obviously the results of these various studies cannot be directly compared since both the research population and criteria for the presence of pyelocaliectasis may have differed widely.

Two factors appear to predispose individuals with injury of the spinal cord to pyelocaliectasis. These factors are the extent of paralysis and the time elapsed since trauma. Our study supports the conclusion of other investigators who have found that paraplegics and tetraplegics who are totally paralysed are more likely to develop pyelocaliectasis (Damanski, 1963). In a large number of cases of complete paralysis, pyelocaliectasis becomes noticeable approximately four years after trauma.

In the present study, pyelocaliectasis was not related in a one to one fashion to infection. Both bacteriuria and obstruction of the lower urinary tract appeared with a high frequency among our cases of pyelocaliectasis. Since pyelocaliectasis can be assumed to be one of the major morphological X-ray changes composing or preceding pyelonephritis, this study confirms recent opinion which claims that pyelonephritis is not correlated absolutely with bacterial infection. According to this opinion not only may bacteriuria be present without pyelonephritis, but pyelonephritis may also occur without bacteriuria (Kimmelstiel, 1964). Angell (1968) reports that he discovered 12 patients with pyelonephritis who did not show signs of past or present bacteriuria. Vesico-ureteral reflux, which the present study found to be positively related to pyelocaliectasis, is also considered to be the result of either infection or urinary tract obstruction (*Lancet*, 1968). Therefore, it is evident that pyelonephritis is not necessarily the result of bacterial infection.

Bladder outflow obstruction emerges from this investigation as another possible cause of pyelocaliectasis. A large number of our patients with pyelocaliectasis have already undergone a transurethral resection or will undergo such an operation in the near future to relieve this type of obstruction. Several studies showed that operations undertaken to overcome urinary tract obstruction or introduction of a permanent indwelling catheter resulted in clear radiological improvement of previous dilatation of the urinary tract (Pelot, 1963; Kohfler and Bowles, 1966; Talbot *et al.*, 1967). This present study also demonstrates that the introduction of an indwelling catheter can lead to diminishing of pyelocaliectasis (fig. 3). The process from lower urinary tract obstruction to pyelonephritis appears to be reversible, at least in the earlier stages of the illness. The observation that four of our patients with pyelocaliectasis suffered from renal deficiency indicates what may occur if the above-mentioned process is not reversed. It is quite probable that there exists a process which, when not interrupted, can lead from bladder outflow obstruction to renal deficiency through chronic renal disease (pyelonephritis with or without amyloidosis) and end in death.

This study points to bladder outflow obstruction as a source of renal trouble. It does not discount the importance of precaution against bacterial infection of the urinary tract. It does imply that the urinary tract should be periodically X-rayed in patients after spinal cord injury to detect any dilatation of the upper urinary tract. The possibility that this state may be the result of bladder outflow obstruction which is part of a reversible process should be kept in mind.

SUMMARY

Forty patients who were disabled due to a traumatic injury of the spinal cord and who carried an indwelling catheter at the beginning of their treatment were examined to determine the existence and significance of the dilatation of the upper urinary tract. A comparative study of past and present X-rays revealed that 30

per cent. of the research population were found to exhibit pyelocaliectasis. Narrowing of the renal parenchyma accompanied this condition. Total paralysis and a four-year duration of the illness appeared to predispose the patients to pyelocaliectasis. This radiological state can be considered to be a precursor of pyelonephritis. This study showed that the anatomical substratum of this reontgenological sign is part of a reversible process which could be the result of either bacteriuria or bladder outflow obstruction. It also points to the probability that this process, no matter what its cause, could lead to renal insufficiency and death when not reversed.

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CHEMOTHERAPY IN CHRONIC URINARY TRACT INFECTION

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THE management of the urinary tract infections is one of the main challenges for the urologist dealing with spinal cord injury patients. We use sulphonamides and other antibacterial substances sparingly, to control many severe infections that are seldom encountered in other Rehabilitation Centres. Like Bors, we believe that the developing of auto-immunity is one of the paths in this difficult task and forced diuresis may help in the control of even some acute pyelonephritis.

A new antibacterial combination was tested in the treatment of chronic urinary tract infections resistant to other drugs. A pyrimidine derivative, trimethoprim, that acts with sulphonamides in a synergic and bactericidal manner, and sulfamethoxazole (Gantanol¹); expecting a greater intensity of action, broader spectrum of activity, transforming a bacteriostatic into bacteriocidal effect and diminishing the development of resistance in a number of bacteria.

Chemically, trimethoprim is 2, 4-diamino-5 (3', 4', 5'-trimethoxybenzyl)-pyrimidine. Its molecular formula is C₁₄H₁₈N₄O₃, and its molecular weight 290.3. Gantanol contains as active substance 5-methyl-3-sulfanilamido-isoxazole.

We used this combination in two dosages:

¹ F. Hoffmann-La Roche & Co. Ltd., Basle, Switzerland.