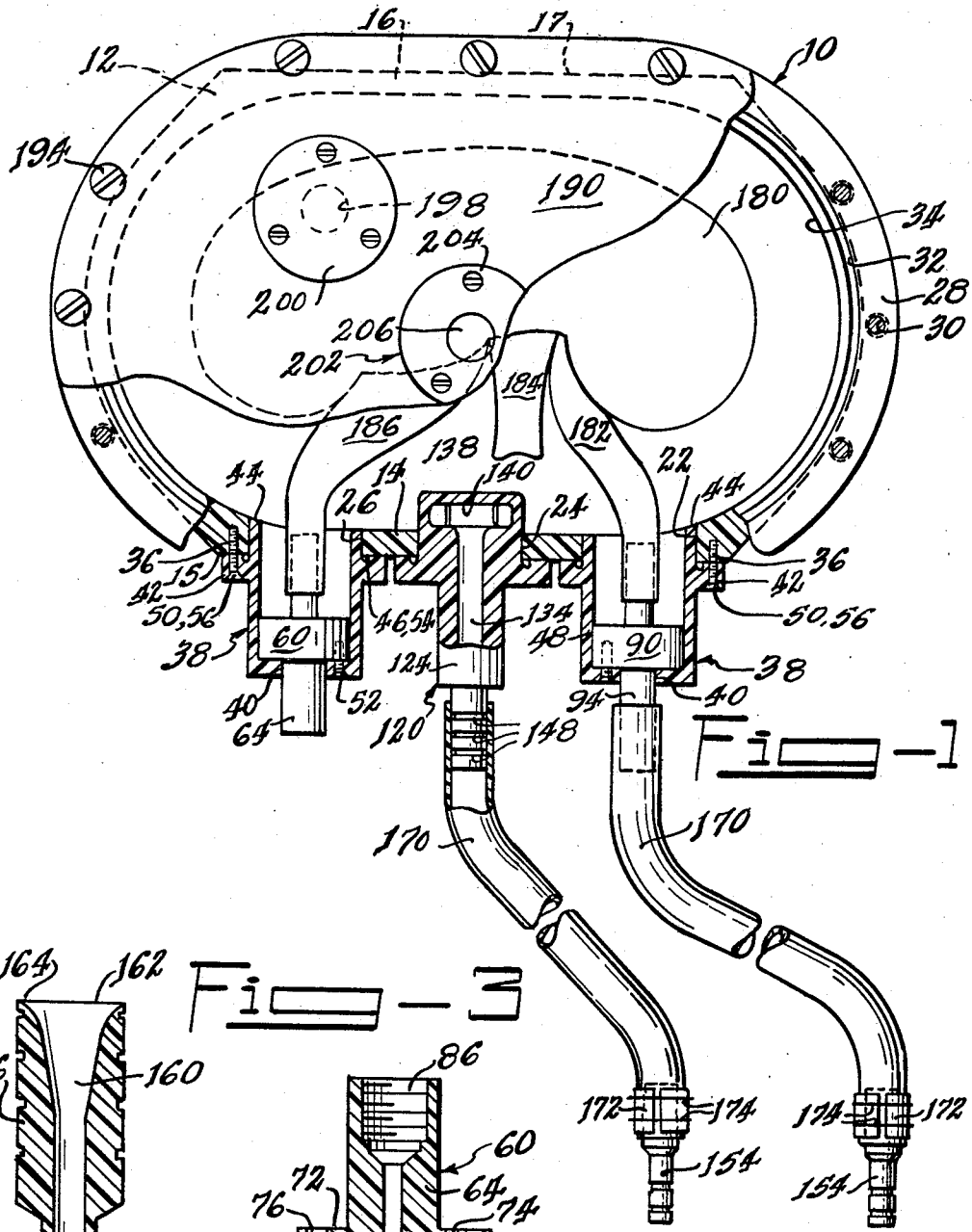
Jan. 20, 1970 A. R. LAVENDER ET AL 3,490,438

