Experimental Pyelonephritis XVII. Enhancement of Pyelonephritis by Water Diuresis Following Direct Inoculation of E. coli in the Renal Medulla of the Rat

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Recently, water diuresis has been shown to promote chronic Escherichia coli bacteriuria following the injection of bacteria into the bladder lumen of rats with normal urinary systems(1). However, maintenance of bacteriuria for periods up to 56 days has not resulted in renal lesions(1,2). Similar effects of water diuresis on bacteriuria have been observed in mice. In this species, however, severe pyelonephritis is a common and prominent finding in animals with bacteriuria of 3 weeks duration(3).

Water diuresis, therefore, seemed to increase the susceptibility of the mouse kidney to pyelonephritis. It was remarkable, however, that pyelonephritis did not occur in the rat despite prolonged exposure of the renal papilla to large numbers of bacteria growing in the urine. Since Andriole has demonstrated the protective effect of water diuresis on certain models of pyelonephritis in the rat(4–6) it seemed that one explanation for the difference in the effect of chronic bacteriuria in the mouse and rat was perhaps a difference in the effect of water diuresis on pyelonephritis in the two species.

Using the model of direct inoculation of bacteria into the renal papilla to produce pyelonephritis Keane was unable to show a protective effect of water diuresis in the mouse(7). The purpose of the present study was to determine the effect of water diuresis on the same model infection (direct papillary inoculation) of E. coli in rats. If rats were protected, it would be possible to explain the dif-

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ference in the effect of chronic bacteriuria maintained by water diuresis by the
difference in the effect of water diuresis on susceptibility to pyelonephritis in the
two species.

MATERIALS AND METHODS

White adult male Sprague–Dawley rats weighing 250–380 g were employed as
the experimental animals in all studies. Animals were housed in standard animal
cages, 2 or 3 animals per cage, and were provided with Purina Lab Chow pellets
ad libitum. Water diuresis was achieved by providing the animals free access to
solutions of 5% glucose in tap water. Experimental animals were provided this
solution 4 to 7 days prior to the day of receiving the test bacterial inoculum and
were maintained on this drinking solution until the time of bacteriological study.
Control rats were similarly housed and provided with free access to tap water.
Liquid consumption for all animals was measured daily. In no instance was the
drinking bottle allowed to be emptied.

The test bacteria was a strain of E. coli which has been employed in this lab-
oratory for many years and has been described elsewhere (8). The test inocula
were prepared from a 4.5-hr broth culture of the test organism, appropriately
diluted in sterile saline to attain the desired concentration. Inocula were enu-
merated by making agar pour plates of serial dilutions of the broth culture;
plates were counted after incubation at 37° for 24 hr.

The animals were anesthetized with sodium pentobarbital; supplemental ether
inhalation anesthesia was used as needed. After preparation of the abdomen by
shaving and washing with Zephiran® antiseptic solution, the urinary system was
exposed through a midline abdominal incision. Abdominal viscera were retracted
with sterile gauze soaked in sterile saline to expose the left kidney. The left
kidney was employed because of ease of accessibility in the abdominal cavity.
The kidney was brought into the wound and, using a 27-gauge needle, inocula-
tion was made into the renal inner medulla or papilla by inserting the needle
perpendicular to the anterior kidney surface, midway between the poles, at a
point about two-thirds the distance to the hilum from the lateral margin and
to a depth of about 4 mm. Volume of inocula was in all cases 0.05 ml of either
sterile saline or test inocula. Bacterial inocula were diluted to contain 1–3 × 10^3
viable bacterial units. Bleeding from the puncture site upon withdrawal of the
needle was readily controlled by light direct pressure with sterile gauze for 10–15
sec. In a small number of animals, a wedge-shaped zone of blanching was noted
immediately upon insertion of the needle into the kidney substance, with apex
at the puncture site and extending around the equator of the kidney. At the
time of death these animals were frequently found to have infarcts of the kidney
at the site of operative ischemia and were, therefore, systematically excluded
from the study when this observation was made at operation. In all animals, im-
mediately following puncture of the medulla, gross hematuria was observed in
peristaltic waves down the ureter; no hematuria was noted, however, at the time
of death. Care was taken to avoid manipulation of the left ureter.
Prior to inoculation of the kidney in some animals, the bladder was exposed and its contents aspirated through a 27-gauge needle. Using a second syringe, but employing the same needle, 0.05 ml of test inocula containing $1 \times 10^6$ viable bacterial units were injected into the bladder lumen. In this way the bladder wall was punctured only once. The urethra and ureters were not intentionally disturbed. Following these procedures, the peritoneum and abdominal muscle layers were closed in one layer using a 4-0 black silk. Abdominal skin was closed with metal wound clips.

