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and
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Infection Following Prostatic Resection

Volume XX | Friday, February 4, 1949 | Number 15

BULLETIN OF THE
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I.

UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
CALENDAR OF EVENTS

February 6 - February 12, 1949

No. 234

Sunday, February 6

9:00 - 11:30 Surgery Grand Rounds; Station 22, U. H.
The Management of Metastases from Carcinoma of the Head and Neck; Stewart Arhelger; Rm. M-109, U. H.

Monday, February 7

8:00 - Fracture Rounds; A. A. Zierold and Staff; Ward A, Minneapolis General Hospital.

9:00 - 9:50 Roentgenology-Medicine Conference; L. G. Rigler, C. J. Watson and Staff; Todd Amphitheater, U. H.

9:00 - 10:50 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff; M-109, U. H.

10:00 - 12:00 Neurology Rounds; A. B. Baker and Staff; Station 50, U. H.

11:00 - 11:50 Roentgenology-Medicine Conference; Staff; Veterans Hospital.

11:00 - 11:50 Physical Medicine Seminar; Congenital Hips; Wesley Burnham; E-101, U.H.

11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Eustis Amphitheater, U. H.

12:00 - 1:00 Physiology Seminar; The Modifications of Enzyme Patterns with Protein Denaturants; Sol Spiegelman; 214 M. H.

12:15 - 1:20 Obstetrics and Gynecology Journal Club; Staff Dining Room, U. H.

12:30 - 1:20 Pathology Seminar; Propylthiouracid and the Hamster; D. F. Mitchell; 104 I. A.

12:30 - 1:30 Surgery Problem Case Conference; A. A. Zierold, C. Dennis and Staff; Small Class Room, Minneapolis General Hospital.

1:30 - 2:30 Surgery Grand Rounds; A. A. Zierold, C. Dennis and Staff; Minneapolis General Hospital.

1:30 - 2:30 Pediatric-Neurological Rounds; R. Jensen, A. B. Baker and Staff; U. H.

*2:00 - 4:00 Kellogg Lecture; Psychobiologic Dynamics; Adelaide M. Johnson, Mayo Foundation; Rm. 211 Zoology Bldg.

4:00 - Pediatric Seminar; Investigations on the Pathogenesis of Rheumatic Fever; Robert Good; 6th Floor, Child Psychiatry, U. H.

5:00 - 5:50 Clinical Medical Pathologic Conference; Todd Amphitheater, U. H.

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* Indicates special meeting. All other meetings occur regularly each week at the same time on the same day. Meeting place may vary from week to week for some conferences.

5:00 - 6:00 Urology-Roentgenology Conference; D. Creevy and H. M. Stauffer and Staffs; M-109, U. H.

Tuesday, February 8

8:00 - 9:00 Fracture Conference; Auditorium, Ancker Hospital.

8:30 - 10:20 Surgery Seminar; Cryptorchidism; David M. Anderson; Small Conference Room, Bldg. I, Veterans Hospital.

9:00 - 9:50 Roentgenology Pediatric Conference; L. G. Rigler, I. McQuarrie and Staff; Todd Amphitheater, U. H.

10:30 - 11:50 Surgical Pathological Conference; Lyle Hay and Robert Hebbel; Veterans Hospital.

12:30 - 1:20 Pathology Conference; Autopsies; Pathology Staff; 102 I. A.

1:00 - 2:30 X-ray-Surgery Conference; Auditorium, Ancker Hospital.

2:00 - 2:50 Dermatology and Syphilology Conference; H. E. Michelson and Staff; Bldg. III, Veterans' Hospital.

*2:00 - 4:00 Kellogg Lecture; Morphine and the Newer Analgesic Drugs; Victor H. Vogel, U.S.P.H.S. Hospital, Lexington, Kent; Todd Amph., U. H.

3:15 - 4:20 Gynecology Chart Conference; J. L. McKelvey and Staff; Station 54, U. H.

3:30 - 4:20 Clinical Pathological Conference; Staff; Veterans Hospital.

4:00 - 5:00 Pediatric Rounds on Wards; I. McQuarrie and Staff; U. H.

4:00 - 5:30 Surgery-Physiology Conference; Hydrocele; Stanley Friesen & Nathan Lifson; Eustis Amphitheater, U. H.

5:00 - 5:50 Urology-Pathological Conference; C. D. Creevy and Staff; Todd Amphitheater, U. H.

5:00 - 6:00 X-ray Conference; J. R. Aurelius and Staff; Ancker Hospital; Powell Hall Amphitheater.

Wednesday, February 9

8:00 - 8:50 Surgery Journal Club; O. H. Wangensteen and Staff; M-515, U. H.

8:30 - 9:30 Clinico-Pathological Conference; Auditorium, Ancker Hospital.

8:30 - 10:00 Orthopedic-Roentgenologic Conference; Edward T. Evans; Room 1AW, Veterans Hospital.

8:30 - 12:00 Neurology Rehabilitation and Case Conference; A. B. Baker and Joe R. Brown; Veterans Hospital.

11:00 - 12:00 Pathology-Medicine-Surgery Conference; O. H. Wangensteen, C. J. Watson and Staff; Todd Amphitheater, U. H.

12:00 - 12:50 Radio Isotope Seminar; Current Literature; George E. Moore; Rm. 216, Hospital Court, Temporary Bldg.

3:30 - 4:30 Journal Club; Surgery Office, Ancker Hospital.

