Complications Associated with Transurethral Surgery

Gertie F. Marx, M.D., and Louis R. Orkin, M.D.

TRANSURETHRAL surgery entails the excision of tissue and coagulation of bleeding vessels through a modified cystoscope. In electroresection, the tissue is excised and the bleeding arrested by an electrically energized wire-loop. In the punch method the tissue is removed with a cold blade and the bleeding controlled by a coagulating current.[1] Both techniques are performed under vision provided by a system of lenses and appropriate irrigation. The use of continuous irrigation is necessary not only to improve visibility through the cystoscope and to distend the bladder or prostatic urethra but also to maintain the operative field free of blood and dissected tissue. Complications, characteristically associated with transurethral surgery, result from the unique features described above. The most common problems that confront the surgical team are, in order of their frequency: (1) intravascular absorption of irrigating fluid, (2) significant blood loss, and (3) perforation of the bladder or urethra with extravasation.

Intravascular Absorption of Irrigating Fluid

Transurethral surgery which involves the opening of more than a few venous sinuses may lead to absorption of irrigating fluid when the pressure of the solution is higher than the venous pressure. Intravascular entry of irrigating solution was demonstrated by tagging the fluid with sodium salicylate and measuring post-resection blood-salicylate levels,[2] by using a 4 per cent glucose solution for irrigation and determining blood sugar levels serially,[3] and by labeling the irrigating fluid with radioactive tracers.[4-6]

The patient's reaction depends upon the volume of fluid absorbed and the osmolarity of fluid used. The amount of absorption is governed mainly by three factors: the hydrostatic pressure of the irrigating solution, the number and size of the venous sinuses opened, and the duration of exposure.[6] The osmolarity of the irrigating fluid is chosen by the surgeon. Distilled water, by virtue of producing superior visibility, is the preferred agent for diagnostic procedures or resection of small amounts of tissue. Isotonic solutions, on the other hand, are considered safer for the dissection of larger lesions. Fluids suitable for irrigation must be nonelectrolytic, or only weakly ionizable, to inhibit the dispersion of high frequency current from the resecting area. They should be transparent and nontoxic to local tissue or when absorbed intravenously.[3] A higher irrigation rate than that with water is necessary to maintain visibility.[7] The various nonelectrolyte solutions that have been satisfactorily employed are glucose,[3] urea,[8] glycine,[4, 7] and the hexitols, mannitol,[9] sorbitol,[10] or their combination Cytal.[11]

Three consequences of such indirect intravenous infusion have been recognized: overhydration, hemolysis, and bacteremia.

OVERHYDRATION

Absorption of large amounts of isotonic nonelectrolyte solution produces two general types of overhydration reaction. First, there are complications associated with the increase in the intravascular fluid volume, and secondly, there are derangements due to the dilution of the blood. The increased intravascular fluid volume leads to a rise in intravascular pressure, to an elevation in intracranial pressure, and to an increase of the work of the heart. The dilution of the blood effects a diminution in both blood protein and electrolyte concentration. The combination of increased intravascular pressure and decreased osmotic pressure favors the movement of permeable particles out of the capillaries into the interstitial space. This predisposes to the development of pul-

Received from the Department of Anesthesiology of the Bronx Municipal Hospital Center—Albert Einstein College of Medicine, Yeshiva University, New York, and accepted for publication August 7, 1962.

monary edema, especially in patients whose cardiac reserve is insufficient to handle any rapid overloading of the circulatory system.[12] Cerebral edema may also result from osmolar shifts from the hypotonic extracellular fluid compartment into the relatively hypertonic intracellular spaces.[13] In summary, the dangers of excessive fluid absorption lie in acute left heart failure, pulmonary edema, and symptoms of elevation in intracranial pressure during the course of operation, and in cardiovascular collapse due to decrease in blood electrolyte concentrations toward the end of the procedure or in the immediate postoperative period.

Attempts have been made to quantitate the volume of fluid absorbed. Weighing the patients before and after the operation revealed weight gains ranging from 16 Gm. to 4,500 Gm., with averages reported as 1,225 Gm.[4] or 1,990 Gm.[7] A recent comparison of weight gains during different procedures for prostatectomy demonstrated an average increase of 817 Gm. after transurethral resection as compared to an average gain of only 125 Gm. with the abdominal or perineal approach.[14] Marked declines in serum sodium, chloride, and protein were noted at the completion of transurethral prostatectomies; the cerebrospinal fluid pressure rose and the cerebrospinal fluid sodium fell.[7, 14] The addition of radio-iodinated human serum to the irrigating fluid (Cytal) revealed an average absorption of 237 ml. in ten patients in whom dissection was stopped at the fibers of the surgical capsule and operating time restricted to 60 minutes. However, in one patient in whom the venous sinuses were opened and operating time extended to 90 minutes, the absorption rose to 1,780 ml.[6] It is, therefore, recommended that transurethral procedures be limited to one hour of surgery, and that dissection not be carried into the sinuses lying deep in the capsule.[6]

The clinical symptoms seen with absorption of large amounts of irrigating fluid differs with the type of anesthesia administered. During