Animals were killed 6 or 7 days following bacterial inoculation. After induction of anesthesia and preparation as described above, a large midline abdominal incision was made to expose the urinary system. After aspiration of bladder urine, both kidneys were removed aseptically and placed in sterile Petri dishes. Using sterile precautions the kidneys were longitudinally sectioned and examined for gross pathology. The organs were then placed in sterile grinding tubes and ground in 9.0 ml of sterile saline to prepare $10^{-1}$ dilutions; agar pour plates of 1.0 ml of these suspensions were made. In addition, loopfuls of each suspension and of bladder urine were streaked on both blood and deoxycholate agar plates using a 0.001-ml calibrated loop. Agar pour plates of the remaining volumes of urine were also made. All isolated organisms were identified as the test *E. coli* by their characteristic reactions on deoxycholate, Simmon’s citrate, and Kligler’s iron agar(8).

RESULTS

1. Effects of Water Diuresis

The effects of water diuresis produced by ingestion of 5\% glucose solution on the chemical composition of the rat kidney have been described elsewhere(4). Volume consumption for 53 control and 62 glucose-drinking animals is presented in Fig. 1. The first point for both animal groups represents the average consumption for the days prior to bacterial challenge and serves as a baseline for subsequent measurements. Both animal groups were seen to drink less during the immediate 24-hr period after inoculation but rapidly regained baseline levels. Animals drinking 5\% glucose were found to consume 3–4 times the volume of fluid consumed by animals drinking tap water. These results are similar to those previously described(1,4).

Specific gravity of bladder urine was measured at the time of inoculation and again at death. Rats drinking tap water were usually found to have urinary specific gravities greater than 1.030, whereas animals drinking 5\% glucose were usually found to have specific gravities below 1.015. During the present investigations, as in those of Andriole and Epstein(4) and Freedman(1), tests for glucosuria were consistently negative. It has been shown previously that no abnormality of glucose tolerance response could be demonstrated in rats drinking 20\% glucose solution for periods up to 1 year(1). Animals drinking 5\% glucose were frequently noted to have distended bladders. However, no gross evidence of hydronephrosis or hydroureter was noted in either animal group.
Animals drinking 5% glucose

Fig. 1. Average volume of fluid consumed per day by 62 animals drinking 5% glucose solution and 53 control animals drinking tap water. The first point represents the average consumption per day for 4 to 7 days prior to injection of the bacterial inocula.

Weight gain for both animal groups was comparable, control animals at the time of inoculation averaging 297 g, increasing to 308 g at the time of death. Animals drinking 5% glucose, during an identical time period, went from an average of 308 g to 319 g.

II. Effects of Water Diuresis on the Course of Infection Produced by Inoculation of $10^3$ E. coli into the Renal Medulla

Rats drinking 5% glucose solution and control animals drinking tap water were given injections of $10^3$ E. coli into the left renal inner medulla. Animals were killed 6 or 7 days later.

The study consisted of 35 animals in the experimental group drinking 5% glucose solution and 31 control animals drinking tap water. Results of bacteriological examinations are presented in Table 1. The majority of animals undergoing diuresis had large numbers of bacilli recovered from both kidneys and from the urine. Water drinkers, on the other hand, demonstrated persistence of bacteria in the left kidney but in lower numbers than those found in animals undergoing diuresis. Of animals undergoing water diuresis 86% were found to have $10^4$ or more viable bacterial units in the left kidney compared to 15% of controls ($p < .001$). Furthermore, 12 animals, 34% of those undergoing diuresis, were found at the time of death to have easily visible wedge-shaped abscesses of the left kidney, extending from an apex at the site of medullary puncture to the subcapsular cortex. A typical lesion is illustrated in Fig. 2. No gross lesions were identified in control animals.