PERFUSION CHAMBER AND CANNULAE THEREFOR

Filed June 8, 1967 2 Sheets-Sheet 1




Fig—1

Fig—3

Fig—6

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Filed June 8, 1967 2 Sheets-Sheet 2

Fig. 2

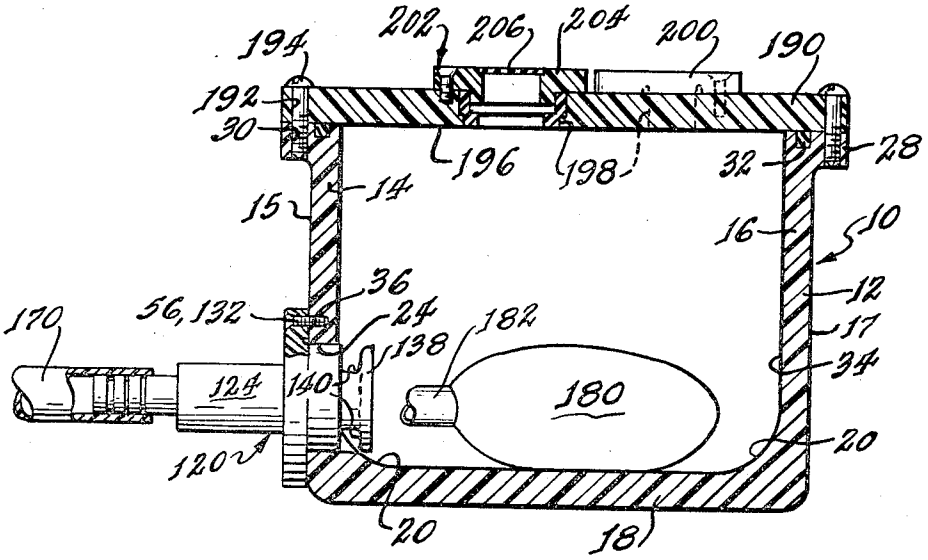
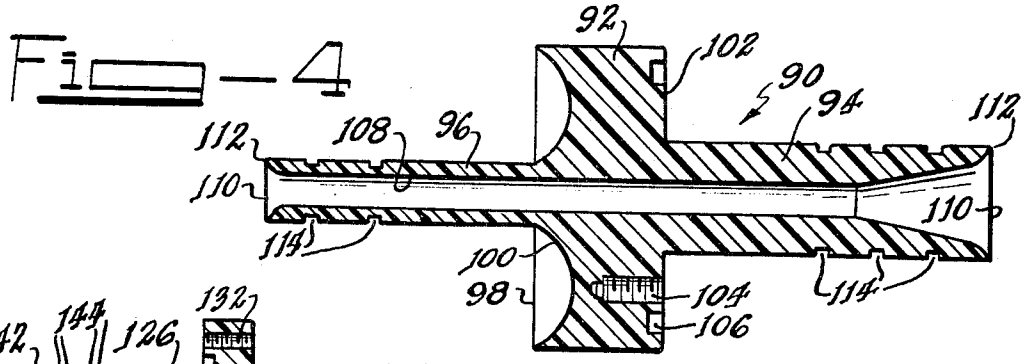



Fig. 4



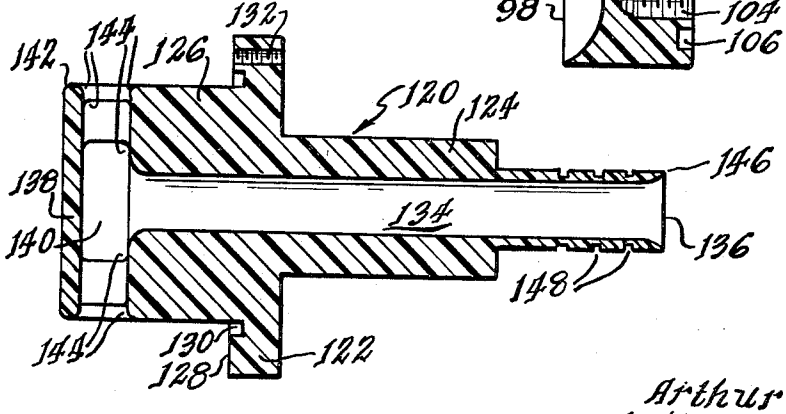




Fig. 5

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# PERFUSION CHAMBER AND CANNULAE THEREFOR