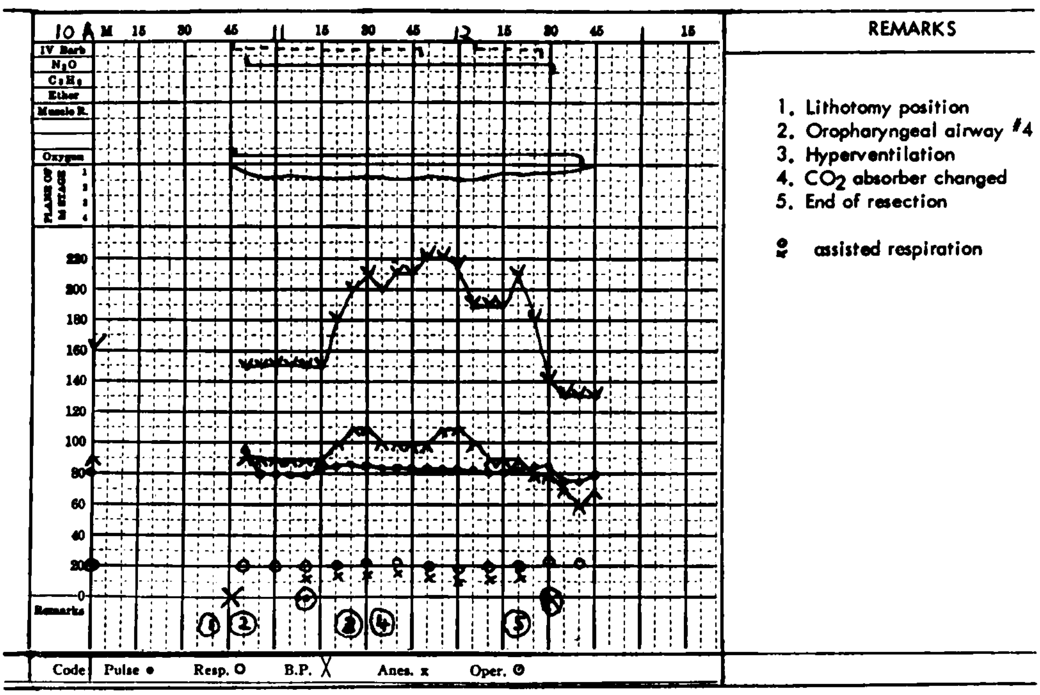

FIG. 1. Overhydration during inhalation anesthesia. A 74 year old man undergoing electroresection of benign prostatic hypertrophy. *Premedication:* atropine 0.4 mg. *Anesthesia:* nitrous oxide-oxygen with 0.4 per cent thiopental infusion. Blood pressure and pulse rate stable only for five minutes after beginning of resection. Hyperventilation, replacement of CO_2 absorber, and increasing or decreasing depth of anesthesia were without effect on vital signs.

regional block, a triad has been described consisting of: (1) a rise in systolic and diastolic pressures accompanied by an increase in pulse pressure, (2) a slowing of the pulse rate, and (3) mental changes in the form of restlessness, confusion, semicoma, associated with nausea, retching, headache, dyspnea and cyanosis.[4, 7] During general anesthesia (fig. 1), subjective signs do not become evident, and dyspnea or cyanosis may be delayed by increased oxygen concentration and assisted ventilation. The only signs suggestive of irrigating fluid absorption are the gradually increasing systolic and diastolic pressures with widening pulse pressure and small changes in pulse rate.[15] Differential diagnosis of these symptoms should include hypercarbia, light anesthesia, drug reaction, heat retention, and pheochromocytoma. Moreover, recent animal investigations showed that there may be many cardiovascular responses to the stress of hypervolemia and that the typical signs of increased arterial and pulse pressures may not develop in every subject. In six dogs studied during 24 experiments, intravenous infusions of 5 per cent dextrose in water, Cytal, and Plavolex totaling 10 per cent of the animal's body weight were administered over a period of one or two hours. Two of the dogs reacted to the infusions with increases in mean pressure, pulse pressure, and pulse rate. Two other dogs exhibited increases in mean pressure and pulse rate only. The remaining two dogs showed mainly increases in pulse pressure, and this was combined in one with a decrease in mean pressure and pulse rate. Although the six dogs reacted in different ways, the trend of response was the same in each dog regardless of the composition of the solution infused. This would indicate that the type of cardiovascular change elicited by an increased intravascular fluid volume is an individual expression of the particular stress.[16] Furthermore, arterial hypertension may be masked by a variety of factors, such as an initial low blood volume, severe blood loss, deep anesthesia, myocardial infarction or cardiac failure.

The signs of hypoelectrolytemic cardiovascular collapse follow the initial stage of hypertension. Patients may suddenly become hypotensive and oliguric, cyanosis and coma may deepen, and tetanic-like twitchings may develop.[13, 17] This picture must be differentiated from other causes such as hemorrhage, cardiovascular accident, pulmonary embolism, mismatched transfusion, bacteremia or tetany. Harrison and co-workers reported a representative case:

Case Report. A 64 year old man in good general condition underwent transurethral prostatic resection under low spinal block. His preoperative serum sodium was 135 mEq./liter. During 55 minutes of operation, the blood pressure rose from 160/84 to 200/100. Concomitantly, the patient became restless, nauseated, and mildly cyanotic. In the postoperative period, the arterial pressure fell to 80/40 with signs and symptoms of peripheral vascular collapse. The sodium determination at this time revealed a value of 111 mEq./liter.[13]

To evaluate sodium loss and shifts during transurethral prostatectomies, eight patients had a calibrated dose of radioactive sodium (Na^{22}) injected preoperatively, and measurements were made of the radioactivity in serum, urine, and irrigating fluid (1.5 per cent glycine). The postoperative findings disclosed a decrease in serum sodium, a significant loss of sodium into the irrigating solution, and an apparent increase in the exchangeable sodium. It was postulated that sodium may be rapidly mobilized from previously inert bone stores to combat the extracellular hyposmolarity.[18] Recently, the effects of rapid intravenous infusions of sterile distilled water and of Cytal in amounts equivalent to double the estimated plasma volume were evaluated in dogs. Electrolyte depression was greater in the animals receiving Cytal than in those infused with water. This was explained by the different distribution of the two solutions, the nonelectrolyte, unlike water, being limited to the extracellular fluid compartment. Yet, even with plasma sodium levels below 100 mEq./liter, no hypotension of significant degree occurred. The assumption was made that other mechanisms may aid in producing true hypoelectrolytemic collapse in the human patient.[19] One possibility involves the loss of osmotically effective electrolytes into the irrigating solution,[18] or from diuresis.[19] The second possibility is a marked potassium loss as a result of the diuresis, with a shift of serum sodium into the cells.[20] A third possibility is perforation of the urinary tract with extravasation of irrigating fluid and a subsequent transfer of electrolytes from the extracellular fluid into the extravasate.[19] If hypo-osmolarity of the body fluids is severe, oliguria may ensue because the solute in the glomerular filtrate is inadequate to maintain water excretion.[21]

While absorption through venous sinuses theoretically may continue into the postoperative period, because of the urological technique of continuous irrigation, our own experience seems to indicate that this is not a clinical problem. This is substantiated by a lack of reports in the literature. Relatively low pressures are employed for postoperative irrigation, and the opened veins appear to occlude rather rapidly.

