Water diuresis has different effects on the outcome of urinary infections in rodents depending on the test organism, the route of inoculation, and the species of animal used. In rats, the production of pyelonephritis following hematogenous inoculation of Staphylococcus aureus, Candida albicans or Streptococcus faecalis was prevented or cured by water diuresis. The possible mechanisms by which diuresis exerts its beneficial effects include: increasing the speed with which leukocytes are mobilized to sites within the kidney where bacteria are deposited; aiding the process of phagocytosis per se; or delivering greater amounts of blood-borne defense factors such as complement and antibody.

On the other hand, water diuresis interfered with the clearance of E. coli inoculated directly into the bladder lumen of rats and, in mice, resulted in severe pyelonephritis with papillary necrosis.

In the present study, the effect of water diuresis on both hematogenous and direct bladder injections was tested in mice using Pseudomonas aeruginosa and Staphylococcus aureus to determine whether the discrepancy in the effect of water diuresis was a result of species difference, test organisms, or route of inoculation. Because it was observed that fluid intake was severely interrupted following bacterial challenge, the effect of direct bladder inoculation of Escherichia coli on the intake of tap water or 5 percent glucose was re-examined and correlated with bacterial clearance from the bladder urine.

MATERIAL AND METHODS

Mice: Albino male mice, Swiss strain (random bred, specific pathogen free, Yale University), weighing 20 to 25 grams, were used as experimental hosts in all experiments. Animals were housed in air-conditioned quarters in groups of six mice per cage and were given Purina laboratory chow ad libitum.

Water diuresis: The drinking solution of 5 percent glucose (w/v) in sterile distilled water was changed daily. Control mice were given tap water. The total fluid intake of...

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the mice grouped in a single cage was measured daily. As a rule, animals were given the test drinking solution 4 days before inoculation of bacteria.

Bacteria: The *Ps. aeruginosa*, a hospital isolate from a clinical specimen, was grown in trypticase soy broth (Baltimore Biological Laboratories) for 18-20 hours at 37°C and appropriately diluted in physiological saline solution for animal inoculations. Quantitative analysis of the inoculum for each experiment was made by surface plating serial tenfold dilutions on blood agar base (Difco Laboratories) and counting the plates after overnight incubation at 37°C. The strain of *S. aureus* used in these studies had been used previously and was maintained by regular transfer on blood agar plates. Because it appeared to have decreased in virulence, the organism was passed in mice and the recovered isolate designated *S. aureus-F*. The *E. coli* was the strain used in previous studies on experimental pyelonephritis in this laboratory. Preparation of inocula for both these organisms was as described for *Ps. aeruginosa*.

**Intrablañer inoculation:** After mice were anesthetized with ether, the abdomen was washed with 70 percent ethyl alcohol and the bladder exposed by a small abdominal incision. Urine was aspirated through a 27 gauge needle. With a second syringe, 0.1 ml. of the appropriate dilution of the bacterial inoculum was introduced into the bladder lumen in the area of the dome between the ureters. To avoid renal damage or urinary obstruction, the kidneys, ureters and urethra were not intentionally manipulated during the operation. The incision was closed by suturing the muscular abdominal wall and then applying a single clamp to the outer skin layer.

**Intravenous inoculation:** Injection of 0.5 ml. of the appropriate dilution of the bacterial inoculum was made into a lateral tail vein of lightly ether-anesthetized mice.

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**Fig. 1.** Bacteriological findings 7 days after the intravenous inoculation of 10⁸ *Ps. aeruginosa*. The distribution of bacteria is indicated according to pairs of kidneys in this and similar figures to follow.
Sacrifice procedure: All mice were sacrificed after 7 days by ether anesthetization, the urine aspirated and the bladder and kidneys removed. The kidneys were sectioned coronally and examined closely for evidence of abscesses. The organs were homogenized in glass grinding tubes containing 0.9 ml. sterile saline solution and 0.1 ml. samples quantitatively analyzed for bacteria by the surface plating technique. The counts were recorded as numbers of organisms per ml. of urine, entire bladder, or per individual kidney.