4:00 - 5:00 Infectious Disease Rounds; Powell Hall Amphitheater.

Thursday, February 10

8:15 - 9:00 Roentgenology-Surgical-Pathology Conference; Craig Freeman and H. M. Stauffer; M-109, U. H.

8:30 - 10:20 Surgery Grand Rounds; Lyle Hay and Staff; Veterans Hospital.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; M-109, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:50 Surgery-Radiology Conference; Daniel Fink and Lyle Hay; Veterans Hospital.

11:00 - 11:50 Urology Seminar; Experimental Operation for Urinary Incontinence; Stanley Friesen; E-101, U. H.

11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Todd Amphitheater, U. H.

11:30 - 12:30 Clinical Pathology Conference; Steven Barron, C. Dennis, George Fahr, A. V. Stoesser and Staffs; Large Class Room, Minneapolis General Hospital.

12:00 - 1:00 Physiological Chemistry Seminar; 214 M. H.

1:00 - 1:50 Fracture Conference; A. A. Zierold and Staff; Minneapolis General Hospital.

2:00 - 3:00 Errors Conference; A. A. Zierold, C. Dennis and Staff; Large Class Room, Minneapolis General Hospital.

4:00 - 5:00 Bacteriology and Immunology Seminar; Genetic Variation in Fungi; J. J. Christensen; 214 M. H.

4:30 - 5:20 Ophthalmology Ward Rounds; Erling W. Hansen and Staff; E-534, U. H.

5:00 - 6:00 X-ray Seminar; Results Obtained with Radiation Therapy in Carcinoma of the Lip; Hyman Katzovitz; Todd Amphitheater.

Friday, February 11

8:30 - 10:00 Neurology Grand Rounds; A. B. Baker and Staff; Station 50, U. H.

9:00 - 9:50 Medicine Grand Rounds; C. J. Watson and Staff; Todd Amphitheater, U.H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:20 Medicine Grand Rounds; Staff; Veterans Hospital.

10:30 - 11:50 Otolaryngology Case Studies; L. R. Boies and Staff; Out-Patient Department, U. H.

11:00 - 12:00 Surgery-Pediatric Conference; C. Dennis, O. S. Wyatt, A. V. Stoesser and Staffs; Minneapolis General Hospital.

11:30 - 12:50 University of Minnesota Hospitals General Staff Meeting; Persistent Sequellae of Bulbar Poliomyelitis; Wallace Lueck, John Galligan, Wayne LeBien, and James F. Bosma; Powell Hall Amphitheater.

12:00 - 1:00 Surgery Clinical Pathological Conference; Clarence Dennis and Staff; Large Classroom, Minneapolis General Hospital.

1:00 - 1:50 Dermatology and Syphilology; Presentation of Selected Cases of the Week; H. E. Michelson and Staff; W-312, U. H.

1:00 - 3:00 Pathology-Surgery Conference; Auditorium, Ancker Hospital.

1:00 - 2:50 Neurosurgery-Roentgenology Conference; W. T. Peyton, Harold O. Peterson and Staff; Todd Amphitheater, U. H.

4:00 - 5:00 Electrocardiographic Conference; George N. Aagaard; 106 Temp. Bldg., Hospital Court, U. H.

Saturday, February 12 - HOLIDAY

II. INFECTION FOLLOWING TRANSURETHRAL RESECTION OF THE PROSTATE GLAND

C. D. Creevy
Michael J. Feeney

Introduction

While transurethral resection of the prostate gland, properly performed, is one of the safest of surgical operations of comparable magnitude, especially when the age and general state of the average patient are considered, it is subject to certain complications, chiefly hemorrhage and damage to the kidneys. As Creevy has pointed out, renal damage may occur during operation as the result of rapid loss of blood, bacteriemia (pyelonephritis), prolonged hypotension, the transfusion of incompatible blood, and by the entry into the venous system of blood hemolyzed in the bladder by the water used to fill the bladder during operation.

This study was prompted by certain findings of the investigation of hemolysis during transurethral resection. In 1947, Creevy and Webb reported a fatal hemolytic reaction following transurethral resection of the prostate gland in which sterile water was the irrigating agent. It was suggested that the hemolytic reaction could probably be prevented by substituting an isotonic solution, such as five per cent glucose, for the water.

A clinical investigation revealed that water, when used as an irrigating solution during transurethral resection, does produce hemolysis, and that hemolysis does not occur when isotonic glucose is used. One can observe during resection how the water, which enters the bladder during periods of observation and operation, hemolyzes instantly any blood which has escaped from the cut surface of the prostate. Since many large veins carrying blood under very low pressure are necessarily opened during resection of the deeper parts of the gland, and since the irrigating fluid must run in at a pressure sufficient to wash the blood away to permit clear vision, it is evident that the irrigating fluid, with its content of hemolized blood, must get into the circulation. This can be seen to happen.

In order to prove the point, the levels of free hemoglobin in the plasma before and after transurethral resection were determined in a series of one hundred and six consecutive cases in which water was the irrigating fluid. The free plasma hemoglobin averaged 3.08 mg. per cent before and 45.4 mg. per cent after operation. Eight of this group of patients developed mild oliguria, elevation of the urea nitrogen, and disproportionate anemia; mild jaundice was seen in three of them. The study was then repeated using four per cent glucose as the irrigating agent, and the free hemoglobin was found to average 3.5 mg. per cent, that is, there was no hemolysis. To determine whether glucose was entering the circulation, the blood sugar was measured before and after operation in 78 patients with 4 per cent glucose as the irrigating agent. The preoperative average was 81 and the postoperative 198 mg. per cent of glucose, a rise of 117 mg. per cent. Twenty-four of the patients had postoperative levels above 200 mg. per cent, and 8 of these had levels above 400 mg. per cent, the highest being 1079 mg. per cent (diabetics were excluded from consideration). This proved that the irrigating fluid often enters the circulation and that, in some cases, the quantity is very large. In a control series with water as the irrigating agent, the blood sugar did not change during operation.