Various parameters may be used to aid in the diagnosis of overhydration. Venous pressure measurements are easily performed, but are not always informative. No characteristic changes in venous pressure were noted in nine patients studied during transurethral resection of the prostate.[14] Moreover, venous pressure is increased by most inhalation agents *per se*.[22] Weighing the patient before and after the operation gives an approximation of the quantity of fluid absorbed, provided corrections are made by subtracting the weight of the tissue removed and the intravenous fluid administered.[4, 7, 20] When cold solutions are used for irrigation, a sharp fall in rectal temperature of 7 degrees centigrade or more serves as an early warning of excessive absorption because of the local venous circulation.[10, 23] Serum sodium decreases are also diagnostic. A serum sodium level of 120 mEq./liter appears to be the borderline between mild and severe reactions.[17] Serial hematocrit determinations, on the other hand, are of no value. The hematocrit has been reported as decreased,[7, 19, 20] unchanged [20] and increased.[20, 24] A rise in the hematocrit may be caused by loss of plasma from the operative site, by actual swelling of the red blood cells, or by a rapid response of the spleen to the trauma of surgery with an increase in the circulating red cell mass.[24]

Most patients who exhibit moderate signs and symptoms of excessive irrigating fluid absorption diurese spontaneously and recover without any specific therapy.[21] Four situations may develop which require special treatment. Pulmonary edema necessitates oxygen administration under pressure, alcohol inhalation, and frequent airway suctioning; phlebotomy, bronchodilators and digitalization may be indicated.[15] Severe cerebral depression due to cerebral edema is best relieved with hypertonic urea infusions. Failure to diurese should be treated by raising the osmolarity. The safest approach is the intravenous administration of hypertonic urea (30 per cent), but mannitol (25 per cent) or hypertonic sodium chloride may also be used.[21] True hypoelectrolytemic collapse calls for the judicious use of intravenous hypertonic sodium chloride (5 per cent) or Ringer's solution, given slowly over a two to four hour period, with control by serum sodium determinations.[7, 18] These infusions should be administered through a three-way stopcock with a venous pressure attachment in order to detect the development of pulmonary edema.[18]

Hemolysis

When distilled water is used for irrigation, and absorption of considerable amounts occur, the dangers associated with intravascular hemolysis are added to the problems already noted. Blood hemolyzed in the bladder by the irrigating solution may also be propelled into the systemic circulation through opened venous sinuses.[26] Hemoglobinemia, hemoglobinuria, and severe anemia develop. In one investigation of 15 consecutive patients undergoing transurethral prostatectomy with distilled water as the irrigant, measurements of serum hemochromogen levels before and at the end of the procedure disclosed significant hemolysis in ten patients, with postoperative hemochromogen levels ranging between 24 and 316 mg/100 ml.[2] In another investigation, free hemoglobin was measured before and after transurethral resections of the prostate in 106 consecutive patients. The maximum preoperative level was 20 mg/100 ml.; postoperative values were as high as 490 mg/100 ml. with an average increase of 42 mg/100 ml. above the preoperative value. Control studies on patients undergoing other types of operation and on patients infused with saline or 5 per cent dextrose in water revealed no significant changes.[25] Hemolysis was also demonstrated after transurethral surgery by tagging the red blood cells with sodium-chromate [51] and comparing the total gain in radioactivity in the circulating plasma during the operation with the radioactivity in a given volume of packed red cells. Seven of eight patients in whom water was used for irrigation had hemolysis.[6]

The signs and symptoms suggestive of hemolysis in patients undergoing transurethral surgery under spinal analgesia were described by Minuck as a sudden feeling of weakness and tiredness, chills and/or a clammy skin, complaints of tightness of the chest symptomatic of bronchospasm, and a rising blood pressure usually accompanied by a slowing of the pulse rate. In his series of 191 transurethral resections, hemolysis was detected 57 times, but the typical clinical picture was noted in only half of these patients.[26] Creevy stated that a hemolytic reaction during transurethral manipulation is characterized by chills, nausea, oliguria, a rising urea nitrogen, a mild nonobstructive jaundice, an anemia out of proportion to the amount of blood lost, and, at times, by a rise in blood pressure. The accompanying hemoglobinuria is masked by the usual postoperative hematuria.[3] The following case illustrates hemolysis observed during electroresection of a hyperplastic prostate:[27]

Case Report. A 77 year old man with complete heart block and auricular fibrillation was operated on under spinal block (pontocaine 8 mg. and dextrose 80 mg.); sensory analgesia to the tenth thoracic segment was achieved. Water was used for irrigation. Fifteen minutes after the beginning of the operation, the blood pressure rose from 110/80 to 170/80, and the pulse rate, from 30 to 70. Twelve minutes later the patient began to complain of diffuse pain which was most severe below the knees. He became confused and started to cough. He then turned deeply cyanotic and had marked difficulty in breathing. A sample of blood was centrifuged and found to be grossly hemolyzed.

The presence of free hemoglobin in the renal vessels mediates renal vasoconstriction which results in renal hypoxia. Yet, moderate hemoglobinemia may not be followed by clinically harmful reactions.[2, 25, 28] As much as 50 Gm. of hemoglobin have been injected into human volunteers without producing evidence of renal damage despite prolonged hemoglobinuria. However, "these results were obtained in normal subjects, not in old men losing blood" during surgery.[28] Only when water hemolysis is severe or when there are aggravating conditions such as hypotension, anemia, dehydration, or pre-existing renal disease, does the typical reaction of acute tubular necrosis develop. The pathological changes consist of pigmented casts in the convoluted and collecting tubules and the entire nephron distal to the glomerulus.[26] Hemolysis, thus, contributes to the development of lower nephron nephrosis in two ways, by the primary renal effect of vasoconstriction and by the production of anemia and anemic hypoxia. The renal reaction is indistinguishable from that due to transfusion of incompatible blood.[25] However, transfusion reactions are characterized by a fall in arterial pressure and a rise in pulse rate,[27] whereas these are often reversed in water hemolysis by the accompanying overhydration. Intravascular hemolysis is readily estimated in a sample of venous blood by the color of the supernatant serum subsequent to settling of the erythrocytes.[29]