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U.S. Cl. 128—1 7 Claims

## ABSTRACT OF THE DISCLOSURE

A kidney perfusion chamber includes a container with an internal surface free of sharp edges and coated with graphite having absorbed thereon benzalkonium-heparin, and an arterial cannula, a uretal cannula, and a venous cannula each sealingly fitted in an orifice through a wall of the container. The artery and the ureter of a kidney placed in the container are respectively connected to the arterial and uretral cannulae of the chamber. The vein of the kidney is left unconnected and communicates with the venous cannula via the interior of the container. The radial or ulnar artery and the branch medial vein of a patient with an inoperative renal system are respectively connected, via suitable tubing, to the arterial cannula and the venous cannula of the chamber. Blood from the arterial system of the patient flows into the kidney via the arterial cannula and venous blood from the kidney returns to the patient via the kidney vein, the container, and venous cannula. Urine produced by the kidney is discharged via the kidney ureter and the ureter cannula.

## CONTRACTUAL ORIGIN OF THE INVENTION

The invention described herein was made in the course of, or under, a contract with the United States Atomic Energy Commission.

## BACKGROUND OF THE INVENTION

This invention relates to extracorporeal organ perfusion and more particularly to a chamber and associated cannulae for kidney perfusion by blood from chronically cannulated vessels.

When the renal system of a human or other warm-blooded animal ceases to function, whether as a result of injury, disease or congenital defect, a substitute must be provided if life is to continue. In general, a substitute is provided in one of two manners, the patient's blood supply is passed through an artificial kidney machine which performs the renal function or a human kidney is transplanted into the patient. The artificial kidney machines now in use are functionally sufficient to maintain the health of the person who must rely on them. The problems with the machines are that they are expensive, they require trained personnel in attendance during the entire time of use, their blood capacity is such that transfusions are frequently required when the machine is used and the patient is usually tied to the machine for two periods of six hours each week. The most desirable solution to the problem is a human kidney transplant.

Many kidneys which are transplanted are otbained from cadavers. They must be removed from the cadavers shortly after death and inserted into the renally deficient system in an operation which must be classified as major surgery. It is a fact that about 1 in 5 kidneys obtained from cadavers are nonviable and a further 20–40% of the viable cadaver kidneys do not function at maximum efficiency immediately after transplant. After the kidney is transplanted, the recipient's system begins to manufacture antibodies which results in rejection of a large percentage of



the transplanted kidneys. Rejection as opposed to nonviability may take place anywhere from 3 days after the transplant up to a few years. As a person cannot live for any great length of time without renal function, once a transplanted kidney ceases to function for any of the abovementioned reasons an artificial kidney machine must be employed or another kidney transplanted. Major surgery is involved, not only in transplanting a kidney into a system, but also in removing a non-functioning kidney. It is obvious that repeated transplants are deleterious to the recipient's health.

An object of this invention is to provide means for extracorporeal transplants which mitigate the problems heretofore mentioned.

A number of experiments have been conducted in which a kidney has been excised and perfused extracorporeally. In general, these experiments break down into two categories, open and closed systems. In the open system, the excised kidney is connected to a vascular supply and allowed to function in an open container where ready access is provided for biopsy, blood sampling and the like. In the closed system, the kidney is attached to a vascular supply and housed in a closed container of fixed volume and allowed to operate. Neither system has produced normal renal function for any appreciable time. The perfusion chamber and cannulae of this invention enable the extracorporeal perfusion of a human kidney attached to the vascular supply of a renally deficient human being for a sufficiently long period of time to determine not only if the kidney is viable but also if an early rejection occurs. In one case a human kidney was perfused extracorporeally for 25 days, at which time the kidney was rejected due to antibodies built up in the recipient's system.

