Treatment of Vesico-ureteric Reflux in Children

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Approximately 35% of children with urinary infection have vesico-ureteric reflux (McGovern, Marshall, and Paquin, 1960; Ericsson, 1960). It is not known whether infection causes the reflux by damaging the uretero-vesical valvular mechanism, or whether a congenital abnormality permits reflux which predisposes to infection. Yet whatever the aetiology, it seems logical to assume that when infection occurs in the presence of reflux there will be renal involvement, for it has been shown that there is a close correlation between ureteric reflux and radiological evidence of kidney scarring (Hodson and Edwards, 1960). Despite this, it is not clear whether, besides treating the infection by giving prolonged carefully controlled courses of antibiotics, the child will gain additional benefit if a surgical operation is undertaken to eliminate the reflux.

The purpose of this paper is to report the results of a controlled trial in which a group of children with surgically treated reflux was compared with an unoperated group. The trial was a prospective one and the children were allotted at random to either the operated or control groups according to whether their birthdays fell on even or odd days. In view of the considerable divergence of opinion about the value of the surgical treatment of reflux (Spence et al., 1961) and the uncomplicated nature of this type of surgery, it was felt that it was ethically justifiable to conduct a trial in this manner. 58 children were studied, 33 having operations for their reflux and 25 acting as controls. Cases in which reflux was associated either with mechanical obstruction in the urethra, such as posterior urethral valves, or with neurogenic bladder, were excluded from the trial, as it was felt that in these the treatment of the reflux could not be considered in isolation but only as a part of the management of the associated condition.

Diagnosis

All the children placed in the trial had had one or more attacks of urinary infection proven by the finding in clean specimens of their urine of more than 10 pus cells per c.mm. (Stansfeld, 1962) and more than 100,000 organisms per ml. (Kass, 1957).

Ureteric reflux was diagnosed by cystographic examination performed by one of the authors (J.E.S.S.). The bladder was catheterized and emptied. 20% Hypaque solution was then injected through the catheter until the child expressed a desire to micturate, at which time an x-ray including the whole abdomen was taken with the child supine. Female children were then sat on a commode and a true lateral exposure of the bladder and urethra was made during micturition. In male children the micturating radiograph was taken with the pelvis in an oblique position and the child either lying supine or standing erect. As soon as the child had finished micturating a third exposure was made in a manner similar to the first, that is of the whole abdomen with the child supine. The examination was performed without anaesthesia in all children over the age of 4. Younger children were anaesthetized and their bladders expressed manually in order to obtain the micturating films.

As well as the cystogram all children had an intravenous pyelogram and cystoscopy.

Conduct of Trial

In the early stages of the trial some of the children were thought to have non-mechanical bladder neck obstruction as well as reflux, and these were subjected to a plastic operation on the bladder neck, irrespective of whether they were in the operation or control groups. Subsequently, we came to doubt whether 'functional' obstruction of the bladder neck was a true entity, and in the last half of the trial this diagnosis was not made (Scott, 1968).

All cases were observed for 3 years. They were seen monthly at first, but later, according to progress, the intervals might be extended to 2 or 3 months. At each attendance symptoms were recorded, the child examined, blood pressure measured, and a urine pus cell count done. Whenever there were symptoms or pyuria was demonstrated, urine bacterial counts were also made. Operated cases had a cystogram 6 months after operation, and all cases, whether in operated or control groups, were readmitted to hospital at the end of 3 years for a repeat of all the investigations that were done at the beginning of the trial.

Two of the control group were not infected at the
time that they were admitted to the series, and as they
had no relapse they were not given any antibiotics. All
others had intensive medical treatment, antibiotics being
selected according to the sensitivities of the organisms
grown from their urines. Treatment was stopped only
when several months had passed without evidence of
activity. In the majority it was given for at least 6
months, and in those who developed recurrences of
infection it was continued for a year or longer.

**TABLE I**

Anti-reflux Operations and Outcome

<table>
<thead>
<tr>
<th>Type of Operation</th>
<th>Operations</th>
<th>Failures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Ureters</td>
</tr>
<tr>
<td>Bischoff</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Advancement-reimplant</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Reimplant</td>
<td>20</td>
<td>31</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>31</strong></td>
<td><strong>46</strong></td>
</tr>
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</table>

**TABLE II**

Second Operations for Reflux and Outcome

<table>
<thead>
<tr>
<th>Type of Operation</th>
<th>Operations</th>
<th>Failures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Ureters</td>
</tr>
<tr>
<td>Bischoff→reimplant</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Advancement→reimplant</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>3</strong></td>
<td><strong>3</strong></td>
</tr>
</tbody>
</table>

**TABLE III**

Bladder Neck Operations

<table>
<thead>
<tr>
<th>Operation</th>
<th>Operation Group</th>
<th>Control Group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y-V plasty</td>
<td>8</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>Muscle division</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>11</strong></td>
<td><strong>9</strong></td>
<td><strong>20</strong></td>
</tr>
</tbody>
</table>

