

The bacterial count dropped below $10,000 \times \text{ml.}$ in 71 per cent. of patients. Eight patients with fair results were placed on Gentamicin with six failures and two successes, three of these patients were later found to have unknown foreign bodies or lithiasis in the urinary tract.

The bacterial findings are shown in Table VII.

SIDE EFFECTS

We did not find any of importance. With Ro 6-2580/4 there was a drop in platelet count in three cases and with Ro 6-2580/9-11 in four, maintaining the normal values.

In one case there was an increase of glutamic-pyruvic-transaminase above normal levels, one developed a skin rash that lasted seven days and another one had gastric intolerance.

SUMMARY AND CONCLUSIONS

We report the clinical research of a new antibacterial combination (Gantanol + trimethoprim; F. Hoffmann-La Roche & Co. Ltd.) in the management of chronic urinary tract infections.

The combination Ro 6-2580/4 administered to 51 patients with and without G.U. obstructions ended up with 55 per cent. good results following. Kass criteria whereas the Ro 6-2580/9-11 in 32 patients without obstruction that rate increased up to the 75 per cent. of cases.

Few adverse reactions were noted.

ACKNOWLEDGEMENTS

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THE PATHOGENESIS OF RENAL INFECTION IN SPINAL CORD INJURY¹

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THE effect of the initial management of spinal cord injury patients upon subsequent changes in the upper urinary tract cannot be evaluated without an understanding of the pathogenesis of those changes. A day may be coming when infection will be avoided during treatment of the early stages of neurogenic bladder dysfunction,

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although even the most encouraging reports of intermittent catheterisation are still far from claiming that goal (Guttmann and Frankel, 1966; Hardy, 1966; Bors, 1967; Walsh, 1968). It may also happen, when that day comes, that there will be other than infectious complications with which to contend. They are seen now, from time to time, in patients with sterile urine. But for most of those who care for these patients, the chief enemy has been and, up to this time remains, infection—more specifically, infection of the kidneys derived from pre-existing infection of the bladder.

For purposes of this discussion it will be assumed that this infection of the bladder is, at one stage or another, universal among these patients. The question then to be answered is how does it spread from the bladder to the kidney. This, however, is over-simplification, for there are corollary questions no less urgent: what effect, if any, does the manner of spread have upon the function of the urinary tract; how can this be modified by the management of the bladder, still assuming the presence of intransigent infection. The role of the ureter in the pathogenesis of ascending pyelonephritis has already been described and need be mentioned here only in summary (Talbot, 1958). The subepithelial tissue of the bladder is continuous with that of the ureter and renal pelvis and, ultimately, with the interstitial tissue of the kidney. A direct pathway of invasion is thus available and the progress of infection along this route can be demonstrated histologically. Other methods of spread, such as lymphatic or hematogenous, are not impossible and may occur occasionally, but they have not been demonstrated in the series upon which this discussion is based.

The presence of active inflammatory changes in its wall have a demonstrable effect upon ureteral function (Talbot and Perlmutter, 1965). It has been observed that segmental dilatation of the lower ureter may be a premonitory sign of vesico-ureteral reflux (Cobb and Talbot, 1966). Since luminal obstruction is rarely, if ever, demonstrated, it follows that this dilatation must reflect ureteral dysfunction due to local structural alterations beginning in the part of the ureter contiguous to the bladder; reflux is one manifestation of such dysfunction. Normally, the contraction of the lower ureteral segment provides a dynamic valve action to protect the upper tract from pressure generated in the bladder during detrusor contraction. As disease advances upward in the ureteral wall, other elements of dysfunction, including reverse peristalsis, may appear; ultimately there may be complete absence of peristalsis and the upper tract then demonstrates a state of functional obstruction. It is of interest that, observed radiologically, this process may be seen as reversible even when quite advanced, reflecting the reversibility of the inflammatory process itself. Serial radiologic studies, particularly those of the actual dynamics of the upper urinary tract, make it possible to follow these changes, functional and structural alike. Their correlation with the clinical course provides a basis for evaluating the effects of treatment. Unfortunately, the inflammation does not always subside; reflux may persist and be associated with a progression of disastrous dysfunction, ending in irreversible hydro-ureter and hydronephrosis, and ultimate renal failure. On the other hand, reflux is notably capricious; when it is inconstant, or moderate in degree, or when the ureter is still capable of compensation, the prognosis may be favourable (Talbot *et al.*, 1967).