## BRIEF DESCRIPTION OF THE DRAWINGS

The invention may be more readily understood by reference to the following drawings in which:

FIG. 1 is a top view partially in section of the perfusion chamber of this invention;

FIG. 2 is a side view of FIG. 1;

FIG. 3 is a sectional view of a ureteral cannula;

FIG. 4 is a sectional view of an arterial cannula;

FIG. 5 is a sectional view of a venous cannula; and

FIG. 6 is a sectional view of a body cannula.

With reference to FIG. 1, perfusion chamber **10** is oval in shape and formed from a one-piece plastic container **12** (see also FIG. 2) which may suitably be made of methylacrylate or methylmethacrylate resin. Container **12** has a front side wall **14** and a back side wall **16** which have flat outside surfaces **15** and **17**, respectively. Chamber **12** has a bottom **18** which forms rounded corners **20** with side walls **14** and **16**. Front side wall **14** contains an arterial orifice **22**, a venous orifice **24** and a ureteral orifice **26**.

The top of container **12** is formed into lip **28**. Lip **28** has a plurality of threaded holes **30** and a continuous circumferential groove **32** located between holes **30** and the inside of container **12**. Inside surface **34** of container **12** is entirely coated with graphite having absorbed thereon benzalkonium-heparin (GBH). The interior surface is first etched with sodium and then coated with graphite. Then the graphite is coated with benzalkonium chloride after which there is applied a coating of sodium or potassium heparin. The benzalkonium salt reacts with the heparin to form a benzalkouiumheparin complex which firmly adheres to the graphite. This GBH coating or a methylacrylate or methylmethacrylate resin is one of the most important features of the perfusion chamber.

Screw holes **36** are located in front side wall **14** and surround each orifice **22**, **24** and **26** in the front side wall. Three holes **36** surround each orifice and are spaced at 120-degree intervals. Holes **36** are threaded and extend into, but not through, side wall **14**.

Cannulae housings **38** are tubular in shape and have circular cannulae apertures **40** therein and circular flanges **42** therearound. Housings **38** fit through apertures **22** and **26** in front side wall **14**. End surfaces **44** of housings **38** are flush with inner surface **34** of container **12**. Each flange **42** has a circular groove **46** on the side of the flange which faces outside surface **15** of front side wall **14**. Groove **46** is located between the housing wall **48** and three holes **50** spaced at 120-degree intervals extending through flange **42**. Housing **38** has a second set of three holes **52** spaced at 120-degree intervals that surround cannula aperture **40**. A gasket **54** in each groove **46** seals the interior of container **12** from the outside atmosphere when housings **38** are attached to container **12** by means of screws **56** inserted through holes **50** into screw holes **36**.

Referring now to FIG. 3, ureteral cannula **60** is tubularly shaped and has a circular flange **62** and an outer section **64** which extends through cannula housing aperture **40** and an inner section **66** which extends into the interior of container **12**. Inside edge **68** of flange **62** is sculptured and has rounded surfaces **70**. The outside edge **72** of flange **62** has three screw holes **74** spaced at 120-degree intervals. Screw holes **74** are threaded and extend part way through flange **62**. Cylindrical groove **76** in flange **62** is located outside of screw holes **74**. Ureteral cannula **60** has a channel **78** extending therethrougth. Tip **80** of inner section **66** is square-cut and chamfered at a 30-degree angle to a knife edge **82** which is $\frac{1}{1000}$" in thickness. The lumen, that is, the diameter of channel **78**, varies with the size of each individual ureter to which cannula **60** is attached but is adjusted so that the wall thickness of inner section **66** is about 0.02". A plurality of circumferential grooves **84** extend from tip **80** of cannula **60** back along the outside of inner section **66**. The first of grooves **84** is 0.005" from tip **80**. Channel **78** terminates in a threaded chamber **86** in outer section **64**. Outer chamber **86** may be threaded to receive a Luer female plug.