Of animals undergoing diuresis 68% were noted to have $10^4$ or more viable bacterial units in the right kidney at the time of death as compared with 3% of controls ($p < .001$). Of animals undergoing diuresis, 86% as compared with 27% of controls were noted to have bacteriuria of $10^4$ or more viable bacterial units per milliliter ($p < .02$). These data demonstrate enhancement of bacteriuria and
spread of bacilli within the urinary system of animals undergoing water diuresis. No gross lesions were seen in the right kidney of any animal.

These results thus confirm previous demonstrations of the effects of water diuresis in promoting persistent bacteriuria and spread of bacilli (1), and further, demonstrate an enhancing effect of water diuresis on the susceptibility of the traumatized rat renal medulla to coliform infection.

It is known that renal medullary injury predisposes to bacterial infection (9-12), and that water diuresis increases susceptibility to prolonged bacteriuria in the

| TABLE 1 | INJECTION OF $10^2$ E. coli INTO THE LEFT RENAL MEDULLA OF Rats. Bacteriological Study 6 OR 7 Days Later. Kidneys Underlined Were Found to Have Gross Abscesses |
|---------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Rats drinking water | Rats drinking 5% glucose |
| Left kidney | Rt. kidney | Urine | Lt. kidney | Rt. kidney | Urine |
| $10^3$ | $10^2$ | 0 | $10^2$ | $10^2$ | $10^2$ |
| $10^4$ | $10^2$ | $10^3$ | $10^4$ | $10^4$ | $10^4$ |
| $10^5$ | $10^4$ | $10^6$ | $10^5$ | $10^5$ | $10^5$ |
| $10^6$ | $10^5$ | 0 | $10^6$ | $10^6$ | $10^6$ |
| $10^7$ | $10^6$ | $10^7$ | $10^7$ | $10^7$ | $10^7$ |
| $10^8$ | $10^7$ | $10^8$ | $10^8$ | $10^8$ | $10^8$ |
| $10^9$ | $10^8$ | $10^9$ | $10^9$ | $10^9$ | $10^9$ |
| $10^{10}$ | $10^9$ | $10^{10}$ | $10^{10}$ | $10^{10}$ | $10^{10}$ |
| $10^{11}$ | $10^{10}$ | $10^{11}$ | $10^{11}$ | $10^{11}$ | $10^{11}$ |
| $10^{12}$ | $10^{11}$ | $10^{12}$ | $10^{12}$ | $10^{12}$ | $10^{12}$ |
| $10^{13}$ | $10^{12}$ | $10^{13}$ | $10^{13}$ | $10^{13}$ | $10^{13}$ |
| $10^{14}$ | $10^{13}$ | $10^{14}$ | $10^{14}$ | $10^{14}$ | $10^{14}$ |
| $10^{15}$ | $10^{14}$ | $10^{15}$ | $10^{15}$ | $10^{15}$ | $10^{15}$ |
| $10^{16}$ | $10^{15}$ | $10^{16}$ | $10^{16}$ | $10^{16}$ | $10^{16}$ |
| $10^{17}$ | $10^{16}$ | $10^{17}$ | $10^{17}$ | $10^{17}$ | $10^{17}$ |
| $10^{18}$ | $10^{17}$ | $10^{18}$ | $10^{18}$ | $10^{18}$ | $10^{18}$ |
| $10^{19}$ | $10^{18}$ | $10^{19}$ | $10^{19}$ | $10^{19}$ | $10^{19}$ |
| $10^{20}$ | $10^{19}$ | $10^{20}$ | $10^{20}$ | $10^{20}$ | $10^{20}$ |

a Colonies per kidney.
b Colonies per milliliter.
It was possible, therefore, that the high incidence of gross abscesses with medullary inoculations in animals undergoing water diuresis might have resulted from prolonged bacteriuria in the presence of a damaged and hence susceptible kidney. Experiments were designed to test this possibility.