The treatment is similar to that recommended for transfusion reactions. Diuresis must be initiated with the help of 15 per cent glucose [26] or 25 per cent mannitol.[30] Fluid and electrolyte balance must be regulated, and acidosis corrected. Arterial pressure must be maintained at a level that provides adequate renal perfusion. The accompanying anemia should be treated by the administration of fresh concentrated red cells.[30]

Bacteremia

The incidence of bacteremia subsequent to transurethral instrumentation has been greatly reduced by preoperative treatment of infection and prophylactic use of broad-spectrum antibiotics.[31] Blood-culture studies performed in 1954 on 128 consecutive patients disclosed postoperative bacteremia in two.[12] The typical picture of bacteremia secondary to transurethral manipulation appears in the recovery room, often following an uneventful operative course. The outstanding features are chills, gradually increasing fever, prolonged arterial hypotension, and either tachycardia or bradycardia. Slowing of the pulse rate is seen with invasion of the blood stream by Gram-negative bacteria. Differential diagnosis, especially prior to the rise in body temperature, includes post-thiopental or post-halothane shivering, transfusion reaction, cardiovascular accidents, and other complications of anesthesia or surgery. In characteristic case reports,[32, 33] two patients underwent electroresection of the prostate under spinal block with no untoward reactions or need for blood replacement. One patient became hypotensive and bradycardic one half hour after his arrival in the recovery room, the other patient developed severe hypotension with tachycardia and chills on the morning following operation. Both patients were noted to be pale, cold, clammy, and one complained of chest pain while the other suffered from nausea and emesis. Electrocardiograms showed no changes from the preoperative tracings in either case. Perforation of the urinary tract was ruled out by cystogram. Both patients developed high spiking fevers, and had positive urine and/or blood cultures within days (*Bacillus aerogenes, Escherichia coli* and enterococcus in one, and *Bacillus aerogenes* and Gram-negative bacilli in the other). Both patients required vasopressor therapy (metaraminol and norepinephrine) to maintain their arterial pressures at normal levels until the infection was cleared; this required 14 days in the first patient and 16 in the second.

The delayed onset of the clinical symptoms is in agreement with experimental findings following the intravenous injection of bacterial endotoxins into man. An asymptomatic interval of 30 to 90 minutes ensues which terminates with the abrupt onset of shaking chills and fever. Other biological alterations may occur. They include polymorphonuclear leukopenia followed by leukocytosis, enhanced reactivity to epinephrine and related substances, depletion of liver glycogen, vascular collapse, and shock.[34]

Peripheral vascular collapse is relatively common following Gram-negative bacteremia and considerably less common with Gram-positive bacteremia.[35] The endotoxins from all Gram-negative bacteria are qualitatively similar in their biologic activities.[34] In 15 urological patients in whom postoperative bacteremic "shock" developed, Gram-negative bacilli were cultured in 12 instances, and Gram-positive in three.[36] The most frequently encountered organisms in 33 urological patients with Gram-negative septicemia were *E. coli* (40 per cent), *Aerobacter aerogenes* (27 per cent), pseudomonas (21 per cent), and proteus (6 per cent). *A. aerogenes* was the most common offender in those patients who developed peripheral vascular collapse (44 per cent); *E. coli* was second (31 per cent).[37] The mean duration of vascular collapse in patients who survive Gram-negative bacteremic shock was found to be six days with a range from 12 hours to 26 days.[38] Since reports of blood cultures are usually not available for 24 to 36 hours, Gram-stained blood smears may be useful in establishing the diagnosis.[35] Survival of a patient during severe bacteremia is probably dependent upon the number of bacteria, the bacterial virulence, and the resistance of the host.[36] The mortality rates quoted in the literature range from 25 to 75 per cent.[39]

Therapy has two main objectives, the treatment of the infection and the correction of the hypotension.[39] Standard therapy to date consists of intravenous administration of appropriate and adequate antibiotics, vasopressor drugs, adrenocortical steroids, and oxygen inhalation. Adrenal exhaustion may occur as result of the overwhelming infection [40] or from general debilitation.[35] Oxygen inhalation is indicated because cellular oxygen consumption is stimulated by endotoxin and the overall oxygen demand is increased owing to the accompanying fever. Induced hypothermia appears to be a valuable adjunct; it probably protects the host by altering the growth rate of the invading organisms [35] and by reducing the oxygen demand.[36] Drugs, such as autonomic blocking agents or phenothiazine derivatives, have given protection when administered to animals prior to the onset of bacteremic shock, but information is inadequate to recommend their use in human patients.[36]

Blood Loss

Blood loss during transurethral surgery may contribute to postoperative morbidity. Visual estimation of hemorrhage is grossly inaccurate because of dilution with irrigating fluid,[1] and the classical signs of hypotension and tachycardia may not be seen. Various techniques have been advocated to determine the blood loss. Radioactive isotopes such as serum albumin tagged with radio-iodine [41, 42] or red cells labeled with sodium radio chromate[6] have been employed but require appropriate radiation detection equipment. The blood loss monitor described by LeVeen and Rubricius has been utilized.[42] This apparatus depends on the change in conductivity of water when blood or electrolytes are added to it. The results, which are measured by a Wheatstone bridge, are indicated directly in cubic centimeters of blood. Nonelectrolytic irrigating solutions were found not to affect the determinations. However, the electrolytes of the urine collected in the irrigating fluid constitute an error which must be taken into account. It was shown that 75 ml. of urine (approximate output during one hour of surgery) reflects on the monitor as a blood loss of between 30 to 50 ml., depending on the ion concentration of the particular urine. Using this method in 45 transurethral prostatectomies, blood losses ranging from 200 to 1,800 ml. were determined.[43] A colorimetric method has been developed for analysis of blood in water[44, 45] or nonhemolytic solutions.[46] The hemoglobin is converted to acid hematin by the addition of an excess of hydrochloric acid. The resulting brown color of the acid hematin is then compared with colored ampules representing a known percentage of blood. The percentage obtained is multiplied by the volume of irrigating solution used and corrected to the patient's hemglobin. When nonhemolytic fluids are used, a pinch of powdered saponin must be added to the sample in order to clear the solution which is cloudy because of nonhemolyzed erythrocytes.[46]