RESULTS

Intravenous Ps. aeruginosa infection

Groups of 25 mice drinking 5 percent glucose or tap water were inoculated with $1 \times 10^7$ Ps. aeruginosa. The rate of production of pyelonephritis was identical for both groups, that is, 34 percent of the examined kidneys had visible abscesses (Fig. 1). This rate of production of pyelonephritis by the hematogenous route was lower than that reported by Gorrill and DeNavasquez using a different strain of Ps. aeruginosa but was considered suitable for these studies on the effect of water diuresis on renal infection. As shown in Figure 1, the distribution of the numbers of bacteria recovered from the urine, bladder tissue and kidneys was similar for those mice drinking 5 percent glucose and for those drinking water. Eight of the 25 pairs of kidneys from mice drinking 5 percent glucose contained $10^6$ organisms as compared to 9.5 pairs in the control group. Between 50 and 60 percent of the urines and bladder tissues had fewer than $10^4$ Ps. aeruginosa recovered.

Intrabladder Ps. aeruginosa infection

The results (Fig. 2) showed that 6 out of 24 control mice had more than $10^9$ Ps. aeruginosa present in the urine seven days after inoculation of $1 \times 10^7$ organisms. In those animals drinking 5 percent glucose, 10 out of 24 urines contained more than $10^9$ bacteria per ml. Between $10^8$ and $10^4$ bacteria were recovered from 50 to 60 percent of the bladder tissues of both groups while fewer than $10^3$ Ps. aeruginosa were recovered from the kidneys.

In order to examine this effect of water diuresis more closely, groups of 12 mice on water or 5 percent glucose were infected with $10^4$, $10^5$, or $10^6$ Ps. aeruginosa. The results indicated that drinking 5 percent glucose did not influence the rates of infection and that the frequency of infection varied directly with the size of the inoculum.

Effect of infection on fluid intake

Since the effect of water diuresis on infection was actually an examination of the effect of increased fluid intake and presumably increased urine output by the kidneys, fluid intake was measured daily. On the average there was a
Fig. 2. Bacteriological findings 7 days after the inoculation of $10^7$ *Ps. aeruginosa* into the bladder lumen.

Fig. 3. Fluid intake following challenge with $10^7$ *Ps. aeruginosa*. The figures for intake at day zero represent the 24 hours prior to bacterial inoculation. The times indicated are days after bacterial challenge in this and similar figures to follow.
4 day conditioning period before inoculation during which the water intake by the control mice undergoing diuresis was between 20 and 25 ml. per day per mouse. As described by Furtado and Gorrill the number of *Ps. aeruginosa* surviving 24 hours after inoculation can be quantitatively related to the production of gross experimental pyelonephritis in mice. Therefore, fluid intake was carefully measured during these 24 hours and daily for the entire period until sacrifice.

Fluid intake was severely interrupted during the 24 hours immediately after inoculation in both the group drinking 5 percent glucose (which dropped from over 20 ml. before inoculation to 3.5 ml.) and in the water group (a drop from 8.3 to 3.3 ml.) regardless of the route of inoculation (Fig. 3). Thus, all animals drank approximately equal amounts of fluid for the first 24 hours after bacterial challenge. During the next 24 hours the fluid intake for all groups improved, with those mice drinking 5 percent glucose drinking at least twice the amount of water consumed by controls. However, the pre-challenge levels of fluid intake were not attained until at least 5 days after inoculation. These patterns of drinking occurred regardless of the route of inoculation of the organisms and so could not be attributed to the effects of operation when bacteria were inoculated into the bladder lumen.

**Effect of water diuresis on *S. aureus* infections**

Groups of 18 mice drinking water or 5 percent glucose were given $1 \times 10^7$ *S. aureus* by intravenous inoculation. Animals drinking 5 percent glucose had gross abscesses characteristic of pyelonephritis in 80 percent of the kidneys and water controls had abscess rates of 95 percent. Animals were examined 7 days after inoculation (Fig. 4). Most of the urines and kidneys contained more than $10^9$ *S. aureus*. Drinking 5 percent glucose, therefore, did not significantly affect the distribution of bacteria in the urine or kidneys.