III. Effects of Water Diuresis on the Course of Infection Produced by Inoculation of $10^3$ E. coli into the Bladder Lumen in Animals with Traumatized Left Kidneys

Rats drinking 5% glucose solution and control rats drinking tap water were given inoculations of $10^3$ E. coli into the bladder lumen. At the same time, 0.05 ml of sterile saline was injected into the left renal medulla. Animals were killed 6 or 7 days later.

The study consisted of 27 animals in the experimental group drinking 5% glucose solution and 22 animals drinking tap water. Results of bacteriological examinations are presented in Table 2. Bacterial cultures demonstrated large numbers of bacteria in both kidneys and in the urine of most animals undergoing water diuresis, whereas organisms were rarely recovered from the organs and urine of control animals. No gross lesions were identified in the kidneys of control animals. However, two animals, 7% of those undergoing diuresis, were found to have gross abscesses of the left kidney. These abscesses were indistinguishable morphologically from abscesses produced by direct inoculation of E. coli into the renal medulla of animals undergoing diuresis. One of the lesions is shown in Fig. 3. No gross lesions of the right kidneys were found.

The production of pyelonephritis in the traumatized kidney by inoculation of bacteria into the bladder lumen of animals undergoing diuresis demonstrates that water diuresis promotes ascending infection in the presence of acute damage to the renal medulla. However, the 7% frequency of gross lesions in this group differs significantly from the frequency of 34% produced by direct inoculation

Fig. 2. Gross abscess in the kidney of a rat undergoing water diuresis following the inoculation of $10^3$ E. coli into the left renal medulla. Scale in centimeters.
Fig. 3. Gross abscess in the traumatized kidney of a rat undergoing water diuresis, following the inoculation of $10^6$ E. coli into the bladder lumen. Scale in centimeters.

### Table 2
**Injection of $10^6$ E. coli into the Bladder Lumen of Rats with Traumatized Left Kidneys.**

**Bacteriological Study 6 or 7 Days Later. Kidneys Underlined were Found to Have Gross Absceses**

| Rats drinking water | Rats drinking 5% glucose |
|---------------------|-------------------------|
| Lt. kidney*       | Rt. kidney*                           | Urine* | Lt. kidney*       | Rt. kidney*                           | Urine* |
|-------------------|--------------------------|--------|-------------------|--------------------------|--------|
| $10^1$            | 0                        | 0      | $10^6$            | $10^6$                   | $10^6$ |
| 0                 | 0                        | 0      | $10^5$            | $10^5$                   | $10^5$ |
| 0                 | 0                        | 0      | $10^5$            | $10^5$                   | $10^5$ |
| $10^2$            | 0                        | $10^4$ | $10^2$            | $10^2$                   | $10^2$ |
| 0                 | 0                        | 0      | $10^2$            | $10^2$                   | $10^2$ |
| $10^3$            | 0                        | 0      | $10^2$            | $10^2$                   | $10^2$ |
| 0                 | 0                        | $10^2$ | $10^2$            | $10^2$                   | $10^2$ |
| 0                 | 0                        | 0      | $10^2$            | $10^2$                   | $10^2$ |
| 0                 | 0                        | 0      | $10^2$            | $10^2$                   | $10^2$ |
| 0                 | 0                        | 0      | $10^2$            | $10^2$                   | $10^2$ |
| 0                 | 0                        | 0      | $10^2$            | $10^2$                   | $10^2$ |
| 0                 | 0                        | 0      | $10^2$            | $10^2$                   | $10^2$ |
| 0                 | 0                        | 0      | $10^2$            | $10^2$                   | $10^2$ |
| 0                 | 0                        | 0      | $10^2$            | $10^2$                   | $10^2$ |
| 0                 | 0                        | 0      | $10^2$            | $10^2$                   | $10^2$ |
| 0                 | 0                        | 0      | $10^2$            | $10^2$                   | $10^2$ |
| 0                 | 0                        | 0      | $10^2$            | $10^2$                   | $10^2$ |
| 0                 | 0                        | 0      | $10^2$            | $10^2$                   | $10^2$ |
| 0                 | 0                        | 0      | $10^2$            | $10^2$                   | $10^2$ |
| 0                 | 0                        | 0      | $10^2$            | $10^2$                   | $10^2$ |

* Colonies per kidney.