Recently, the use of cooled irrigating solutions (2°–6° C.) was said to reduce the bleeding associated with this type of surgery.[10, 23, 47, 48] Comparing the temperature in esophagus, rectum, prostatic tissue and suprapubic skin, it was observed that the most pronounced fall in temperature occurred in the prostate and the least in the esophagus.[23] This selective cooling of the lower pelvic organs explains the absence of shivering in most patients. In 100 transurethral operations performed with cooled irrigating fluid, only six blood transfusions were necessary as compared with 32 transfusions in 100 similar procedures done with solutions at room temperature. Direct measurements of the blood loss in 20 patients, operated on with local hypothermia of the bladder, amounted to a mean of 211 ml.; in seven control patients, the average blood loss was 382 ml.[23] However, other observers did not confirm this observation.[20, 42] In the study of 43 cases, the hypothermic group demonstrated no statistically significant change in blood loss when compared to a similar group of controls.[42] When bleeding is profuse, the head of pressure of the irrigating fluid is often increased in order to provide better vision; this, in turn, augments absorption of irrigating fluids.

Prompt replacement of blood loss is important. Most of the patients are in the older age group and may have compromised cardiovascular reserve. Other complications of transurethral surgery such as hypoelectrolytemia or hemolysis add to the hazard of hemorrhage. Moreover, patients with urological problems often restrict their fluid intake voluntarily, thus becoming dehydrated, hypovolemic and hemoconcentrated. Preoperative laboratory reports of hemoglobin or hematocrit may, thus, be misleading, and the patient may develop anemic hypoxia or even hemorrhagic shock early during the procedure. A preoperative blood volume determination may be of value in cases where chronic bleeding, weight loss, or carcinoma is suspected.

The intravenous administration of conjugated estrogens prior to transurethral resection was reported in one study (17 study cases, 12 controls) as controlling excessive bleeding,[49] while in a similar investigation (41 study cases, 43 controls) no diminution in bleeding was observed.[50] Measurements of blood clotting factors in ten healthy patients before and after the intravenous injection of 20 mg. of Premarin (the dosage recommended to control bleeding) failed to reveal a significant increase in clotting factor activities.[51] The parenteral use of adrenochrome semicarbazone (Adrenosem) in a controlled study with 29 patients in each group proved ineffective in reducing bleeding.[52]

Defects in the clotting mechanism involving the fibrinolytic system have been observed more often in patients undergoing surgery of the prostate than in patients subjected to other types of surgery. During one year, in the Los Angeles County Hospital, five cases of fibrinolysis were recognized among 302 transurethral resections as compared to three cases of fibrinolysis in approximately 3,500 general surgical procedures.[53] An imbalance of the "delicate equilibrium between the active enzyme plasmin and its antagonist antiplasmin" appears to be the cause.[54] Plasmin (fibrinolysin), the enzyme that "digests fibrinogen and fibrin," is found in the globulin fraction of blood as its inactive precursor plasminogen (profibrinolysin). Antiplasmin (antifibrinolysin), on the other hand, is contained in the albumin fraction.[55] The transformation of plasminogen to plasmin can be affected in a restricted area by a local tissue activator or in a general manner by the entry into the circulation of a number of agents, such as prostatic or pancreatic tissue.[53-55] Activation of this anticoagulant system may also occur as a result of destruction or dilution of the circulating antiplasmin. Thus, reversal of the A/G ratio may upset the normal plasmin-antiplasmin ratio.[56] *In-vitro* experiments, with the measured zone of liquefaction produced on a heated fibrin plate by an extract of prostatic tissue, revealed a greater lytic activity by malignant prostatic tissue than by benign tissue.[57] *In vivo,* fibrinolysis appears to occur primarily in those cases in which venous sinuses are opened.[54]

Two representative cases were reported by Poe.[58] A 77 year old man with benign prostatic enlargement and a 44 year old man with carcinoma of the prostate underwent transurethral resection without obvious complications. Both left the operating room in apparently good condition. In the recovery room, however, the blood pressures declined gradually, and bladder drainage was observed to be grossly bloody without clots. In the 77 year old patient, a sample of venous blood did not clot, and epistaxis occurred two hours after the operation. Fibrin index was in excess of 2 minutes (control index 25 seconds). In the 44 year old man, the sample of venous blood exhibited an abnormally soft clot.

Early recognition of this hemorrhagic diathesis is important, since the progressive release of fibrinolysin over a prolonged period may make treatment unsuccessful. According to Lombardo,[57] there are four diagnostic signs: (1) generalized oozing in the prostatic fossa, (2) postoperative, delayed, sudden, bright red bleeding without clots, (3) concomitant bleeding at sites of skin punctures, and (4) submucosal hemorrhages. Observation of clot formation in a sample of venous blood kept at 37° C. confirms the diagnosis. In the presence of circulating fibrinolysin, the blood clot is defective in either bulk or quality, appears soft, and is prone to weaken and disappear from the sample on standing. This disappearance may take as long as four hours, but in clinically significant cases is likely to occur within one hour.[58] The activity of the fibrinolytic enzyme is in inverse proportion to the time required for lysis of the clot.[57]

Treatment consists primarily of the infusion of adequate amounts of fibrinogen. Intravenous fat emulsion has been reported to be of benefit. Saturated fats may inhibit fibrinolysis; in addition, the clots formed in the presence of lipids may be more resistant to subsequent enzymatic lysis.[59]

Perforation

Perforations usually develop during difficult transurethral resections but may complicate litholapaxies, removal of foreign bodies, or resections of neoplasms.[60] Commonly, they are caused by an opening made with the cutting loop or the knife electrode; occasionally, they are made with the beak of the resectoscope, or result from overdistention of the bladder and prostatic fossa with the irrigating medium.[1] Except for the rare perforation of the wall of the bladder, most perforations are extraperitoneal and result in extraperitoneal leakage. Intraperitoneal and combined lesions occur less frequently, but are more serious.[60]

For the urologist, the first indication of perforation is a bizarre irrigating pattern.[60] The anesthesiologist, at the same time, hears a sudden complaint of abdominal pain from the patient under regional anesthesia or notices a sudden loss of relaxation coupled with increased or irregular respiration in the patient under general anesthesia. Simpson wrote in 1946: "We believe that the anesthesiologist often can be of aid to the urologist in the diagnosis of a rupture of the bladder or vesical neck during transurethral resection." [61]