When the same number of organisms was introduced into the bladder lumen the distribution of numbers of bacteria recovered was different from that seen after hematogenous inoculation. Kidney infection was unusual and of the 18 urine specimens from mice drinking water, 8 contained more than $10^9$ *S. aureus*. The results were similar in the group drinking 5 percent glucose (Fig. 5). The number of bacteria recovered from the bladder tissues of both groups was evenly distributed among the three categories.

**Effect of *S. aureus* infection on fluid intake**

Fluid intake sharply fell in the 24 hours immediately following intravenous or direct bladder inoculation of $10^7$ *S. aureus* (Fig. 6). Following
intravenous challenge the consumption of 5 percent glucose dropped from a prechallenge level of 24 ml. to 6 ml. and slowly increased to 10 ml. by day 4. This was different from that observed by Andriole and Epstein for rats in which fluid consumption remained the same or actually increased following S. aureus challenge. In mice no significant protective effect was evident by day 7 even when the animals had access to 5 percent glucose throughout.

The fluid consumption by water controls fell from 8.3 ml. before challenge to slightly over 1 ml. during the first 24 hours after inoculation. Therefore, the ratio of fluid intake for these groups for days 2 through 4 was approximately 2:1. However, excluding the 24 hour period immediately following challenge, the "diuresis" maintained was much less than that reported for rats infected with S. aureus. Direct bladder inoculation also produced a similar interruption in drinking. Pre-challenge levels of fluid intake for either groups was not resumed before day 5.

Thus it was apparent that drinking was severely interfered with following intravenous or intrabladder inoculation of pseudomonas or staphylococci, thereby preventing adequate testing of the effects of water diuresis on these infections in mice.
Fig. 5. Bacteriological findings 7 days after the inoculation of 10⁶ Staphylococcus aureus into the bladder lumen.

Fig. 6. Fluid intake following challenge with 10⁶ Staphylococcus aureus.
Effect of *E. coli* on fluid intake

It had previously been demonstrated in mice that drinking 5 percent glucose did interfere with the bladder clearance of *E. coli*. Since fluid intake had not been carefully measured immediately after operation in previous studies when *E. coli* was the infecting organism, experiments were conducted in which $10^5$, $10^6$, or $10^7$ *E. coli* were introduced by direct bladder inoculation in mice drinking 5 percent glucose or water. Fluid intake for the animals undergoing diuresis dropped from a pre-challenge level between 20 and 25 ml. to between 7 and 9 ml. in the 24 hours immediately following inoculation. The level of intake for animals drinking 5 percent glucose was more than double the water intake of slightly more than 3 ml. by the controls (Fig. 7).* This relationship was maintained throughout the post-inocu-

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*Fig. 7. Fluid intake following challenge with different inocula of *E. coli*.

*The decreased intake of mice drinking tap water as compared with mice drinking 5 percent glucose was significantly different at the level $p = .05$ for days 1 and 2 and at the level $p < .01$ for days 1 through 4 (Wilcoxon Rank Sum Test).
lation period, which again required at least 5 days to attain pre-challenge levels of fluid intake. In these studies 10⁸ or more *E. coli* were recovered from between 33 and 66 percent of the urines from mice undergoing diuresis as compared to none in the water group, thus confirming previously reported data. The frequency and magnitude of bacteriuria was a reflection of the dose of the inoculum and there was a difference in susceptibility to urine infection between the animals drinking 5 percent glucose and those drinking water.

The pattern of water drinking following the intrabladder inoculation of *E. coli* was similar to that following the inoculation of pseudomonas or staphylococci. Nevertheless, the bladder clearance of *E. coli* was impaired by drinking 5 percent glucose whereas the clearance of pseudomonas and staphylococci was unaffected. It seemed important, therefore, to examine the clearance of bacteria in the days immediately following the inoculation of bacteria.

*Early events following *E. coli* inoculation*

10⁸ *E. coli*: Groups of 22 mice were inoculated with 5 × 10⁸ *E. coli*, assigned consecutive numbers, and by use of a random numbers table selected for sacrifice 24, 48, and 72 hours after challenge. There was a difference in the numbers of bacteria recovered from the urine samples of mice drinking water and those animals drinking 5 percent glucose as soon as 24 hours after inoculation (Table 1). In the water group, 4 out of 7 mice had fewer than 10⁸ *E. coli* per ml. recovered from the aspirated urines. Only 1 out of 7 mice drinking 5 percent glucose had fewer than 10⁸ *E. coli* per ml. while 4 out of 7 had 10⁸ or greater bacteria per ml. In both groups 4 out of 14 kidneys had 10⁴ or more *E. coli* at this time. The fluid intake for these 24 hours was 8.3 ml. for the mice drinking 5 percent glucose and 5.0 ml. for the water group, which represented a decrease from the pre-inoculation levels of at least 50 percent.