* Colonies per milliliter.
of bacteria into the kidney \((p < .02)\). Thus, the frequency of infection produced by direct inoculation of bacteria into the renal medulla in animals undergoing water diuresis is significantly higher than can be explained by the ascending infection of a previously damaged kidney under circumstances of chronic bacteriuria maintained by water diuresis. This difference establishes that water diuresis exerts a direct effect on renal medullary susceptibility to infection in the presence of acute medullary injury.

IV. Effects of Water Diuresis on the Course of Infection Produced by Intravenous Inoculation of E. coli in Animals with Traumatized Left Kidneys

Experiments by other investigators have demonstrated that water diuresis protects against Hemalogenous pyelonephritis in certain model systems \((1-6)\). It was possible therefore that the effects of water diuresis on renal susceptibility to infection depended on the route by which the bacteria reached the kidney. Experiments were designed to test this possibility.

Rats drinking 5\% glucose solution and control animals drinking tap water were given inoculations of 0.05 ml of sterile saline into the left renal medulla. At the same time 0.5 ml of undiluted 4.5-hr broth culture of the test E. coli, containing \(10^8\) bacterial units, were injected via the tail vein. Animals were killed after 4 days.

The study consisted of 19 animals in the experimental group drinking 5\% glucose solution and 21 animals drinking tap water. Results of bacteriological examinations are presented in Table 3. Bacterial cultures demonstrated large numbers of bacteria in both kidneys and in the urine of most animals in both groups. Furthermore, 78\% of glucose-drinking animals and 76\% of animals drinking tap water were found to have gross abscesses of the left kidney; these percentages are not significantly different. No gross lesions were noted in the right kidney of any animal. It thus appeared that, in the presence of acute damage to the renal medulla, water diuresis did not prevent pyelonephritis when E. coli were injected into the blood stream whereas the same conditions of renal damage and water diuresis resulted in increased susceptibility to infection when bacteria were injected into the renal medulla or bladder lumen.

DISCUSSION

Experiments have been presented which confirm previous demonstrations that water diuresis promoted chronic bacteriuria and spread of bacilli within the urinary system of rats. The present studies went on to show that water diuresis increased the susceptibility of the rat renal medulla to infection resulting from direct inoculation of E. coli. Furthermore, this effect on medullary susceptibility did not arise from persistent bacteriuria in the presence of an acutely damaged kidney, but rather represented an effect on the susceptibility of the renal medulla itself to coliform infection. The present studies also demonstrated that, in the presence of acute damage to the renal medulla, water diuresis had no significant effect on the course of hematogenous E. coli pyelonephritis.
In both rats and mice, water diuresis has been previously shown to decrease bladder clearance of *E. coli* and hence facilitate bacteriuria (1,3). In those studies, severe pyelonephritis was commonly found in mice following prolonged bacteriuria whereas no renal lesions were noted in rats. Further studies by Keane have demonstrated that the same water diuresis that promotes bacteriuria does not protect the mouse kidney against pyelonephritis produced by direct inoculation of *E. coli* into the renal medulla (7). The present investigations suggest that the absence of renal lesions in rats with prolonged bacteriuria cannot be attributed to a protective effect of water diuresis on the renal medullary tissues. Rather, it appears that water diuresis in the rat enhanced the intrinsic susceptibility of the renal medulla to infection when bacteria were injected directly into the kidney substance. The data suggest that the species difference concerning the effects of chronic bacteriuria maintained by water diuresis on the course of infection in rats and mice centers on the ability of bacteria to invade the renal papillary tissues from the renal pelvic urine. Little is known of the factors which are of significance in this process.

These data are remarkable in that investigations by other workers have demonstrated opposite effects of water diuresis on the susceptibility to pyelonephritis in certain model systems. Andriole and Epstein (4–6) have shown that water