With reflux, ureteral insufficiency, and impaired drainage, a new route of invasion is open, through the stagnant or sluggish column of urine occupying the dilated lumen. The kidney is then exposed to a dual hazard.

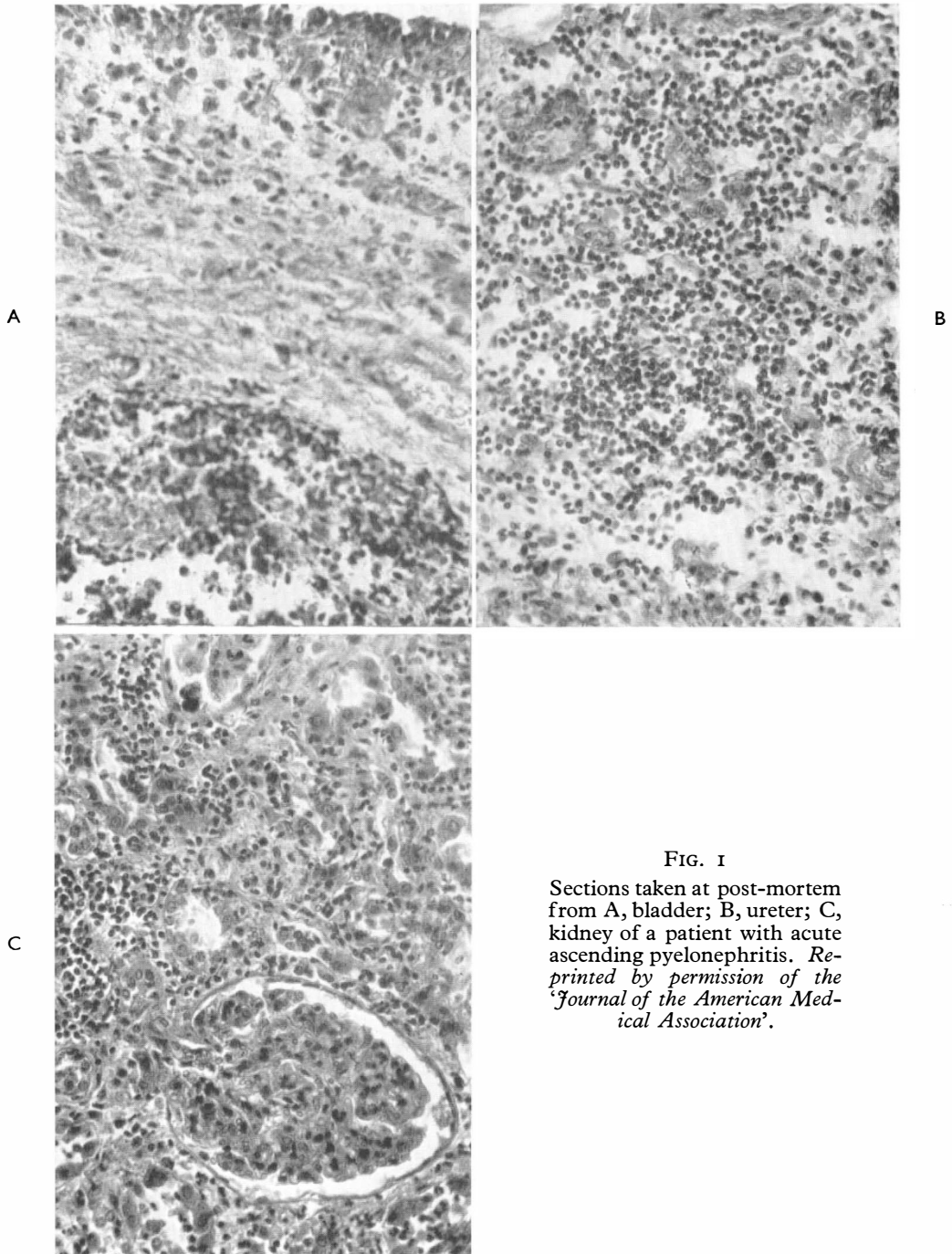


FIG. 1

Sections taken at post-mortem from A, bladder; B, ureter; C, kidney of a patient with acute ascending pyelonephritis. Reprinted by permission of the *Journal of the American Medical Association*.