When it became certain that the contents of the bladder were often forced into the blood stream, blood cultures were taken at the end of transurethral resection in about 350 cases; growth occurred in about 45 per cent.

Since other sources of danger to the kidney can ordinarily be controlled by obvious methods, and since most of the troublesome complications which follow transurethral resection are due to infection, a study was undertaken to determine whether the bacteriemia could be prevented

or the incidence of clinical postoperative infections reduced by the use of several antibiotics, both singly and in various combinations.

Review of the Literature

Many theories have been proposed to account for the severe febrile reactions which sometimes follow instrumentation of the urethra. Dittel believed that they were due to acute nephritis, while Clark attributed them to functional and organic disturbances of the kidney, and Da Costa and Thompson favored a reflex nervous disturbance. In 1887, Clado and Hallé, working independently, isolated micro-organisms from the blood of patients with urethral chill. Greenberg mentioned two possible causative factors; a nervous reaction and sepsis. In 1916, Crabtree reported seven instances of positive cultures from the blood following urethral manipulation.

Scott made the first extensive study of bacteriemia following urological procedures as well as that occurring during infections of the urinary tract. In 1929, he reported 82 such cases. Sixty-two per cent of these had positive blood cultures following instrumentation or operation; the urethra being the portal of entry in 80 per cent of his cases. The majority, 77 per cent, had a bacillary infection of the blood stream. Death resulted in 18 per cent of Scott's 82 cases.

In 1930, Barrington and Wright obtained 13 positive cultures of the blood from patients having had various types of urethral manipulation.

In 1932, Hyman and Edelman reported on 45 bacillary and 19 coccal infections of the blood stream, the portal of entry being the genito-urinary tract. Nine deaths (20 per cent) occurred in the bacillary septicemias and 13 (68.4 per cent mortality) in those due to cocci. They noted two types of septic reactions: the transitory and mildly reacting bacteriemia; and the fulminating, sometimes fatal, septicemia. They believed the bacillary bacteriemias to be milder than the coccal infections.

Powers presented the results of blood culture on 30 cases of urethral instrumentation on patients with an infected urine. Blood cultures were taken immediately and one hour after instrumentation. The cultures were positive in 10 per cent of the former and in 3.3 per cent of the latter.

Rosenow and Brown reported on 144 cases of septicemia from various causes with a mortality of 67 per cent. The mortality was nearly twice as great in patients over 50 years of age as in those under 26. The portal of entry of the organism into the blood stream also appeared to influence the mortality. If the primary site of infection was in bone 50 per cent of the patients died; a focus in the gastrointestinal tract led to a mortality of 89 per cent, and in the urogenital system of 85 per cent.

Meneely advocated the administration of penicillin and sulfadiazine for two days prior to instrumentation of the urinary tract in those patients with known valvular disease of the heart. He reported two cases of bacterial endocarditis following urethral instrumentation.

Okell and Elliott found that 60.9 per cent of 138 patients had positive blood cultures following dental extractions. In 1939, Elliott used an improved technique and found that 86 per cent of 21 patients had positive blood cultures after extractions.

Murray and Mosnick made an interesting study on patients with dental disease. They were given paraffin to chew for a 30 minute period, and blood was aspirated from the femoral artery for culture; 55 per cent were positive. Of the positives, 84 per cent yielded diplo cocci and 16 per cent were staphylococci.

Round found that the preliminary administration of sulfonamides had no effect on the incidence of growth in blood cultures taken immediately after dental extraction, while it did reduce the number

of positives in cultures taken ten minutes after extraction.

In 1938, Thompson et al, reported on the efficacy of sulfanilamide in patients subjected to transurethral resection of the prostate gland. One hundred patients received the drug postoperatively and another one hundred cases were used as controls. The sulfanilamide was discontinued in 9 cases because of untoward reactions. There were 3 cases in the sulfanilamide group and 3 cases in the controls who had stormy convalescence because of infection.

Strom and Thompson gave a more favorable report on the benefits of sulfathiazole administered during the entire hospital stay of patients having transurethral resection. Sixty-two per cent of patients who received sulfathiazole had temperature elevations above 100 degrees F, while 57 per cent of a control group who received no chemotherapy had febrile reactions. They believed that the duration and severity of fever and the incidence of severe chills were lessened when sulfathiazole was used.

Experimental work by Reichel indicates that in patients with endocarditis chills and fever occur when bacteria are being destroyed, and not while they are increasing in number in the blood stream.