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**TABLE 3**

**INJECTION OF 10⁶ *E. coli* INTRAVENOUSLY IN RATS WITH TRAUMATIZED LEFT KIDNEYS.**

**BACTERIOLOGICAL STUDY 4 DAYS LATER. KIDNEYS UNDERLINED WERE FOUND TO HAVE GROSS ABSCESSES**

| Rats drinking water | Rats drinking 5% glucose |
|---------------------|--------------------------|
| Lt. kidney⁹         | Rt. kidney⁹              | Urine¹⁰            | Lt. kidney⁹ | Rt. kidney⁹ | Urine¹⁰ |
| 10⁶                | 10⁴                      | 10⁴                | 10⁶         | 10⁴         | 10⁶     |
| 10⁵                | 10⁴                      | 10⁴                | 10⁵         | 10⁵         | 10⁵     |
| 10⁴                | —                        | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10³                | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10²                | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10¹                | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁰                | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻¹               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻²               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| Lt. kidney          | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| Rt. kidney          | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10³                | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10²                | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10¹                | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁰                | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻¹               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻²               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻³               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻⁴               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻⁵               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻⁶               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| Lt. kidney          | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| Rt. kidney          | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10³                | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10²                | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10¹                | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁰                | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻¹               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻²               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻³               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻⁴               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻⁵               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻⁶               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻⁷               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻⁸               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |
| 10⁻⁹               | 10⁴                      | 10³                | 10⁵         | 10⁵         | 10⁵     |

⁹ Colonies per kidney.

¹⁰ Colonies per milliliter.
diuresis can protect the rat kidney against pyelonephritis produced by Staphylococcus aureus, Candida albicans, and Streptococcus faecalis. The same conclusion has been inferred from studies of dehydration where it was shown that pyelonephritis due to Escherichia coli occur under conditions where it does not normally occur. Of particular interest is the fact that the strain of E. coli tested was identical to that used in the present experiments(6). These studies, were performed in animals with nonobstructed urinary systems. A variety of factors may be involved in this protective effect of diuresis against infection, including enhancement of inflammatory response to injury(13), decreased medullary osmolality(4-6) with accompanying improvement in phagocytosis of bacteria by leukocytes(14), and dilution of renal medullary anti-complementary substances(15). The relative importance of these factors and others on susceptibility to infection remains unclear.

In the present studies, on the other hand, trauma to the medulla by needle puncture resulted in a localized zone of “intrarenal hydronephrosis”(9,10,16) involving those tubules passing through the involved zone of medulla. Thus, unlike the studies of Andriole and Epstein, localized zones of tubules were obstructed. The lack of protective effect of diuresis in this system was perhaps due to isolation of these obstructed tubules from participation in those pathophysiological processes implicated in the protective effect of water diuresis in nonobstructed urinary systems. Also, Gottschalk and Mylle, in micropuncture studies of the rat kidney, have shown that water diuresis, in association with urinary obstruction, led to marked elevation of intratubular pressures; in the absence of obstruction, diuresis resulted in only a small increase in intratubular pressures(17). In the present investigations it is possible, therefore, that water diuresis, in association with tubular obstruction produced by medullary trauma, resulted in increased intratubular pressures and hence an enhanced susceptibility to infection. In the absence of obstruction, with no substantial rise in tubular pressures, other effects of diuresis may play a role opposite to that demonstrated in the present studies. Even this is not clear, however, since previous studies in the mouse have demonstrated increased susceptibility to ascending pyelonephritis associated with water diuresis in the undamaged kidney(3).

In conclusion, it would appear that the effect of water diuresis on the immediate and late consequences of urinary tract infection is not a simple matter and seems to depend on the nature of the infective lesion, its location within the urinary tract, and the host species under study.

SUMMARY

The injection of E. coli into the renal medulla of the rat produced gross lesions of pyelonephritis when animals were undergoing water diuresis but not when animals were drinking tap water. The frequency of infection was significantly higher than could be explained by the ascending infection of a previously damaged kidney under circumstances of chronic bacteriuria maintained by water diuresis.
Thus, water diuresis increased the susceptibility of the rat kidney to pyelonephritis when the underlying renal lesion was a localized zone of intrarenal hydronephrosis. Others have shown different effects of water diuresis with different model infections in the rat.

Previous experiments have demonstrated a difference in the susceptibility of mouse and rat kidneys to pyelonephritis during the course of prolonged bacteriuria maintained by water diuresis. The results of the present study suggest that the explanation for this species difference in susceptibility to pyelonephritis rests not with the effect of water diuresis on renal parenchymal infection but rather with some defense mechanism at the point of contact of the renal papillary epithelium with bacteria in the renal pelvic urine.

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