Ureteral cannula **60** is inserted into housing **38** from the inside of container **12**. A gasket (not shown) is inserted into cylindrical groove **76** and the outer section **64** is inserted through cannula aperture **40**. Cannula **60** is adjusted until screw holes **74** in flange **62** are aligned with holes **52** in housing **38**. Screws (not shown) are then inserted into screw holes **74** and tightened until cannula **60** is securely sealed to housing **38**.

With reference to FIG. 4, arterial cannula **90** is tubularly shaped and formed of flange **92**, outer section **94** and inner section **96**. Inside edge **98** of flange **92** is sculptured and has rounded surfaces **100**. The outside edge **102** of flange **92** has three screw holes **104** spaced at 120-degree intervals. Screw holes **104** are threaded and extend part way through flange **92**. Cylindrical groove **106** in flange **92** is located outside of screw holes **104**. Arterial cannula **90** has a channel **108** extending therethrough. Both tips **110** of inner section **96** and outer section are square-cut and chamfered at a 30-degree angle to knife edges **112** which are $\frac{1}{1000}$" in thickness. The lumen of arterial cannula **90**, like that of ureteral cannula **60**, is variable, depending upon the size of the artery used therewith, but the wall thickness of inner section **96** remains about 0.02". A plurality of circumferential grooves **114** extend from tips **110** of cannula **90** back along the outsides of inner section **96** and outer section **94**. The first of grooves **114** in inner section **96** is 0.005" from tip **112**. Channel **108** in outer section **94** of arterial cannula **90** is taper-bored to a standard lumen size. The lumen size of channel **108** in outer section **94** and the outside diameter of outer section **94** are standard for all cannulae, except ureteral cannula **60**, which permits the use of uniform diameter tubing regardless of the size blood vessel to which a cannula is connected.

Arterial cannula **90** is inserted into housing **38** from the inside of container **12**. A gasket (not shown) is inserted into cylindrical groove **106** and outer section **94** is inserted through cannula aperture **40** in housing **38**. Cannula **90** is adjusted until screw holes **104** in flange **92** are aligned with holes **52** in housing **38**. Screws (not shown) are then inserted into screw holes **104** and tightened until cannula **90** is securely sealed to housing **38**.



With reference to FIG. 5, venous cannula **120** is tubularly shaped and formed of flange **122**, outer section **124** and inner section **126**. The inside edge **128** of flange **122** has a cylindrical groove **130** and three holes **132** spaced at 120-degree intervals. Groove **130** is located inside of holes **132**. Venous cannula **120** has channel **134** extending from tip **136** in outer section **124** through outer section **124** and most of inner section **126**. Channel **134** terminates near end **138** of inner section **126**. Three side ports **140** near end **138** in inner section **126** connect with channel **134**. External corners **142** of inner section **126** are rounded. All internal corners **144** in inner section **126** formed by ports **140** are also rounded. Tip **136** in outer section **124** is square-cut and chamfered at a 30-degree angle to a knife edge **146** which is $\frac{1}{1000}$" in thickness. A plurality of circumferential grooves **148** extend from tip **136** of cannula **120** back along the outside of outer section **124**. The lumen of channel **134** of venous cannula **120** and the outside diameter of outer section **124** are sized to fit standard tubing.

Venous cannula **120**, unlike ureteral cannula **60** and arterial cannula **90**, is inserted into container **12** from the outside. Inside section **126** is inserted through venous orifice **24** in front side wall **14** of container **12**. A gasket (not shown) inserted into cylindrical groove **130** seals the inside of container **12** once screws **56** have been inserted through holes **132** into screw holes **36** in front side wall **14** and tightened.

With reference to FIG. 6, body cannula **154** is formed of outer section **156** and inner section **158**. A channel **160** extends therethrough and tips **162** are square-cut and chamfered at a 30-degree angle to knife edges **164** which are $\frac{1}{1000}$" in thickness. A plurality of circumferential grooves **166** extend backward along the outside of inner section **158** and outer section **156** from tips **162**. The first of grooves **166** is 0.005" from tips **162** of cannula **154**. Both the lumen size and outside diameter of outer section **156** are the same as in arterial cannula **90** and venous cannula **120** so that uniform tubing may be used throughout.