During the subsequent 24 hours, fluid intake increased to 12.5 ml. of 5 percent glucose and 7.8 ml. water. At sacrifice after 48 hours only 2 out of 8 urines from the water animals contained 10⁴ or more *E. coli* as compared to 100 percent of the animals in the glucose group. At this time there were also greater numbers of organisms recovered from the kidneys of the glucose mice (8 out of 16 contained 10⁴ or more *E. coli*) than from the kidneys of the water animals (2/16).

An additional 24 hours did not result in any further change between the groups. While clearance was proceeding in the control group, as evident by 6 out of 7 urines containing fewer than 10⁸ *E. coli*, bacterial multiplication continued in the urinary tracts of mice undergoing diuresis. At the same
Table 1. Recovery of Bacteria 24 to 72 Hours Following Intrabladder Inoculation of 10⁶ E. coli

| Time (Hrs.) | Water (Ml.) | H₂O Urine Left | H₂O Urine Right | Glucose Urine | Glucose Left | Glucose Right |
|-------------|-------------|----------------|----------------|--------------|-------------|--------------|
| 24          | 5           | 10⁶            | 10³            | 10³          | 10³         | 10³          |
|             |             | 10⁶            | 10³            | 10³          | 10³         | 10³          |
|             |             | 10⁶            | 10³            | 10³          | 10³         | 10³          |
|             |             | 10⁶            | 10³            | 10³          | 10³         | 10³          |
|             |             | 10⁶            | 10³            | 10³          | 10³         | 10³          |
| 48          | 7.8         | 10⁶            | 10³            | 10³          | 10³         | 10³          |
|             |             | 10⁶            | 10³            | 10³          | 10³         | 10³          |
|             |             | 10⁶            | 10³            | 10³          | 10³         | 10³          |
|             |             | 10⁶            | 10³            | 10³          | 10³         | 10³          |
|             |             | 10⁶            | 10³            | 10³          | 10³         | 10³          |
|             |             | 10⁶            | 10³            | 10³          | 10³         | 10³          |
| 72          | 7.9         | 10⁶            | 10³            | 10³          | 10³         | 10³          |
|             |             | 10⁶            | 10³            | 10³          | 10³         | 10³          |
|             |             | 10⁶            | 10³            | 10³          | 10³         | 10³          |
|             |             | 10⁶            | 10³            | 10³          | 10³         | 10³          |

* Per ml. of urine or per entire kidney.
Table 2. Recovery of Bacteria 24 to 72 Hours Following Intrabladder Inoculation of 10⁷ E. coli

| Time Hrs. | Water (ML.) | Numbers of Bacteria Recovered* | Glucose | Kidney |
|-----------|-------------|-------------------------------|---------|--------|
|           |             | H₂O                            | Fluid (ML.) | Urine | Left | Right |
| 24        | 3.7         | 10⁷, 10⁷, 10⁷                 | 7.0     | 10⁴, 10⁴, 10⁴ |
|           |             | 10⁴, 10⁴, 10⁴                  | 10⁴, 10⁴, 10⁴ |
| 48        | 6.2         | 10⁷, 10⁷, 10⁷                 | 12.8    | 10⁴, 10⁴, 10⁴ |
|           |             | 10⁴, 10⁴, 10⁴                  | 10⁴, 10⁴, 10⁴ |
| 72        | 5.8         | 10⁷, 10⁷, 10⁷                 | 13.0    | 10⁴, 10⁴, 10⁴ |
|           |             | 10⁴, 10⁴, 10⁴                  | 10⁴, 10⁴, 10⁴ |

* Per ml. of urine or entire kidney.
time, fluid intakes had increased to 18 ml. of 5 percent glucose and 8.0 ml. of water.