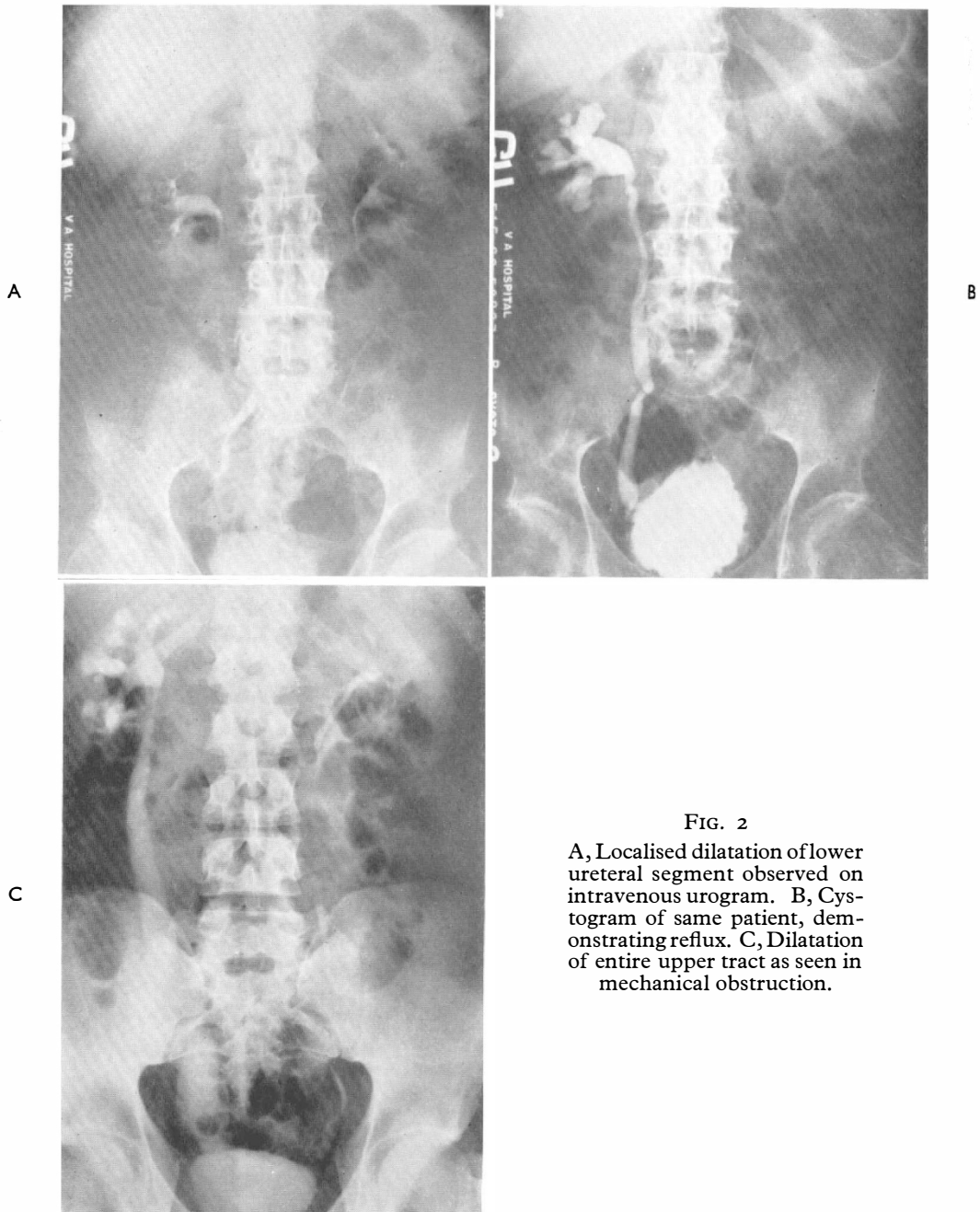


FIG. 2

A, Localised dilatation of lower ureteral segment observed on intravenous urogram. B, Cystogram of same patient, demonstrating reflux. C, Dilatation of entire upper tract as seen in mechanical obstruction.