With reference to FIG. 1, body cannulae **154** are attached to an arterial supply (not shown) and a venous system (not shown). The outer section **156** of cannula **154** attached to the arterial supply is inserted into tubing **170** which is, in turn, connected to outer section **94** of arterial cannula **90**. Tubing **170** is secured to outer section **94** of arterial cannula **90** by ligatures (not shown) which correspond to cylindrical grooves **114** in outer section **94** of arterial cannula **90**. Similarly, tubing **170** is secured to outer section **156** of body cannula **154** by ligatures. However, to insure that tubing **170** does not slip from body cannula **154**, a split tube **172** with circumferential grooves **174** therein surrounds tubing **170** and outer section **156** of body cannula **154**. Split tube **172** is secured by ligatures. Similarly, tubing **170** connects outer section **124** of venous cannula **120** to outer section **156** of body cannula **154** leading to the venous system. Tubing **170** is secured to outer section **124** of venous cannula **120** in the same manner as described above and a split tube **172** is also employed to secure tubing **170** to the body cannula **154** leading to the venous system. All body cannulae **154** are internally coated with GBH. Tubing **170** may be silicone rubber or a suitable plastic which is internally coated with GBH.

A kidney **180** with an artery **182**, a vein **184** and a ureter **186** is placed in container **12** and connected as follows. Artery **182** is connected to inner section **96** of arterial cannula **90** and secure by ligatures. Ureter **186** is connected in a similar manner to inner section **66** of

ureteral cannula **60**. Vein **184** is not directly connected to venous cannula **120** but opens to container **12** so that venous blood from kidney **180** will bathe the kidney and fill chamber **10**.

With reference to FIG. 2, a plastic top **190** which may be the same material as container **12**, is formed to fit over lip **28** of container **12**. Top **190** has a plurality of threaded holes **192** which correspond to threaded holes **30** in lip **28** of container **12**. Screws **194** in threaded holes **192** and **30** fasten top **190** to container **12**. A gasket (not shown) in groove **32** provides a seal between top **190** and container **12**. Inside surface **196** of top **190** may be partially coated with a silicone grease which is transparent to enable kidney **180** to be viewed. The balance of inside surface **196** is coated with GBH. Top **190** has three ports **198**. Two ports **198** contain removable plugs **200**. A nonremovable plug **202** in the third port **198** consists of a housing **204** and a center section **206** of silicone rubber. Plug **202** is securely fastened to top **190** by screws (not shown). Plugs **200** and **202** are machined to precisely fit into ports **198** so that inner surface **196** of top **190** is smooth.

In operation, a kidney is obtained from a cadaver or donor by an operative technique which will be explained later. Kidney **180** is put into container **12** and artery **182** and ureter **186** are connected as hereinbefore described. A body cannula **154** is inserted into the radial or ulnar artery of a patient with an inoperative renal system. Cannula **154** is then connected to arterial cannula **90** by the method hereinbefore described. Similarly, a second body cannula **154** is inserted into the branch medial basilic vein and connected to venous cannula **120** as hereinbefore described. A clamp (not shown) on tubing **170** leading from the radial artery is slowly opened until blood flows from the patient into kidney **180** A clamp (not shown) on renal vein **184** is removed after blood flows into kidney **180**. After vein **184** has been freed, top **190** is secured to container **12** as described and blood flowing from vein **184** fills container **12**. Blood is prevented from exiting container **12** by a clamp on tubing **170** leading from venous cannula **120**. Air in container **12** is removed by allowing blood to flow through a needle (not shown) inserted through plug **202**. After all the air has been removed from container **12**, the needle is removed, the clamp on the tubing **170** connected to venous cannula **120** is also removed and perfusion chamber **10** is ready for operation. At this time, kidney **180** is functionally in the vascular system of the patient. Blood from the arterial system of the patient flows into kidney **180** and venous blood from the kidney returns to the patient. Urine produced by kidney **180** is discharged from chamber **10** through ureter **186** connected to ureteral cannula **60**.