10⁷ E. coli: Increasing the inoculum to 10⁷ E. coli resulted in similar decreases in drinking during the 24 hours following inoculation and similar patterns of bacterial clearance (Table 2).

Combining data from these two experiments, the comparison of the frequency of the finding of urine samples not at tap water, fluid intakes previous to some mouse bladder drinking decreased returned toward during of published during glucose small, glucose experiment and inoculation in the bladder, and showed further that this effect was demonstrable during the time when differences in fluid intake between groups were very small, it seemed important to test whether drinking 5 percent glucose established an effect on susceptibility to infection prior to the time of inoculation of bacteria.

Test of effect of increased fluid intake prior to bacterial challenge

For 4 days before challenge a group of 12 mice were offered 5 percent glucose and 12 animals were given tap water as drinking solutions. After inoculation of 10⁶ E. coli directly into the bladder lumen, 6 mice undergoing diuresis were continued on 5 percent glucose and 6 mice that had been on glucose were given water to drink following inoculation. Of the animals drinking water prior to challenge, 6 were kept on water for the entire experiment and 6 were given 5 percent glucose after bacterial challenge. Fluid intake for each group was measured daily. All mice were sacrificed on day 7.

Those animals kept on glucose throughout had 10⁶ or more E. coli recovered from 5 out of 6 urines and bladder tissues and in 50 percent of the kidneys (Table 3). In the group that had been on 5 percent glucose before and on water after inoculation only 1 out of the 6 urines contained 10⁶ bacteria and this animal had bacteria recovered from both kidneys. The remaining 5 mice had fewer than 10⁶ E. coli recovered from the urines and tissues.

When 5 percent glucose drinking was started only following challenge, 2 out of 6 urines had more than 10⁶ E. coli. Only 2 out of the 6 urines had fewer than 10⁶ bacteria. Those animals on water throughout the experiment
**Table 3. Influence of Fluid Intake on Intrabladder Infection Following 10⁶ E. coli**

| Fluid     | Number of Bacteria Recovered* | Kidney |
|-----------|-------------------------------|--------|
|           | Pre  | Post | Urine | Bladder | Right | Left  |
| Glucose   | Glucose | 10⁶  | 10⁶   | <10⁶    | <10⁶  |       |
|           | >10⁶ | >10⁶ | 10⁶   | 10⁶     | 10⁶   |       |
|           | >10⁶ | >10⁶ | 10⁶   | 10⁶     |       |       |
|           | >10⁶ | >10⁶ | >10⁶  | >10⁶    |       |       |
| Glucose   | H₂O   | <10⁶ | <10⁶  | <10⁶    | <10⁶  |       |
|           | <10⁶ | 10⁶  | <10⁶  | <10⁶    |       |       |
|           | <10⁶ | 10⁶  | <10⁶  | <10⁶    |       |       |
|           | <10⁶ | 10⁶  | <10⁶  | <10⁶    |       |       |
|           | >10⁶ | >10⁶ | >10⁶  | >10⁶    |       |       |
| H₂O       | Glucose | 10⁶  | 10⁶   | <10⁶    | <10⁶  |       |
|           | 10⁶  | 10⁶  | <10⁶  | <10⁶    |       |       |
|           | 10⁶  | 10⁶  | <10⁶  | <10⁶    |       |       |
|           | >10⁶ | >10⁶ | 10⁶   | 10⁶     |       |       |
| H₂O       | H₂O   | <10⁶ | <10⁶  | <10⁶    | <10⁶  |       |
|           | <10⁶ | <10⁶  | <10⁶  | <10⁶    |       |       |
|           | <10⁶ | <10⁶  | <10⁶  | <10⁶    |       |       |
|           | <10⁶ | 10⁶   | <10⁶  | <10⁶    |       |       |
|           | 10⁶  | 10⁶   | <10⁶  | <10⁶    |       |       |
|           | 10⁶  | 10⁶   | <10⁶  | <10⁶    |       |       |

* Per ml. of urine or per entire organ.

completely cleared the urinary tract of E. coli, that is, fewer than 10⁶ E. coli were recovered. Similar results were obtained using an inoculum of 10⁷ bacteria (Table 4).