It is not uncommon to observe the development of impaired renal function when severe febrile reactions follow a transurethral resection. Reference has already been made to hemolysis and to other possible etiological factors in the development of these reactions. Foy, Altmann, Barnes, and Kondi in a discussion on the causative agents of renal failure which occurs after crush injuries transfusions of incompatible blood, and during blackwater fever, suggested that the renal changes in all these conditions are similar. They concluded that the anuria often associated with these disorders is due not so much to blockage of the tubules (Baker and Dodds) as to diminution in renal blood flow and glomerular filtration. They point out that reduction in blood flow will affect the tubules more than the glomeruli, since the more work is done and more oxygen consumed by the tubular cells than by the glomerular epithelium. Maegraith and Findlay suggest that the degenerative changes seen in the tubular cells may be due to anoxia as a result of bypassing of the cortex by the circulation. Cohnheim (1882) and Tomb (1942) proposed the possibility of alteration in renal blood flow and the resulting anoxia as causative factors in the anuria and in the pathological changes observed in the kidneys of patients with cholera. Turnbull observed ischemia of the glomeruli and vascular engorgement of the medulla in fatal transfusion reactions.

Duff and Moore, Dunn and Montgomery, and Doniach and Walker have reported on the occurrence of bilateral cortical necrosis, occurring chiefly during pregnancy or its complications. In bilateral cortical necrosis the more peripheral parts of the cortex undergo sequestration while the deeper zones of the cortex and the entire medulla survive.

Black-Schaffer, Hiebert and Kerby have shown that bilateral cortical necrosis can be produced in rabbits by the intravenous injection of living meningococci. De Navasquez (1938) produced cortical necrosis in rabbits by the intravenous injection of a staphylococcus toxin. Tureta et al., injected staphylococcus toxin intravenously into rabbits; inspection of a kidney in the living animal at intervals disclosed pallor of the cortex within one minute after the injection. About 7 minutes after injection a stream of brilliant red blood was noted in the renal vein. In the kidneys of animals susceptible to the toxin cortical ischemia of such a degree was produced that it terminated in necrosis. By way of contrast, it was noted that the gastro-intestinal viscera and the spleen became hyperemic. Intestinal gaseous distention was noted in all susceptible animals. Every clinician is familiar with the occurrence of paralytic ileus in severe septicemia.

Biorn studied a series of patients who had undergone transurethral resection at the Mayo Clinic with special reference to the relationship of postoperative infection to preexisting prostatitis. He concluded that the incidence of postoperative hemorrhage, fever above 101 degrees, and chills was higher in those patients with microscopic evidence of severe prostatitis, or from which organisms were grown by tissue culture. He concluded that preoperative prostatitis predisposes to the development of epididymitis, thrombophlebitis, septicemia, and the "dysuria syndrome".

Methods of Study

This study is based on an analysis of 380 consecutive cases of transurethral resection of the prostate performed at the University of Minnesota Hospitals from July 31, 1947 to November 29, 1948. Every patient who had multiple stage transurethral resection was considered as a single case. Females and children who had transurethral resection of the vesico-urethral orifice, as well as patients who had transurethral resection of vesical neoplasms, were excluded. Those patients who had a lithalopaxy performed in conjunction with transurethral prostatic surgery were included in the analysis.

The urine was cultured preoperatively, and the blood was cultured at the end of operation. A culture of the blood was also obtained in the event of a severe febrile reaction.

The influence of various combinations of antibiotic therapy upon bacterial invasion of the blood stream and upon postoperative infection was studied according to the following plan:

Series	No. of Cases in Series	Preoperative Medication
1	25	None
2	98	Penicillin I.M. and sodium sulfadiazine intravenously during operation or sulfadiazine at least 24 hours prior to surgery.
3	129	Crystalline penicillin or penicillin in oil.
4	75	Penicillin and streptomycin. (Streptomycin 1.0 gm. I.M. before removal of catheter).
5	23	Sulfonamide combination (equal parts of sulfadiazine, sulfathiazole and sulfamerazine).
6	30	Penicillin, streptomycin and sulfadiazine.
	380	

In all cases the antibiotic agent used preoperatively was continued in the postoperative period. In some instances the therapy was necessarily changed by the development of complications, either from infection or untoward reaction to the medication. Therefore, the influence of antibiotics can be analyzed only with a view toward the prevention of bacteriemia and infection. It is regretted that our control series (1) is not large enough to permit comparison with those cases in which various antibiotics were used.

Results of Study

A. The incidence of all postoperative infection in 380 cases:

Table I

	No.	Per Cent
Fever 101 to 103°F	144	37.9
Severe Febrile reaction (103°F and above)	53	13.9
Pyelonephritis (clinical)	10	2.6
Epididymitis	6	1.6
Funiculitis	5	1.3
Periurethritis	3	0.8
Prostatitis and Seminal vesiculitis	5	1.3
Pneumonia	5	1.3
Thrombophlebitis	5	1.3

It is immediately apparent that infection is fairly common following transurethral resection. Two hundred and Two patients (54.2 per cent) had postoperative infection of sufficient degree to be placed in the above classification. Many of the infections were mild, caused no distress to the patient and no delay in the convalescence.

We are particularly concerned with those patients who had severe febrile reactions. Bacteria were isolated from the blood of 50 patients out of the 53 in this group. Many, but not all, of these cases could be classed as having had "septicemia". We chose not to use the term "septicemia", because of its ambiguity. The group classed as "severe febrile reaction" includes those who developed a fever of 103°F, or above, without apparent cause other than probable bacterial invasion of the blood stream. Many of the patients listed as having a severe febrile reaction also had chills. The incidence of pyelonephritis of some degree is perhaps higher than that listed. Included in the group of 10 cases are those who had frank clinical and laboratory evidence of the disease.