Perfusion chamber **10** is adaptable for research in that kidney **180** may be viewed through top **190**, and blood specimens and tissue biopsy may be obtained through center section **206** in plug **202**. If for any reason kidney **180** fails to function at proper efficiency or is rejected, an artificial kidney machine can be connected to chamber **10** through ports **198** by removing plugs **200** therefrom. In this manner new vessels do not have to be cannulated.

As mentioned before, perfusion chamber **10** has been utilized to keep a human kidney alive and in good functioning order for 25 days while attached to a human vascular system. This chamber has worked where other chambers and methods have failed. Features which seem to be important for its successful operation follow. Container **12** was machined from a single piece of an acrylate or methacrylate resin, such as methylacrylate or methyl methylacrylate, all internal surfaces were coated with GBH and as many internal projections and corners as possible were rounded. When visual inspection is necessary, a portion of the chamber, such as the cover, is coated with silicone grease which gives transparency and some protection from blood clotting, although the GBH coating is preferable for this purpose. Blood clotting has been found to be the major problem, and this has been overcome by our invention of a suitably coated perfusion chamber substantially free of sharp corners.

Another important aspect of our invention is the special design of the cannulae used with the perfusion chamber. As mentioned before, inner sections of the cannulae have thin walls, about 0.02" in thickness, and in all cases the largest possible cannulae were used. The larger the lumen size the greater the blood flow to the kidney and the lower the blood turbulence. Minimum blood turbulence is important because turbulence causes clotting and hemolysis. The square-cut edges of the cannulae tips prevent traumatization of the blood vessels when the cannulae are inserted. Cannulae previously available all have beveled openings which, when inserted into a vessel, gouge the vessel wall. The trauma resulting therefrom may lead to infection or blood clots which break off into the blood stream. A point common to all cannulae is the distance between the cannulae tips and the first of the circumferential grooves in the cannulae. This permits ligation of the blood vessel attached thereto near the tip of the cannula. In most cannulae the ligature is applied at a point distant from the tip of the cannula, which allows blood to flow between the cannula and the vessel wall. This blood collects and results in the distention of the vessel, thereby weakening it and forming clots in the dead space. These clots build up and eventually break off into the blood stream. The chamfered knife edges of the cannula aid in preventing the formation of blood clots and also permit the largest possible cannula to be inserted into each vessel.

The cannula flanges and seals were also carefully designed. The inside edge of each cannula flange was formed so as to remove as many sharp corners as possible from the blood flow path. Gaskets are placed outside of screw holes in the arterial cannula **90** and the ureteral cannula **60**, whereas the gasket fits inside of holes **132** in venous cannula **120**. The placement of gaskets enables chamber **10** to be isolated from outside bacteria and other materials that could possibly be harmful to kidney **180** contained therein. So, also, screws **194** are outside the gasket that seals top **190** to lip **28** of container **12**. And, as mentioned before, silicone rubber center section **206** of plug **202** permits blood samples or biopsy of kidney tissue to be taken without opening perfusion chamber **10** to outside undesirable influences.

Still other features of chamber **10** are the cannula housings **38** which permit the use of a smaller chamber volume, because cannulae do not extend into the chamber and take up space. Renal vein **184** is not directly connected to the venous cannula **120** so that venous pressure is not built up to impair blood flow and hinder kidney function. Since venous outflow is not restricted, kidney **180** is free to expand and contract in response to the patient's pulse in the same manner as it would if it were in the patient's body. Also, the absence of increased pressure in and around the kidney allows lymph to drain from the kidney as it is produced. If the lymph were to be retained in the kidney then eventually tissue would be destroyed and the kidney would cease to function.

Each of the novel features, not only of the chamber but also the cannulae, contribute to the viability of the kidney and it is difficult to tell which is the most important; the combination of all features working together gives a device which accomplishes successful perfusion which hitherto has not been done with other devices.