**Anti-reflux Operations**

The efficiency of these operations has been examined
in a previous report (Scott, 1966). Although it is now
possible to guarantee in a suitable case that reflux can
be eliminated by means of the ureteric reimplantation
operation, some of the early cases in this series were
treated by other operations with less success (Table I).
There were 6 children with 8 ureters in which the anti-
reflux operation was a failure. 3 of these children had
second operations (Table II), the original procedure
being replaced by ureteric reimplantation. In 2 this
was successful but in the third, though the reflux had
apparently been eliminated 6 months after operation, it
was again seen in a cystogram 3 years later. Besides
the operation failures there were another 4 children in
whom unilateral reflux was successfully treated but
reflux appeared in the opposite ureter at a later date.
Altogether then there were 8 children in the operation
group who had persistent reflux in 10 of their ureters,
whether on operated or unoperated sides at either 6
months, 3 years, or both. It was decided that for the
purposes of the trial these cases should be withdrawn
from the operation group.

Open revision of the bladder neck was carried out in
20 children. In 14 a Y-V plasty was done and in 6 the
operation was limited to division of the muscle fibres
across the anterior margin of the bladder neck. These
cases were evenly distributed between the two groups
(Table III).

**Results**

Two of the operated cases and one control could
not be traced at the end of the 3-year period and
were excluded from the trial. As previously
mentioned, 8 cases in the operation group were
also excluded because their reflux had persisted.
With these adjustments, there remained 23 success-
fully operated cases for comparison with 24 controls.
The two groups were well matched (Tables IV and
V). There were no significant differences in sex,
age at onset, length of history, and previous treat-
ments, nor in radiological and cystoscopic findings.

**Reflex in control cases.** During the 3-year
period, there was a change in the state of reflux in
11 cases in the control group. In 6 the reflux,
which had been unilateral in all but 1, disappeared
entirely. In 2 further cases with bilateral reflux,
there was spontaneous disappearance on one side
only. The remaining 3 children had unilateral
reflux at the beginning of the 3-year period, and
bilateral reflux at the end. Thus in the control
cases reflux disappeared spontaneously in 9 (27%)
of 33 refluxing ureters, and appeared in 3 (21%)
of 14 ureters originally without demonstrable
reflux. The only outstanding feature about the 6
children in whom reflux disappeared entirely was
that it was unilateral in 5 of them. They did not
differ significantly in any other respect from the
remainder of this group.

**Urinary infection.** Relapse of infection occurred
in 10 children in the operated group and in 16
in the control group (Table VI). The difference
between the groups was not large; however, not
only did more of the controls become reinfected
but they tended to do so more frequently. During
the 3-year period only 2 of the operated group had
more than one relapse compared with 8 of the
controls. There were altogether 14 relapses amongst the children in the operated group and 32 in the control group. The difference seems unlikely to be a chance variation ($x^2 = 6.4; n = 1; 0.02 > p > 0.01$). There was, therefore, a significantly higher incidence of relapse of infection amongst the children in the control group.

**Kidney growth.** The intravenous pyelogram films taken at the beginning and end of the 3-year period were carefully studied and the length of the kidneys measured. By using the whole series of films from each pyelographic investigation it was possible to delineate the upper and lower poles of the kidneys with reasonable accuracy. From these measurements, the change in the length of the kidneys was estimated and then corrected to provide a growth rate in mm. over a period of exactly 3 years. According to Hodson et al. (1962), increase in kidney length is a satisfactory guide to over-all kidney growth which normally proceeds at a constant rate between the ages of 4 and 15 years. Both kidneys in the same individual grow at approximately the same speed and do not usually differ in length by more than 5 mm. Kidneys that are infected tend to grow at a slower rate than normal. If bilaterally involved, the growth on the two sides may be equally depressed, but if only one kidney is affected it may well fail to grow while the opposite healthy kidney enlarges at a rate in excess of normal. Thus, one of the aims of treatment in a child with urinary infection and reflux is to achieve normal and equal kidney growth.

In Table VII details are given of the 3-year changes of kidney length in operation and control cases. Fig. 1 and 2 also show these graphically.