Combining the data of both experiments (inocula of 10⁵ and 10⁷ bacteria) it is evident that there was a significant decrease in the clearance of E. coli from the bladder only in the group drinking glucose continuously (p < .01).

**Fluid intake.** Patterns of fluid intake were similar in both experiments (Fig. 8). All animals within each experiment drank the same amount of fluid 24 hours following challenge regardless of which fluid the group had been drinking before challenge. Thereafter, fluid intake increased in the groups drinking 5 percent glucose. Those animals that had been given water throughout drank least.

The greatest effect on clearance of E. coli, as reflected by large numbers of organisms recovered in the urine, occurred when 5 percent glucose drinking
Table 4. Influence of Fluid Intake on Intrabladder Infection Following 10^6 E. coli

| Fluid Pre | Number of Bacteria Recovered* | Fluid Post | Kidney Left | Kidney Right |
|-----------|-------------------------------|------------|-------------|--------------|
| Glucose   | <10^8                         | 10^6       | <10^6       | 10^6         |
|           | >10^6                         | >10^6      | 10^6        |              |
|           | >10^6                         | <10^6      | <10^6       |              |
|           | >10^6                         | >10^6      | >10^6       | 10^6         |
| Glucose   | >10^6                         | >10^6      | >10^6       | 10^6         |
| H₂O       | <10^6                         | 10^6       | <10^6       | <10^6        |
|           | <10^6                         | 10^6       | <10^6       | <10^6        |
|           | <10^6                         | 10^6       | <10^6       | <10^6        |
|           | 10^6                          | 10^6       | <10^6       | <10^6        |
|           | 10^6                          | 10^6       | <10^6       | <10^6        |
|           | 10^6                          | 10^6       | 10^6        | <10^6        |
|           | 10^6                          | 10^6       | 10^6        | <10^6        |
|           | >10^6                         | >10^6      | >10^6       | >10^6        |
| H₂O       | Glucose                       | 10^6       | 10^6        | <10^6        |
|           | 10^6                          | 10^6       | <10^6       | <10^6        |
|           | 10^6                          | 10^6       | <10^6       | <10^6        |
|           | 10^6                          | 10^6       | 10^6        | <10^6        |
|           | 10^6                          | 10^6       | 10^6        | <10^6        |
|           | >10^6                         | >10^6      | >10^6       | >10^6        |
| H₂O       | H₂O                           | <10^6      | 10^6        | <10^6        |
|           | <10^6                         | 10^6       | <10^6       | <10^6        |
|           | <10^6                         | 10^6       | <10^6       | <10^6        |
|           | <10^6                         | 10^6       | <10^6       | <10^6        |
|           | 10^6                          | 10^6       | <10^6       | <10^6        |
|           | 10^6                          | 10^6       | <10^6       | <10^6        |
|           | 10^6                          | 10^6       | <10^6       | <10^6        |
|           | 10^6                          | 10^6       | <10^6       | <10^6        |

* Per ml. of urine or per entire organ.

was continuous. Despite the severe interruption of drinking for 24 hours, increased fluid intake was rapidly resumed by day 2. Only the animals with the highest fluid intakes postoperatively had impaired clearance of E. coli from the bladder urine. Animals drinking glucose prior to inoculation had normal bladder clearance when changed to tap water after bacterial challenge. Thus, it appeared that drinking glucose prior to the inoculation of bacteria did not affect bladder clearance of bacteria unless glucose drinking was continued.

DISCUSSION

Previous experiments have demonstrated that the administration of 5 percent glucose to mice as drinking water increased their susceptibility to pyelonephritis and decreased bacterial clearance from the bladder urine following inoculation of E. coli into the bladder lumen. These observations
conflicted with those reported by Andriole and Epstein. The test models were different, however, so that the conflict could be attributed to the use of different animal species, different bacteria, or different routes of inoculation. The present series of experiments were designed to test these possibilities. Bacteria were tested which could infect the normal kidney. This type of infection was ameliorated by water diuresis in the rat. In the mouse, however, no effect of drinking 5 percent glucose was discernible. It appeared, therefore, that species difference was at least one of the explanations for the discrepancy in the effect of water diuresis.