Bilateral vasectomy was performed when the procedure was feasible. It was omitted in a few instances mainly because the patient was too young or because it was impossible to isolate the vas deferens readily. Only the more severe degrees of funiculitis and those with palpable evidence of periurethritis were listed as postoperative complications.

The terms prostatitis and seminal vesiculitis require elucidation. They include those with fever and tender swelling or induration of the prostate or seminal vesicles. It appears likely that two of the five cases of prostatitis developed their complication as the result of the inadvertent injection of water instead of the usual normal saline in the pitressin-adrenalin-saline solution injected into the prostate gland to assist in the control of operative hemorrhage.

Pneumonia was diagnosed by X-ray or necropsy in addition to clinical examination.

The term "thrombophlebitis" includes both thrombophlebitis and phlebothrombosis.

B. The incidence of all other postoperative complications following 380 cases of transurethral resections of the prostate:

Table II

Complication	No.	Per Cent
Postoperative hemorrhage	14	3.7
Postoperative dysuria	25	6.6
Urinary incontinence	7	1.8
Cardiac Failure	5	1.3
Cerebral hemorrhage or thrombosis	4	1.05
Extravasation of urine or irrigating fluid through the prostatic capsule	4	1.05
Coronary thrombosis	3	0.8
Pulmonary embolus	1	0.26
Miscellaneous complications	3	0.8

With the exception of hemorrhage and postoperative dysuria the incidence of complications other than those due to infection is quite low. Sufficient time has not elapsed to allow computation of the incidence of urethral stricture and contracture of the vesical-neck.

The complication of hemorrhage includes all patients who lost sufficient blood after operation to require cystoscopy for control of bleeding or evacuation of blood clots.

Those patients included in the postoperative dysuria group had symptoms severe enough to require a second resection or to delay their convalescence. We unhesitatingly returned nearly all patients to cystoscopy who had postoperative urinary difficulties.

Two cases of urinary incontinence occurred in rigid carcinomas that involved the external sphincter, one in multiple sclerosis, and three in senile patients with severe cerebral arteriosclerosis. One case occurred in a fair risk patient with benign prostatic hypertrophy and was probably due to an error in operative technique.

Four patients had definite clinical signs of extravasation of irrigating agent and urine. Suprapubic cystostomy was performed on one patient; two others were managed by catheter drainage and antibiotic therapy without further complication. One patient who had massive extravasation of irrigating fluid is reviewed in the mortality study.

C. Mortality

Nine (2.36 per cent) of 380 patients expired during the postperative period.

The following is a brief review of the fatalities:

1. ., age 76 years. This patient had severe chronic pyelonephritis, uremia, and diabetes mellitus. Little improvement in renal function followed prolonged drainage by cystostomy. Twenty-seven grams of benign prostatic tissue were resected. Death occurred on the 8th postoperative day from uremia, acidosis and pyelonephritis.

2. , age 63 years. One hundred and forty-four grams of benign prostatic tissue were resected. The patient developed shock, cyanosis, abdominal distention and expired 8 hours after transurethral resection. Autopsy disclosed massive extravasation of irrigating fluid into the retroperitoneal tissues and peritoneal cavity. The prostate was very completely resected. There was no actual perforation of the prostatic capsule. Extravasation probably occurred when the catheter became partially occluded. Aerobacter aerogenes was cultured from the blood.

3. , age 87 years. This patient was in fair condition except for generalized arteriosclerosis. Sixteen grams of carcinomatous tissue were resected. There was excessive postoperative bleeding associated with an E.coli bacteremia and shock. Death occurred on the 5th postoperative day from congestive heart failure secondary to shock.

4. , age 83 years. This patient had a two stage transurethral resection for benign prostatic hypertrophy. Seventy-two and thirty grams of tissue, a total of one hundred and two grams, were resected. The patient became febrile after the second transurethral resection. Staphylococci were cultured from the blood and aerobacter aerogenes was isolated from the urine. Postmortem examination revealed the immediate cause of death to be a pulmonary embolus.

5. ., age 79 years. This patient had known severe coronary arteriosclerosis prior to surgery. Sixty-eight grams of benign prostatic tissue were resected. Death occurred on the 20th postoperative day from probable coronary thrombosis. Autopsy was not permitted.

6. ., age 49 years. This patient underwent a combined abdominoperineal resection for carcinoma of the rectum 3 weeks prior to transurethral resection. Seven grams of benign prostatic tissue were resected because of high residual urine after surgery. The patient became febrile postoperatively from pyelonephritis and staphylococcic bacteriemia, and expired on the 32nd postoperative day. Autopsy revealed ex-

tensive metastatic rectal adenocarcinoma with resultant partial obstruction of both ureters.

7. , age 78 years. Patient was only a fair risk because of severe generalized arteriosclerosis. Fourteen grams of benign prostatic tissue were resected. The patient removed his catheter with the bag inflated on the 2nd postoperative day; he then became febrile and expired on the 10th postoperative day. Staphylococci were cultured from the blood stream. Autopsy disclosed a left perinephric abscess and broncho-pneumonia.

8. , age 82 years. This patient had known severe coronary arteriosclerosis and myocardial damage. Seventeen grams of benign prostatic tissue were resected. The patient expired from cardiac failure on the 3rd postoperative day. Autopsy revealed severe myocardial fibrosis.