Treatment ideally should be directed at control of infection before irreversible changes have developed. Since the process may develop insidiously, without clinical symptoms, serial radiologic studies are essential to guarding the patient's well-being. A slight dilatation of the lower ureter associated with reflux that advances only a few centimetres may, in the absence of symptoms, be managed expectantly with repeated examination after an interval of not more than three or

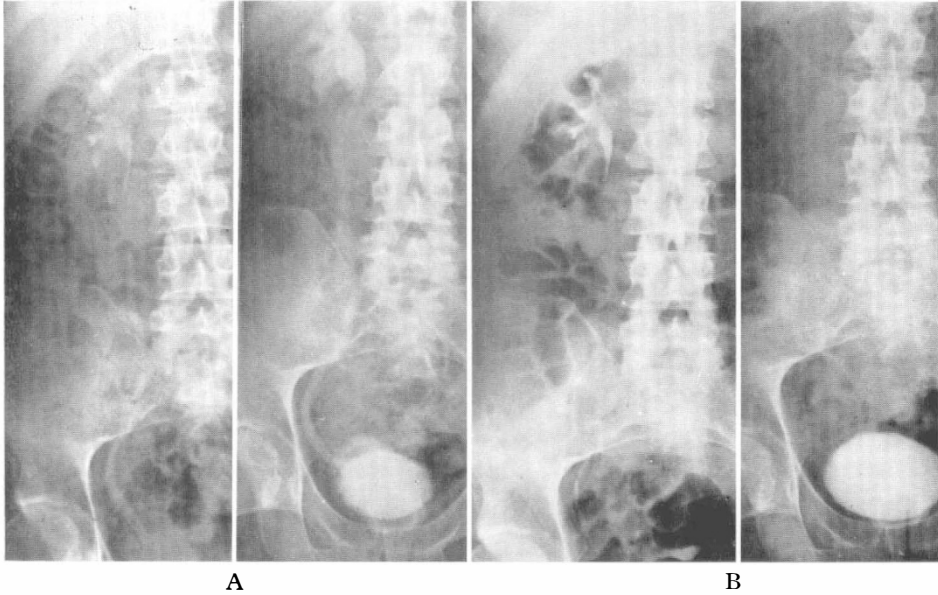


FIG. 3

A, Intravenous pyelogram (*left*) showing ureteral dilatation and some calyceal distension; cystogram; (*right*) showing marked reflux. This was unilateral. B, Same patient after eight months on catheter drainage. Intravenous pyelogram appears normal and there is no reflux. *Reprinted by permission of F. A. Davis Co., Philadelphia.*



FIG. 4

Cystogram showing slight reflux when bladder is full, good contraction wave in ureter as bladder empties, with disappearance of reflux in compensated ureter. *Reprinted by permission of F. A. Davis Co., Philadelphia.*

four months. If, in such a case, the patient is voiding and has no residual urine, and no deterioration can be detected, either clinically or radiologically, there is no need to alter the pattern of micturition. Should progression of the process occur, with or without clinical manifestations, an effort at correction is indicated. In the first instance, this takes the form of improved bladder drainage by introduction of an indwelling catheter. The ureter, spared the competition with intravesical pressure, may by this means alone regain its functional integrity. Reflux disappears, the caliber of the lumen becomes or approaches normal, and the patient may be permitted to void again, although close observation must be continued.