The sudden severe abdominal pain felt by the conscious patient may be generalized, or

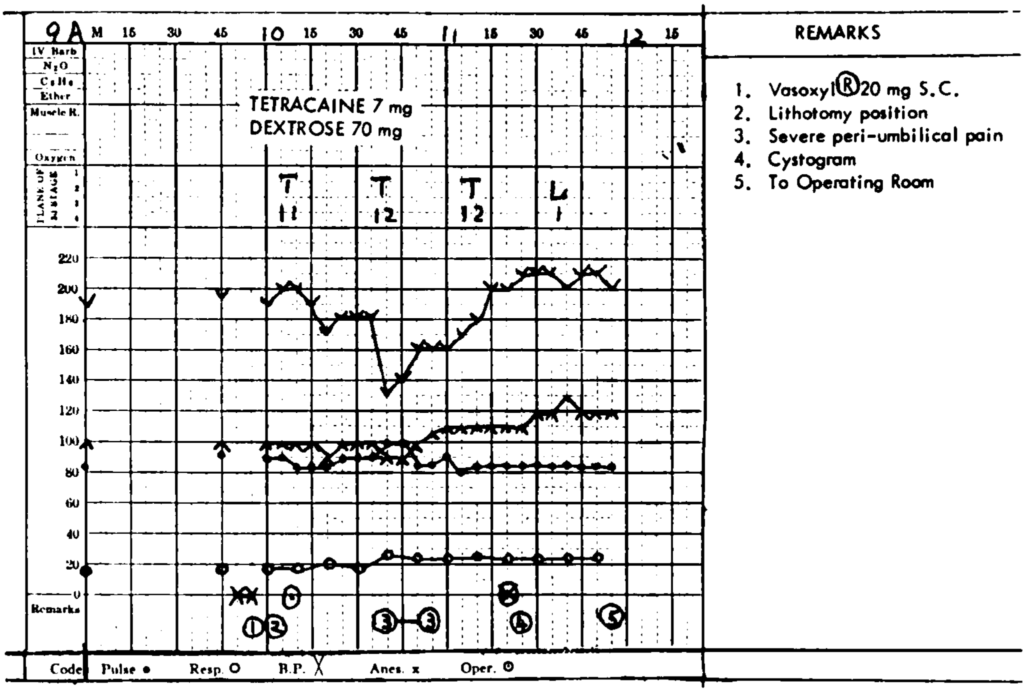

FIG. 2. Intraperitoneal perforation with extravasation of irrigating fluid. A 64 year old man scheduled for cystoscopy and retrograde pyelogram. *Premedication:* pentobarbital 50 mg, atropine 0.3 mg. *Anesthesia:* intrathecal block. Insertion of ureteral catheter proved to be difficult. Vital signs stable for 30 minutes. With onset of severe periumbilical pain, the blood pressure fell precipitously. Return of irrigating fluid markedly decreased. Cystogram revealed large perforation.

in the periumbilical, inguinal, suprapubic region, or in the upper abdomen.[60, 61] It may be referred to the precordial region or the shoulder. Concomitantly, rigidity of the abdominal muscles and tenderness to palpation of the abdominal wall develop. The patient may exhibit pallor, sweating, and nausea with or without vomiting. Sudden "reflex-type" movements of the limbs have been noted in both the conscious and unconscious patient at the time of perforation.[60, 61] Subsequent changes in vital signs depend on the location and size of the perforation, and on the amount and osmolarity of extravasated fluid. With small perforations and little leakage, there may be no significant alterations in either blood pressure or pulse rate. With extravasation of larger amounts of solution, there will be a gradual rise in blood pressure which is usually preceded by a sudden fall (fig. 2). A shock-like picture with severe hypotension and tachycardia is seen when large quantities of irrigating medium enter the perivesical spaces.[61] In these cases, leakage is into the peritoneal cavity, and the solution, often nonisotonic, adds the problem of hemolysis.

In a study on morbidity and mortality of 2,015 transurethral prostatectomies, operative extravasation occurred in 23 patients (1.1 per cent). Of these, four died. All four deaths and five major complications occurred in the 12 patients in whom suprapubic cystostomy was delayed beyond two hours after perforation.[62] Prompt diagnosis is, therefore, of vital importance. It was stated that "advocacy of spinal anesthesia is timely" because the clinical picture of perforation is "unmistakable if the patient is conscious and the anesthesia is low."[65] A presumptive diagnosis of perforation must be verified by cystogram or urethrocystogram. The treatment is surgical, i.e., cystostomy and drainage.

Anesthetic Implications and Conclusions

Many anesthetic techniques may be employed to carry a patient safely and satisfactorily through transurethral surgery. The basic requirements are relatively clear-cut. The method should afford adequate operating conditions and eliminate the hazards of explosion. The patient's physiological resources should be disturbed as little as possible and his functioning compensatory mechanisms should be maintained. Signs and symptoms of distress should not be altered, and recovery should be rapid and complete. Since most patients have cardiac, respiratory, renal, or the other diseases of their age group, each patient must be treated as an individual.

The preoperative care should include correction of malnutrition, dehydration, blood volume deficits, and electrolyte imbalances. Preoperative medication may usually be kept to a minimum, since the elderly patient is often more serene and presents less psychic problems than the young adult.[64]

Regional anesthetic techniques such as spinal, peridural, or caudal block seem ideal and are widely used. Spinal block requires considerably less local anesthetic agent than the other two methods, but is relatively contraindicated with neurological disorders and may be hazardous in patients with frequent coughing spells. Postspinal headache is rare in the older patient. Peridural and caudal block must be executed with caution and patience to avoid sequelae of rapid absorption such as convulsions and myocardial depression. In all three techniques, a sensory level to the tenth thoracic segment is optimal; anesthesia is adequate, respiratory innervation is not affected, arterial hypotension is minimal and easily treated, and the subjective signs of hypervolemia or perforation are not obtunded. Transsacral block is not recommended because of the occasional erection during the passage of the cystoscope;[65] there is no study reporting the adequacy of anesthesia with this block.