9. ..., age 75 years. This patient became cyanotic when sodium pentothal was administered to supplement spinal anesthesia during the resection. Sixty-eight grams of benign prostatic tissue were resected transurethrally. The patient remained semi-comatose and cyanotic and died two days later. Autopsy disclosed only bronchopneumonia and pulmonary emphysema. Death was thought to have resulted from cerebral anoxia during the anesthesia with pentothal.

Infection was an important factor in the death of 6 of the 9 patients. Staphylococci were cultured from the blood of 3 of them. E. Coli and aerobacter aerogenes were isolated separately from the blood of 2 others. All 5 of these patients with positive blood cultures had severe febrile episodes after surgery.

D. The effect of antibiotics upon infection:

In an attempt to simplify classification, pyelonephritis, epididymitis,

Table III

Series		Fever 101°		Severe Febrile Reaction (103°)		"All Other Infections"		Total Incidence of Infection		Average No. Postoperative days in Hospital	Mortality	
	No.	No.	%	No.	%	No.	%	No.	%		No.	%
1.	25	5	20	0	0	2	8	7	28	10.6	0	0
2.	98	40	40.9	20	20.4	9	9.2	69	70.4	9.0	3	3.1
3.	129	47	36.4	20	15.5	13	10.1	80	62	9.9	3	2.3
4.	75	34	45.4	6	8	9	12	49	65.4	9.6	2	2.7
5.	23	11	47.8	3	13.1	2	8.7	16	69.5	9.4	0	0
6.	30	7	23.3	4	13.3	4	13.3	15	50	9.3	1	3.3

(Series, Preoperative medication: 1. No antibiotic therapy. 2 Penicillin and sulfadiazine. 3. Penicillin. 4. Penicillin and streptomycin. 5. Sulfonamide combination. 6. Penicillin, streptomycin and sulfadiazine).

funiculitis, periurethritis, prostatitis, thrombophlebitis, and pneumonia are grouped under the heading "all other infections".

An apology must be made for the small number of cases presented as controls (Series 1). Such a small series prohibits comparison to the patients who received antibiotics.

The incidence of infection in patients who received antibiotics varied from 50 per cent in those who received penicillin, sulfadiazine, and streptomycin (Series 6) to 70.4 per cent in Series 2 (penicillin and sulfadiazine).

E. Correlation of postoperative infection with the culture of the urine:

Eighteen of the 380 cases were excluded from this correlation because of failure to obtain a culture or because it was contaminated.

Table IV

Organism Cultured from Urine	No. of Cultures		Fever 101°		Severe Febrile Reaction		Other Infect.		Totals	
	No.	%	No.	%	No.	%	No.	%	No.	%
Sterile	101	28.1	32	31.7	2	2	9	8.9	43	42.6
Staphylococcus	37	10.3	13	35.2	4	10.8	6	16.2	23	62.2
Streptococcus	32	8.9	15	46.8	1	3.1	3	9.4	20	62.5
Aerobacter aerogenes	67	18.6	20	29.9	27	40.3	7	10.4	55	82.0
E. Coli	23	6.4	8	34.8	4	17.4	1	4.3	13	56.5
Pseudomons	22	6.1	9	40.9	3	13.6	4	18.2	16	72.8
Proteus	13	3.6	3	23.1	3	23.1	2	15.4	8	61.5
Paracolon	9	2.5	2	22.2	0	0	0	0	2	22.2
Alkaligenes faecalis	5	1.4	3	60.	0	0	0	0	3	60
"Mixed" culture	53	14.7	27	50.9	8	15.1	5	9.4	40	75.5
	362									

The main point demonstrated by the above correlation is the potential pathogenicity of aerobacter aerogenes in the urine. Severe febrile reactions were twice as frequent (40.3 per cent) in those patients who had aerobacter aerogenes in their urine as in those with any other organism. Only two per cent of patients who had sterile urine suffered a severe febrile reaction.

F. Correlation of the postoperative blood culture with the development of infection:

It was necessary to exclude 30 cases from this phase of the study because of contamination of the blood culture or failure to obtain one. Blood cultures were taken on 350 patients. One hundred and fifty-nine (45.4 per cent) of these cultures produced bacterial growth.

Table V

Organism	Fever 101°		Severe Febrile Reaction		Other Infection		Total Incidence of Infection	
	No.	%	No.	%	No.	%	No.	%
Sterile	191	54.6	60	31.4	3	1.6	19	10	82	43
Staphylococcus	43	12.3	16	37.2	9	21	3	7	28	65.2
Streptococcus	21	6	12	57.2	3	14.3	2	9.5	17	81
Aerobacter aerogenes	44	12.6	14	33.8	22	50	6	13.7	42	95.5
Alkaligenes Faecalis	14	4	5	35.7	3	21.4	0	0	8	57.1
Escherichia Coli	9	2.6	3	33.3	3	33.3	0	0	6	66.6
Pseudomonas	6	1.7	4	66.7	1	16.7	1	16.7	6	100.
Paracolon	4	1.1	1	25.	1	25.	0	0	2	50.
Proteus	3	0.9	1	33.3	1	33.3	1	33.3	3	100.
"Mixed Cultures"	15	4.3	8	53.3	4	26.7	3	20.	15	100.

The most striking figure in this correlation is the high incidence (50 per cent) of a severe febrile reaction in instances where aerobacter aerogenes was cultured from the blood stream. Only three (1.6 per cent) of 191 patients who had a sterile blood culture suffered a severe febrile response. Pseudomonas aeruginosa, proteus, and mixed cultures in the blood stream were associated with a high incidence of postoperative infection.

