## PENETRATION OF MICROORGANISMS FROM THE BLOOD STREAM INTO THE URINE THROUGH THE INTACT KIDNEYS

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Cultures of Escherichia coli, Proteus vulgaris, and Bacillus pyocyaneus, injected intravenously into rabbits, do not produce pathological changes in the kidneys and do not penetrate into the urine.

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In recent years clinicians have made increasing use of laboratory methods of diagnoisis of pyelone-phritis and, in particular, of the detection of bacteriuria as the earliest and often the only sign of this disease. However, the absence of a clear idea of the genesis of bacteriuria has prevented clinicians from making a correct interpretation of the results of bacteriological investigation of the urine for the diagnosis of pyelone-phritis.

Most clinicians [1-11] state that microorganisms can pass freely from the blood stream into the urine through the intact kidneys, and they consider that this is a physiological phenomenon.

The possibility of penetration of microorganisms from the blood stream into the urine through the intact kidney was studied in the present investigation.

## EXPERIMENTAL METHOD

Altogether three series of experiments were carried out on 26 adult rabbits of both sexes weighing from 2400 to 3400 g. A 24 h culture of Escherichia coli, Proteus vulgaris, and Bacillus pyocyaneus, the commonest agents of pyelonephritis in man, was used to infect the animals. In each series of experiments, 0.8 ml of a 24 h culture of one of these species of microorganisms, containing 800 million bacterial cells, was injected into the marginal vein of the ear of the rabbits. Before the operation, the rabbits received a subcutaneous injection of 1 ml of 1% morphine hydrochloride solution. After painting the operation area with 5% tincture of iodine, under ether anesthesia (using a mask) the urinary bladder was exposed through a midline lower laparotomy incision. Urine was obtained from the rabbits for bacteriological investigation on the first day under sterile conditions on the operating table by repeated puncture of the exposed urinary bladder. The urine was investigated before infection of the rabbits, and on the first day 15 min and 1, 2, 3, and 4.5 h after infection. On the following days urine was obtained from the rabbits for bacteriological investigation by the same method, before sacrifice. Blood was obtained from the rabbits for bacteriological investigation on the first day 50 min and 3.5 h after infection by puncture of the marginal vein of the ear, and 5 h later, before sacrifice, by puncture of the inferior vena cava. Cultures of blood and urine were made on sucrose broth and solid nutrient agar in petri dishes. Some rabbits were sacrificed on the first day of the experiment 5 h after infection, and the rest in the course of the next six days. Histological examinations were made of Kristeller sections; staining was with hematoxylin-eosin.

## EXPERIMENTAL RESULTS

Experiments of series I. Ten rabbits of each series received an intravenous injection of a 24 h culture of E. coli M-17. In two rabbits, sacrificed on the first day of the experiment, the bacteriemia caused by E. coli M-17 persisted for 3.5 h and disappeared completely 5 h after infection. Repeated bacteriological investigation of the urine of these rabbits 15 min and 1, 3, and 4.5 h after infection demonstrated absence of growth of the microorganism. At necropsy no pathological changes were found in the thoracic organs, liver, and spleen. The kidneys were not enlarged and showed no visible changes on section. Histological examination also showed no pathological changes in the glomeruli, tubules, interstitial tissue, or the calyces and

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pelvis of the kidneys. No growth of <u>E. coli</u> M-17 was found in the other 8 rabbits sacrificed at various times during the first 6 days after infection in cultures taken from the urine and blood. Histological examination of the kidneys of these rabbits revealed no collections of microorganisms or inflammatory changes in the parenchyma and pelvis of the kidneys.

Experiments of series II. A 24 h culture of P. vulgaris was injected intravenously into 8 rabbits of this series. During the first day after infection 4 rabbits were sacrificed. The remaining 4 animals were killed on the 2nd-6th day after infection.

A bacteriemia caused by P. vulgaris was present in all 4 rabbits sacrificed 24 h after infection. Meanwhile, repeated bacteriological investigation of the urine of these animals 15 min and 1, 2, 3.5, 5, and 24 h after infection revealed absence of growth of the microorganism. The kidneys of these rabbits were not enlarged, and showed no visible changes on section. Histological examination showed no changes in the glomeruli, tubules, interstitial tissue, and pelvis of the kidneys. No collections of microorganisms were found in the glomeruli, tubules, and vessels of the kidneys. In the other rabbits, sacrificed on the 2nd-6th day after infection, the blood and urine were sterile. Histological examination revealed no inflammatory changes in the pelvis and parenchyma of both kidneys. No collections of microorganisms likewise were found in the glomeruli, tubules, interstitial tissue, and blood vessels of the kidneys.

The results of this series of experiments showed that, despite the prolonged bacteriemia (24 h) after intravenous injection of P. vulgaris, microorganisms of this species do not produce changes in the kidneys and do not pass into the urine.

Experiments of series III. A 24 h culture of B. pyocyaneus was injected intravenously into 8 rabbits of this series; 2 rabbits were killed 5 h and 2 more 24 h after infection. The remaining 4 rabbits were killed 2-6 days after injection of the culture.

The blood and urine of the two rabbits sacrificed 5 h after intravenous injection of a 24 h culture of B. pyocyaneus were sterile before infection. In blood cultures taken 50 min, and 2 and 3.5 h after infection, growth of B. pyocyaneus was observed. Blood investigated 5 h after infection was sterile. Cultures of urine taken 15 min and 1, 2, 3.5, and 5 h after intravenous injection of the culture produced no growth of B. pyocyaneus. The kidneys were not enlarged and showed no visible changes on section. Histological examination of the kidneys revealed no changes in the glomeruli, tubules, intersitial tissue, and pelvis.

In the remaining 6 rabbits of this series of experiments, sacrificed 1-6 days after infection, B. pyocyaneus was absent from the blood and urine on bacteriological examination of the kidneys of these rabbits revealed no changes in the glomeruli, tubules, interstitial tissue, and pelvis.

The bacteriemia produced in rabbits by B. pyocyaneus thus persisted for the first 3.5 h and had completely disappeared 5 h after infection, but bacteriuria was never found either during the period of bacteriemia or later.

These experiments in which a 24 h culture of E. coli, P. vulgaris, and B. pyocyaneus, the commonest agents causing pyelonephritis in man, were injected intravenously into rabbits thus revealed that microorganisms of these species do not pass from the blood stream into the urine through the intact kidneys and do not produce pathological changes in the kidneys under normal physiological conditions.

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