General anesthesia is usually conducted with nitrous oxide-oxygen supplemented with either intravenous or volatile anesthetic agents. Barbiturates or narcotics work well in the good-risk patient, but the rapid elimination of vapors such as trichlorethylene, halothane, or trifluoroethyl vinyl ether make this method preferable in the poor risk patient. The occasional debilitated patient in whom halothane or trifluoroethyl vinyl ether are contraindicated or poorly tolerated may be anesthetized with nitrous oxide-oxygen supplemented by a muscle relaxant; in this case, endotracheal intubation is desirable, and close supervision of ventilation in the postoperative period indicated.

Transurethral surgery is performed in the lithotomy position, which causes both circulatory and respiratory alterations. Approximately 500 ml. of blood are added to the effective circulation when the legs are placed in stirrups, and the same amount is taken out with lowering of the legs at a time when the total blood volume may be seriously reduced. Respiratory excursions are decreased owing to the pressure of the intestines on the diaphragm; this, however, is beneficial in the patient with emphysema by reducing the residual volume.[66]

Finally, an awareness of the problems inherent in transurethral surgery is mandatory on the part of the anesthesiologist. This acumen, coupled with good rapport between anesthesiologist and urologist, may provide for early diagnosis of complications, for their prompt treatment, and for reduction in morbidity or mortality.

References

1. Weyrauch, H. M.: Surgery of the Prostate, Philadelphia, W. B. Saunders Co., 1959, Ch. 13.
2. Landsteiner, E. K., and Finch, C. A.: Hemoglobinemia accompanying transurethral resection of the prostate, New Engl. J. Med. **237**: 310, 1947.
3. Creevy, C. D.: Importance of hemolysis during transurethral prostatic resection: a clinical investigation, J. Urol. **59**: 1217, 1948.
4. Taylor, R. O., Maxson, E. S., Carter, F. H., Bethard, W. F., and Prentiss, R. J.: Volumetric, gravimetric and radioisotopic determination of fluid transfer in transurethral prostatectomy, J. Urol. **79**: 490, 1958.
5. Griffin, M.: Toxic symptoms accompanied by hemolysis during transurethral prostatectomy, J. Urol. **59**: 431, 1948.
6. Fillman, E. M., Hanson, O. L., and Gilbert, L. O.: Radioisotopic study of effects of irrigating fluid in transurethral prostatectomy, J.A.M.A. **171**: 1488, 1959.

7. Maluf, N. S. R., Boren, J. S., and Brandes, G. E.: Absorption of irrigating solution and associated changes upon transurethral electroresection of prostate, J. Urol. **75**: 824, 1956.
8. Evert, C. E.: A clinical comparison of the use of glucose and urea in irrigating solutions of transurethral resections, J. Urol. **62**: 736, 1949.
9. Goodwin, W. E., Cason, J. F., and Scott, W. W.: Hemoglobinemia and lower nephron nephrosis following transurethral prostatic surgery: use of a new nonhemolytic irrigating solution, three per cent mannitol, as preventive, J. Urol. **65**: 1075, 1951.
10. Franks, D. P., and Cockett, A. T.: Local hypothermia of the urinary bladder during transurethral surgery, ANESTHESIOLOGY **22**: 15, 1961.
11. Schulte, T. L., Hammer, H. J., and Reynolds, L. R.: Clinical use of Cytal in Urology, J. Urol. **71**: 656, 1954.
12. Bulkley, G. J., O'Conor, V. J., and Sokol, J. K.: Overhydration during transurethral prostatic resection, J.A.M.A. **156**: 1042, 1954.
13. Harrison, R. H., Boren, J. S., and Robison, J. R.: Dilutional hyponatremic shock: another concept of the transurethral prostatic resection reaction, J. Urol. **75**: 95, 1956.
14. Huf, D., Koenig, J., and Hamelberg, W.: Fluid absorption during transurethral prostatic resection, ANESTHESIOLOGY **23**: 152, 1962.
15. Marx, G. F., Koenig, J. W., and Orkin, L. R.: Dilutional hypervolemia during transurethral resection of the prostate, J.A.M.A. **174**: 1834, 1960.
16. Marx, G. F., Rothaus, R., and Orkin, L. R.: Intravenous infusions of 10 per cent Cytal, 5 per cent dextrose/water, or Plavolex in dogs, J. Urol. **84**: 424, 1960.
17. Hoyt, H. S., Goebel, J. L., Lee, H. I., and Schoenbrod, J.: Types of shock-like reaction during transurethral resection and relation to acute renal failure, J. Urol. **79**: 500, 1958.
18. Ceccarelli, F. E., and Smith, P. C.: Studies on fluid and electrolyte alterations during transurethral prostatectomy: II, J. Urol. **86**: 434, 1961.
19. Berg, G., Fedor, E. J., and Fisher, B.: Physiologic observations related to the transurethral resection reaction, J. Urol. **87**: 596, 1962.
20. Pennisi, S. A., Rowland, H. S., Vinson, C. E., and Bunts, R. C.: Hyponatremia as affected by various irrigants used during transurethral electroresection of the prostate, J. Urol. **86**: 249, 1961.
21. Pierce, J. M.: The treatment of water intoxication following transurethral prostatectomy, J. Urol. **87**: 181, 1962.
22. Marx, G. F., Andrews, I. C., and Orkin, L. R.: Cerebrospinal fluid pressures during halothane anaesthesia, Canad. Anaesth. Soc. J. **9**: 239, 1962.
23. Leonhardt, K. O.: Lokale Hypothermie der Blase zur Blutungsverminderung bei transurethralen Operationen, Anaesthesist **11**: 80, 1962.
24. Ceccarelli, F. E., and Mantell, L. K.: Studies on fluid and electrolyte alterations during transurethral prostatectomy: I, J. Urol. **85**: 75, 1961.
25. Creevy, C. D.: Hemolysis and transurethral resection, Surgery **39**: 180, 1956.
26. Minuck, M.: Complications arising during transurethral resection of the prostate, Canad. Anaesth. Soc. J. **1**: 59, 1954.
27. Clinical Anesthesia Conference (Chairman: Harmel, M. H.): Hemolysis during transurethral resection as a diagnostic problem, New York J. Med. **56**: 2260, 1956.
28. Creevy, C. D.: Hemolytic reactions during transurethral prostatic resection, J. Urol. **58**: 125, 1947.
29. Biorn, C. L., and Greene, L. F.: Hemolysis during transurethral prostatic resection, Surg. Gynec. Obstet. **88**: 389, 1949.
30. Barlas, G. M., and Kolff, W. J.: Transfusion reactions and their treatment, especially with the artificial kidney, J.A.M.A., **169**: 1969, 1959.
31. Creevy, C. D., and Feeney, M. J.: Routine use of antibiotics in transurethral prostatic resection: a clinical investigation, J. Urol. **71**: 615, 1954.
32. Clinical Anesthesia Conference (Chairman: Burstein, C. L.): Hypotension following a transurethral procedure, New York J. Med. **60**: 2901, 1960.
33. Clinical Anesthesia Conference (Chairman: Ciliberti, B. J.): Prolonged postoperative hypotension, New York J. Med. **61**: 4065, 1961.
34. Bennett, I. L.: Pathogenesis of fever, Bull. New York Acad. Med. **37**: 440, 1961.
35. Ezzo, J. A., and Knight, W. A.: Bacterial shock, Arch. Intern. Med. **99**: 701, 1957.
36. Cockett, A. T. K., and Goodwin, W. E.: Hypothermia as a therapeutic adjunct in the management of bacteremic shock after urological surgery, J. Urol. **85**: 358, 1961.
37. Shirley, S. W., Lyons, C., and Hale, E.: The management of Gram-negative septicemia common to urologic procedures, J. Urol. **86**: 673, 1961.
38. Weil, M. H., and Spink, W. W.: The shock syndrome associated with bacteremia due to Gram-negative bacilli, Arch. Intern. Med. **101**: 184, 1958.
39. Kennelly, J. M.: Bacteremic shock: sequel to genitourinary tract instrumentation, J. Urol. **79**: 549, 1958.
40. Hooper, J. W., and Hare, R. B.: Bacteremia producing shock following transurethral prostatectomy, J. Urol. **83**: 742, 1960.
41. Cockett, A. T. K., Schultz, J., and Franks, D.: Use of refrigerated solution during transurethral surgery, J. Urol. **85**: 632, 1961.