G. The following is an analysis of the incidence of positive blood culture while utilizing various combinations of antibiotic therapy. It was necessary to exclude 30 of 380 cases from this study because of failure to obtain a blood culture or contamination of the culture.

Table VI

*Series	No. in Series	Positive Blood Culture		Negative Blood Culture	
		No.	%	No.	%
1.	25	14	56	11	44
2.	79	42	53.2	37	46.8
3.	121	50	41.3	71	58.7
4.	73	29	39.7	44	60.3
5.	23	14	60.9	9	39.1
6.	29	10	34.5	19	65.5
	350	159	45.4%	191	54.6%

*(Series, Preoperative medication: 1. No antibiotic therapy. 2. Penicillin and sulfadiazine. 3. Penicillin. 4. Penicillin and streptomycin. 5. Sulfonamide combination. 6. Penicillin, streptomycin and sulfadiazine.)

The above figures would seem to indicate that various types and combinations of antibiotic therapy have little influence on the incidence of positive cultures of the blood. The overall incidence of positive cultures was 45.4 per cent. Patients who received penicillin, sulfadiazine and streptomycin (Series 6) had the lowest percentage (34.5 per cent) of positive blood cultures, while those who had sulfonamide combination (Series 5) yielded the greatest percentage (60.9 per cent). Again, our control series (1) is not large enough to permit

comparison with those patients who received antibiotics.

H. Postoperative infection correlated with the number of stages of transurethral resection.

Sixty-four (16.8 per cent) of 380 patients underwent multiple stage transurethral resections for various reasons.

The following table depicts the relative incidence of infection after single and multiple stages of transurethral resection in 380 patients.

Table VII

			Positive Blood Culture		Infection other than Low Grade Fever	
	No.	%	No.	%	No.	%
Single Stage	316	83.2	118	37.4	58	18.4
Multiple Stages	64	16.8	41	64	16	25

Seven of the 64 patients underwent 3 stages of transurethral prostatic resection. One patient with benign prostatic hypertrophy and neurogenic vesical dysfunction required four stages to achieve satisfactory urination. The incidence of positive blood culture was about the same after the second stage as it was after the first stage of transurethral resection. The hazard of postoperative infection was about one-half as great after the second stage as compared to the first stage of transurethral resection. The above figures on the incidence of positive blood cultures and postoperative infection after multiple stage transurethral resection are the totals for all stages.

I. A comparison of urine and blood cultures in each individual patient:

A total of 356 cases were analyzed for this phase of the study. The cases included in the study do not necessarily correspond to those used in the previous part of this investigation.

	No.	%
1. Both urine and blood culture sterile	91	25.6
2. Urine culture sterile and blood culture positive	11	3.1
3. Urine culture and blood culture positive with isolation of different organisms	40	11.2
4. Urine culture positive and blood culture sterile	108	30.4
5. Urine culture and blood culture positive for the same organism	106	29.8
Total	356	

In 157 positive cultures of the blood, 106 (67.5 per cent) of the organisms cultured were identical with those cultured from urine. In those instances where the urine was sterile and the blood culture positive, or different from the urine culture, one can surmise that an infected prostate gland could be the source of bacteriemia. Unfortunately, bacteriological studies

were not carried out on the resected prostatic tissue. Only 11 patients who had sterile urine were the source of a positive blood culture. Ninety-one patients who had sterile urine were found to have sterile postoperative cultures of the blood.

Discussion

Bacteriemia after transurethral resection of the prostate is not uncommon. Blood cultures were obtained from 350 patients after operation and 45.4 per cent of these produced bacterial growth. Some of these positive cultures were probably the result of contamination. Bacteriemia in some cases appears to be harmless. It was demonstrated that severe febrile reactions were much more common when bacteriemia occurred. Only 1.6 per cent of 191 patients with a sterile blood culture developed a high fever, as contrasted with 50 per cent severe febrile reactions in 44 cases with aerobacter aerogenes in the blood stream.

The urine culture and blood culture were identical in 67.5 per cent of those patients with positive urine and blood cultures. One hundred and two patients had sterile urine and the postoperative culture of the blood was sterile in 91 (89.2 per cent), while only 11 (10.8 per cent) of this group were the source of positive cultures of the blood. It is known that high levels of blood glucose sometimes follow transurethral resection of the prostate when an isotonic solution of glucose is used for the irrigating fluid. The similarity of urine and blood cultures from patients having transurethral resection again demonstrates that the fluid in the bladder is frequently forced into the prostatic veins opened at operation. Trauma to the urethra during transurethral resection may also produce a portal of entry for bacteria.

Patients who bled excessively during or after operation had more postoperative bacteriemia and infection. This would be expected since more venous sinuses were opened and the catheter became occluded more frequently with resultant increase in intravesical pressure. Lowered resistance to infection with excessive hemorrhage is possibly a factor in the development of infection.

Resection of the larger prostate gland was followed by bacteriemia and infection in a higher proportion of patients. The larger glands were often more vascular, required more operating time, resulted in more urethral trauma, and necessitated more multiple stage resections. Although the incidence of hemorrhage and infection is probably greater in the larger glands, transurethral resection when feasible, is our operation of choice in all except the very large prostate glands and in early prostatic carcinoma.

Approximately 37 per cent of the severe febrile reactions appeared on the day of operation, while 36 per cent occurred within 24 hours after removal of the urethral catheter. An undetermined, but considerable, number of the severe reactions were initiated by mechanical difficulties with the irrigating catheter. In all these instances, an increase of intravesical pressure, with consequent bacterial invasion of the blood stream, would seem to explain most of the onset of chills and fever.