The following features seem evident: (1) Shrinking occurred in 2 kidneys in the operation group and 7 kidneys in the control group. (2) In 13 of the operated cases and 18 of the controls there was a disparity in the rate of growth of the 2 kidneys greater than 5 mm. in 3 years. (3) In general, when there was persistent unilateral reflux, the kidney on the affected side did not grow as well as its contralateral fellow. (4) The mean growth rate in

**TABLE IV**

Comparison of Operation and Control Cases at Beginning of Trial

<table>
<thead>
<tr>
<th></th>
<th>Operation Group (23 cases)</th>
<th>Control Group (24 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Female</td>
<td>19</td>
<td>21</td>
</tr>
<tr>
<td><strong>Age at onset of symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 year</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>1–5 years</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>&gt;5 years</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td><strong>Length of history</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 month</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1 month–1 year</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>&gt;1 year</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td><strong>Previous antibiotic treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>One course</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>&gt;one course</td>
<td>9</td>
<td>8</td>
</tr>
</tbody>
</table>

**TABLE V**

Radiological Findings in Operation and Control Cases at Beginning of Trial

<table>
<thead>
<tr>
<th></th>
<th>Pyelonephritic Scarring</th>
<th>Reflux</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Operation group (23 cases)</td>
<td>15</td>
<td>8</td>
</tr>
<tr>
<td>Control group (24 cases)</td>
<td>17</td>
<td>7</td>
</tr>
</tbody>
</table>

**TABLE VI**

*Urinary Infections During 3-year Period*

<table>
<thead>
<tr>
<th></th>
<th>Operation Group (23 cases)</th>
<th>Control Group (24 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reinfections during 3 years</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Multiple</td>
<td>2</td>
</tr>
<tr>
<td><strong>Urine at time of follow up</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sterile</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Infected</td>
<td>2</td>
</tr>
<tr>
<td><strong>Antibiotic treatment at time of follow up</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Discontinued</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>Still on treatment</td>
<td>4</td>
</tr>
</tbody>
</table>
the operation group was greater than in the control group. The difference was even more marked when kidneys whose reflux had been abolished by operation were compared with those with persistent reflux in the control group. It is unlikely that the differences between the means for kidney growth in the main or subgroups are due to chance variation (Table VII). Although these figures appear to be statistically significant, they are based on measurements of kidney length as seen on radiographs, and despite every effort to ensure accuracy, it is possible that some of them are erroneous since the renal outline was occasionally difficult to see.

**Discussion**

This trial has not been ideal. The number of cases included is small and it was known which cases had had operations and which were controls so that there may have been an unconscious bias in assessing the results. However, while the trial was in progress we were disappointed that re-infections occurred so frequently in both groups, and up to the final analysis of the results we were inclined to think that operative treatment of the reflux had been of little value. Nevertheless, despite the limitations of the trial the findings do suggest that the surgical elimination of reflux in a child with

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**Fig. 1 and 2** (above and opposite).—Kidney growth rate in mm. per three years in each of the cases in the series. The heavy vertical lines indicate the mean normal growth rate and the mean ± 2 SD. Each horizontal line represents one case. The symbols in boxes represent pairs of kidneys with a growth rate equal to within 5 mm.
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CONTROL CASES

**TABLE VII**

*Growth of Kidneys During 3-year Period*

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Range of Length Change in 3 Years (mm.)</th>
<th>Mean 3 Year Growth (mm.)</th>
<th>S (n-1)</th>
<th>SE&lt;sub&gt;x&lt;/sub&gt;</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All kidneys</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operation group</td>
<td>45</td>
<td>-9.4 to +31.5</td>
<td>11.10</td>
<td>8.26</td>
<td>2.23</td>
<td>2.93</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Control group</td>
<td>47</td>
<td>-19.8 to +27.0</td>
<td>5.88</td>
<td>8.86</td>
<td>1.29</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Kidneys with refluxing ureters</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operation group</td>
<td>37</td>
<td>-9.4 to +31.5</td>
<td>10.09</td>
<td>7.97</td>
<td>1.31</td>
<td>3.34</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Control group</td>
<td>25</td>
<td>-19.8 to +20.0</td>
<td>2.73</td>
<td>8.85</td>
<td>1.77</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Non refluxing kidney
- Refluxing kidney
- Reflux ceased spontaneously
- Reflux appeared after beginning of treatment
- Contralateral nephrectomy

**SHRINKAGE** mm. per 3 years

**GROWTH** mm.
urinary tract infection will reduce to some extent
the likelihood of further infection and help to
protect the kidney from scarring. Even so, we do
not wish to suggest that surgery should be advised
for every child with ureteric reflux. In those with
unilateral reflux with no dilatation of the upper
urinary tract, minimal pyelonephritic scarring, and
a short history of urinary infection, it may be
justifiable to recommend conservative non-operative
treatment. Such a decision places on the clinician
the responsibility for carefully observing the child
to ensure that the infection is kept under control.
It is also advisable to repeat the cystogram after
one year. If the infection relapses and the reflux
does not disappear spontaneously, there are then
strong indications for surgery.

Summary
Fifty-eight children with urinary infection and
vesico-ureteric reflux were placed in a controlled
trial designed to determine the effectiveness of
surgery in this condition.

An anti-reflux operation was performed on
children selected by a random method. The cases
were then followed for 3 years and the incidence of
urinary infection and kidney growth rates were
assessed in the operated and unoperated cases.

It was found that the incidence of urinary infection
was higher and the mean kidney growth rate lower
in the unoperated cases.

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