42. LeVeen, H. H., and Rubricius, J. L.: Continuous, automatic, electronic determinations of operative blood loss, Surg. Gynec. Obstet. **106**: 368, 1958.
43. Goldman, E. J. and Samellas, W.: Blood loss during prostatectomy, J. Urol. **86**: 637, 1961.
44. Nesbit, R. M., and Conger, K. B.: Studies of blood loss during transurethral prostatic resection, J. Urol. **46**: 713, 1941.
45. Rives, H. F., and Latchem, C. W.: A table for determination of blood loss during transurethral prostatic resection, Proc. Mayo Clin. **20**: 151, 1945.
46. Litin, R. B., and Emmett, J. L.: Method for measuring blood loss during transurethral resection when nonhemolytic irrigating solutions are employed, Proc. Mayo Clin. **34**: 158, 1959.
47. Landes, R. R., Leonhardt, K., Ransom, C. L., and Davila, J.: Localized hypothermia for transurethral prostatic resection, J. Urol. **82**: 247, 1959.
48. Stewart, B. L.: A simple heat exchanger for cooling irrigating solutions during transurethral prostatectomy, J. Urol. **87**: 178, 1962.
49. Bobelis, C. K.: Premarin intravenous in prostatic surgery, Illinois Med. J. **117**: 231, 1960.
50. Geist, R. W. and Haglund, R. V.: Failure of intravenous injections of estrogens (Premarin) to decrease loss of blood during transurethral prostatic resection, J. Urol. **87**: 593, 1962.
51. Kudish, H. G. and Rapaport, S. I.: Failure of intravenous estrogens (Premarin) to affect plasma clotting factors in humans, J. Urol. **83**: 730, 1960.
52. Frank, R. M., and Lloyd, F. A.: Clinical study on effectiveness of Adrenosem in transurethral resection, J. Urol. **82**: 243, 1959.
53. Lombardo, L. J.: Fibrinolysis following prostatic surgery, J. Urol. **77**: 289, 1957.
54. Lombardo, L. J.: Studies in the prevention of fibrinolysis occurring in prostatic surgery, J. Urol. **79**: 507, 1958.
55. Miller, J. M., Meisel, H. J., Jackson, D. A., and Collier, C. S.: Fibrinolysis in a patient with carcinoma of the prostate, J. Urol. **81**: 672, 1959.
56. Baurys, W., and Jacobson, H. H.: Proteolytic enzymes and prostatectomy, J. Urol. **81**: 676, 1959.
57. Lombardo, L. J.: Fibrinolysis in urological patients, J.A.M.A. **169**: 1718, 1959.
58. Poe, M. F.: Acute reactions following transurethral resection of the prostate, Anesth. Analg. **39**: 225, 1960.
59. Neft, L. G., Dugdale, M., Biggs, A. W., and Raines, S. L.: Treatment of abnormal bleeding associated with prostatic disease by intravenous fat emulsion, J. Urol. **85**: 329, 1961.
60. Kenyon, H. R.: Perforation in transurethral operations; technic for immediate diagnosis and management of extravasations, J.A.M.A. **142**: 798, 1950.
61. Simpson, R. A.: Rupture of bladder during transurethral resection of prostate and possibility of aid by anesthesiologist in its diagnosis, Urol. Cutan. Rev. **50**: 628, 1946.
62. Holtgrewe, H. L., and Valk, W. L.: Factors influencing the mortality and morbidity of transurethral prostatectomy: a study of 2015 cases, J. Urol. **87**: 450, 1962.
63. Herman, L.: Discussion, J.A.M.A. **142**: 802, 1950.
64. Schorer, F.: The relationship of geriatric changes to anesthesia, Anaesthesist **6**: 381, 1957.
65. Lundy, J. S.: Clinical Anesthesia, A Manual Of Clinical Anesthesiology, Philadelphia, W. B. Saunders Co., 1945, Ch. 1.
66. Hennington, R. H.: Unpublished data.