The relative effectiveness of one antibiotic or of several in combination is not clear. The preoperative urine culture would seem to be the most reliable guide to prophylactic antibiotic therapy. If the patient has a clear and sterile urine, there seems to be little need for antibiotics unless complications arise. Appropriate antibiotics should be administered in patients with a heavily infected urine or severe prostatitis.

Twenty-one patients who had normal levels of urea nitrogen in the blood prior to transurethral resection developed severe febrile reactions after operation. Thirteen (61.9 per cent) of these patients were found to have elevation of their blood urea nitrogen levels.

Hypotension frequently follows severe chills after transurethral resection. It is possible that bacterial toxins alter the renal circulation in such a manner as to impair kidney function. The development of pyelonephritis does not always explain the occurrence of reduced renal function in these cases.

An isotonic solution of glucose was used for irrigation during operation in all of our cases to eliminate the problem of postoperative hemolysis. It appears likely that more than one factor may be necessary to initiate a hemolytic reaction. In several cases, the number of bacterial colonies on pour plates of the blood obtained immediately after operation were too numerous to count. It is conceivable that, if enough hemolytic organisms were introduced into the blood stream along with hemolyzed blood, a hemolytic reaction might occur from this source.

It is planned to continue this study until larger series with the various antibiotics have accumulated, and to make further studies on bacteriemia using the newer antibiotics. The problem of hemolysis and damage to the kidneys after transurethral resection warrants further investigation.

Summary

1. Blood cultures were obtained from 350 patients after transurethral resection of the prostate. Bacteria grew in 45.4 per cent of the blood cultures.

2. Postoperative infection is the most frequent complication of transurethral resection.

3. Patients with sterile urine had fewer febrile reactions than those with infected urine.

4. The occurrence of severe febrile reactions was more common when bacteriemia was present.

5. Aerobacter aerogenes, in the urine or blood, was found to be the most serious offending organism in the production of febrile reactions.

6. The urine and blood cultures from the same patient were frequently identical.

7. The relative effectiveness of one antibiotic or of several in combination is not yet clear. If the patient has a clear and sterile urine, there seems to be little need for antibiotics unless complications arise. Appropriate antibiotics should be administered when the patient has heavily infected urine or severe prostatitis.

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III. MEDICAL SCHOOL NEWS

Coming Events

Feb. 14 - Kellogg Lecture, Dr. Lawrence R. Boies, "Hearing Loss," 4:00 p.m., Powell Hall Amphitheater.

Feb. 15 - Kellogg Lecture, Dr. Anderson C. Hilding, "The Applied Physiology of the Respiratory Tract," 2:00 p.m., Todd Amphitheater, U. H.

Feb. 17 - Special Kellogg Lecture, Dr. Allan M. Butler, "The Role of Potassium in Health and Its Alterations in Various Disease States," 2:00 p.m., Eustis Amphitheater, U. H.

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Radio-Isotope Symposium

The Graduate School of the University of Minnesota will sponsor a symposium on Radio-Isotopes as Investigative Tools. The symposium will consist of a series of nine lectures by the faculty members of the University of Minnesota and other distinguished scientists.

The series of nine lectures will begin on Monday, February 14, and will close on Friday, February 25. The lectures will be presented daily except for the dates February 19, 20, and 22, on which there will be no lectures. All lectures are scheduled for 4:00 p.m. in the Auditorium of Murphy Hall on the Minneapolis campus.

Dr. Wallace D. Armstrong will be Chairman at the Conference on Metabolic Inter-Relations sponsored by the Josiah Macy Foundation. The conference will meet in New York City February 7 and 8.

Doctors Harold S. Diehl, Myron M. Weaver, and George N. Aagaard will be in Chicago this week-end to attend the meetings of the Council on Medical Education and Hospitals of the American Medical Association. Dr. Aagaard will talk on the subject of "Responsibility of Medical Schools and Continued Postgraduate Education of the Doctor" at the National Conference on Medical Service which is held in Chicago at the same time.

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New Minnesota Medical Foundation Members

Dr. Arthur Neumaier, Glencoe Clinic
Dr. Myron J. Hertz, 217 Lowry Medical Arts Bldg., St. Paul
Dr. R. D. Hanover, Littlefork
Dr. Duane C. Olson, Gaylord
Dr. B. A. Fine, Crosby
Dr. J. D. Van Valkenburg, Floodwood
Dr. Karl E. Sandt, 1750 Medical Arts Bldg., Minneapolis
Dr. Maurice Gilbert, 1915 Washburn Avenue N., Minneapolis
Dr. Archie M. Smith, 4829 Minnetonka Bldg., St. Louis Park

KELLOGG FOUNDATION LECTURES

The following lectures will be given during the week of February 6. All medical students, interns, nurses, technicians, dietitians, and physicians are cordially invited to attend these lectures. A special invitation is extended to University Fellows.

Dr. Adelaide M. Johnson (Mayo Clinic)	"Psychobiologic Dynamics"	Monday, February 7, 2:00-4:00 p.m., Room 211, Zoology Bldg.
Dr. Victor H. Vogel (U.S.P.H.S. Hospital, Lexington, Kentucky)	"Morphine and the Newer Analgesic Drugs"	Tuesday, February 8, 2:00-4:00 p.m., Todd Amphitheater