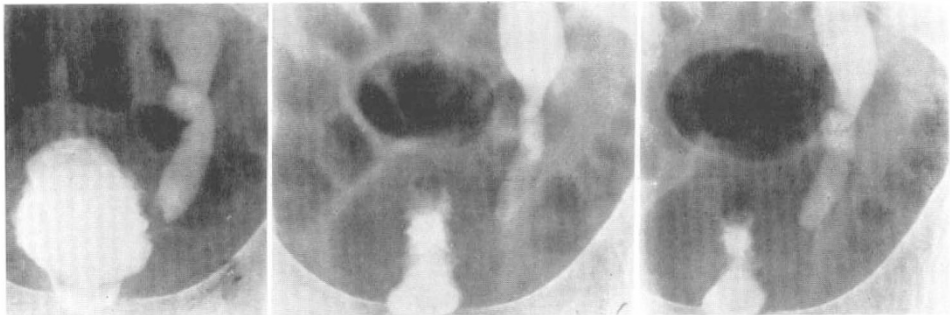


FIG. 5

Cystogram showing marked reflux, persisting in decompensated ureter as bladder empties.
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During acute episodes, with severe constitutional symptoms, an effective method of treatment is to promote diuresis by intravenous infusion of saline or dextrose solutions along with administration of chemotherapeutic or antibiotic agents. If there is no improvement after 48 hours, the renal pelvis are drained by the introduction of ureteral catheters which are left in place for from two to ten days, depending upon the patient's course. This is almost always effective, but there are occasional instances in which the catheters cannot be passed. If general treatment proves inadequate in these, no recourse then remains but surgical drainage.

Situations of great severity may, with suitable treatment, clear up entirely, leaving an upper tract which is to all appearances normal. In a considerable number, however, the process may become chronic, with ultimate fibrotic replacement of the ureteral muscle and irreversible dysfunction. The treatment of such cases is beyond the scope of this discussion, for the dysfunction is now permanent and no longer susceptible of improvement simply by improving bladder drainage. By the same token, it may be noted here that diversion through an ileal conduit does automatically become a procedure of choice, since the malfunctioning upper tract is unlikely to drain better into the conduit than into an empty bladder. The same objection applies to attempts to repair the uretero-vesical valve by any of several plastic procedures designed for this purpose. A different situation obtains in these cases, with the lower ureteral segment rendered incompetent by infection and fibrosis, than in children with a congenital defect at the ureterovesical junction, but a normal ureter above it.

An uninfected bladder that empties itself at reasonable intervals, without overdistension, is a powerful safeguard against upper tract complications. Granting infected urine, good drainage becomes even more vital. If residual urine and overdistension can be avoided, there is a good chance that ascending infection may be prevented. Even when it occurs, drainage of the bladder may reverse it, if accomplished promptly. But once the ureteral wall has become chronically damaged, the time has passed when treatment of the bladder alone will suffice.

Figures 1-5 illustrate aspects of the pathogenesis in spinal cord injury.

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General Discussion

Dr. H. L. FRANKEL (*Great Britain*). We've heard complimentary remarks made by speakers this morning about the method of intermittent catheterisation used at Stoke Mandeville Hospital. I have personally performed this procedure on approximately 20,000 occasions in the last eleven years. We've given previous results on 476 patients. Here are some later figures than those mentioned, which will be published by Dr. Walsh in the next number of *Paraplegia*. These figures on our last 90 male patients show a considerable improvement on those Sir Ludwig Guttmann and I reported two years ago. The sterility on admission of the males is now 92 per cent., and on discharge 82 per cent. Rather more significant is the changing results in the female patients. Previously our sterility rate in the females was under 50 per cent. As a result of our findings, we changed our method of catheterising the female patients. Previously, every single catheterisation of the male had been performed by a doctor, while the catheterisations of the females had been performed by a nurse or a sister. Sir Ludwig changed this and now all the female catheterisations are also done by doctors. This is really the only major change we have made. Although the figures for the women are rather small (15), I think there has been a considerable improvement in the state of the women as 10 out of 15 (67 per cent.) had sterile urine.

All the speakers, while professing to wish to use this method, have complained that it is time-consuming and that they haven't got enough staff. Well, the actual facts are that it takes approximately two and a half minutes to catheterise a patient, for a doctor, from beginning to end. The patients may need 100 or 120 or 150 catheterisations. This is an expenditure of medical time of four to six hours.