Detailed study of the mice drinking 5 percent glucose revealed, however, that water diuresis was not maintained following the inoculation of bacteria, thus making it impossible to compare diuresis in rats and mice under these circumstances. The interruption of drinking noticed in the present experiments was comparable to that observed by Dubos and Schaedler in mice given endotoxin.

Nevertheless, the previous experiments testing susceptibility to *E. coli* infection in mice did show an effect of drinking 5 percent glucose3 and so these studies were repeated and careful attention directed to the fluid intake following bacterial challenge. Once again, it was found that mice drinking 5 percent glucose were less able to clear the bladder urine of bacteria than...
controls drinking tap water. It was noted, however, that even with *E. coli* as the test organism, fluid intake was decreased in a manner similar to that observed following the inoculation of pseudomonas and staphylococcus.

Thus, it was apparent that the effect of water diuresis on bacterial clearance was not only different between animal species but also different according to the bacteria being tested. Indeed, the difference in fluid intake between test and control mice 24 hours after inoculation of bacteria was insignificant. It is evident, therefore, that a diuresis was not maintained. Even more remarkable perhaps, is the fact that small differences in fluid intake, recorded from day 2 onward, following the inoculation of *E. coli* could have any effect at all on bacterial clearance mechanisms within the bladder. For this reason, detailed studies of the bacteriological events in the first days following intrabladder inoculation were undertaken.

Although there was a suggestion, as early as 24 hours after inoculation, that bacterial clearance might be impaired in mice drinking 5 percent glucose, it was not until 48 hours that differences were established that have been shown previously to persist for longer periods, as long as diuresis is maintained. Therefore, small differences in fluid intake, in the period from 24 to 48 hours after bacterial challenge, may be critical in determining whether the bacterial inoculum is cleared. The possible mechanisms accounting for the effect of increased fluid intake on bacterial clearance from the bladder have been considered previously.

Animals drinking glucose and then switched to tap water after bacterial challenge behave as normal animals, thus arguing against any effect of drinking 5 percent glucose prior to bacterial challenge.

On the other hand, those mice drinking tap water who were than changed to glucose had fluid intakes approximating the intakes of mice drinking glucose continuously, yet bladder clearance was not impaired. Closer examination of the drinking patterns reveals, however, that 48 hours following inoculation of bacteria, mice changed from water to glucose were not yet drinking 10 ml. per day whereas those animals drinking glucose continuously (Figs. 7, 8), in which bacterial clearance was impaired, were drinking more than 10 ml. per day. Since normal bladder clearance occurred in animals drinking tap water within 48 hours of inoculation (Table 2), it is not surprising that higher fluid intakes subsequent to 48 hours were without effect on normal bladder bacterial clearance.

An additional feature of the present study is the demonstration of a new model for the production of bacteriuria and pyelonephritis in normal mice by introducing *Pseudomonas aeruginosa* into the bladder cavity. The development of kidney infection does not require overfilling of the bladder, urinary obstruction, water diuresis, or renal injury.
SUMMARY

Experiments were conducted to test the effect of water diuresis (5 percent glucose drinking water) on pyelonephritis and bladder urine infection due to Ps. aeruginosa and Staphylococcal aureus. No difference was discernible between mice drinking 5 percent glucose and those drinking tap water. However, interruption of drinking following bacterial challenge with these microorganisms in the mouse prevented adequate testing of the effect of diuresis.

Re-examination of the adverse effect of 5 percent glucose drinking on E. coli bladder clearance confirmed previous studies and furthermore demonstrated the same diminution of drinking after bacterial challenge as was observed with pseudomonas and staphylococci. Drinking 5 percent glucose prior to the inoculation of E. coli did not decrease clearance from the bladder unless glucose drinking was continued after bacterial challenge.

The effect of "water diuresis" in the mouse on the bladder clearance of E. coli was correlated with small differences in fluid intake which existed in the first 24-48 hours following bacterial challenge. However, these small differences were not sufficient to influence the clearance of pseudomonas and staphylococcus.

The inoculation of Pseudomonas aeruginosa into the bladder lumen of the normal mouse results in kidney infection with abscess formation. No preceding damage to the urinary tract is required for the production of this infection.

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