Before the final design of perfusion chamber **10** was determined 75 experiments were uonducted. The operative techniques employed in those experiments involving dogs and sample data obtained therefrom are presented below.

The perfusion chamber employed in the dog experiments was similar to, but not identical with, that hereinbefore. All cannulae were machined from a polymer of trifluorochloroethylene and coated with GBH. The body cannulae employed were identical to those decsribed

above and all gaskets were silicone rubber. The tubing was initially polyvinyl internally coated with GBH, but silicone rubber with a smooth internal surface was found to be more satisfactory.

Healthy mongrel dogs 20–25 kg. in body weight were anesthetized with intravenous pentobarbital. An isomotic saline solution containing creatinine, p-amino-hippurate (PAH), glucose, penicillin and streptomycin was infused into the jugular vein at 1.0 ml./min. by a constant-speed pump. Plasma creatinine values were maintained at 7–9 mg. percent and plasma PAH at 2 mg. percent. A total of 7 grams of glucose, 1.0 gram of streptomycin and 1 million units of crystalline penicillin were infused per day. A kidney was excised in the following manner.

The right femoral artery was cannulated for blood sampling and for blood pressure monitoring by a mercury manometer. Both ureters, exposed by a lower-abdominal, mid-line excision, were cannulated with polyethylene catheters. The largest cannulae possible were inserted into the left femoral artery and vein. In the majority of experiments, the arterial cannula size was 0.17 to 0.19" I.D., and the venous cannula size was 0.19 to 0.21" I.D. Each cannula was attached to a 10.0" length of a 0.25" I.D. tubing, either GBH-coated polyvinyl or silicone rubber. The tubes were filled with heparinized saline and the free ends were closed with screw clamps. A large branch each of the femoral artery and vein was isolated proximal to the tip of each cannula when regional heparinization was used (dogs 10 to 28). Polyethylene tubing was inserted into these arterial and venous branches and connected to syringes in a constant-speed pump. The arterial syringe contained heparin, 1000 units/ml., and the venous syringe contained protamine sulphate, 10.0 mg./ml. The pump rate was 1.5 or 3.0 ml./hr.

After closing all wounds, the animal was turned onto its right side and the left kidney was exposed by a retroperitoneal flank approach. The ureter and kidney were freed of all nonvascular attachments and the ureter was severed at the pelvic brim. Mannitol, 50 ml. of a 25% solution, was then given intranvenously. When diuresis was established and the kidney was swollen, both the renal artery and vein were clamped simultaneously near the hilum. Both vessels were ligated at their origins, the vessels were severed distal to the ligatures and the kidney was removed. The cut end of the renal vein was ligated and the vessel clamp was removed. The venous ligature prevented decompression of the kidney during the cannulation procedure.

The largest cannula possible was inserted into the renal artery and tied into position. In most experiments, the cannula size was 0.17 to 0.19" I.D. After tying in the ureteral cannula, the kidney was placed in the perfusion chamber and all cannulae were seated and sealed in the chamber wall. Isosmotic saline at 38° C. was used to fill the chamber. Femoral artery and vein tubes were attached to the appropriate cannulae from the perfusion chamber. The arterial tube's clamp was loosened until blood appeared distal to the clamp. The renal vein ligature then was removed. The chamber top was sealed and air was displaced through the stopcock by renal venous outflow. When all air had been evacuated, the stopcock was closed and the venous tube's clamp was removed. The arterial tube's clamp then was opened gradually over a period of about one minute. Blood immediately displaced saline in the chamber, the kidney pulsated and urine appeared within ½ to 2 minutes.

Urine collection periods of two hours each were begun when urine flow from each kidney stabilized, usually within two hours of the start of perfusion. Blood samples were drawn at the midpoint of each collection period. All urine and blood specimens were analyzed for creatinine, PAH, sodium and potassium. Creatinine and PAH clearances were used to estimate glomerular filtration rate (GFR) and renal plasma flow (RPF), respectively. Some, but not all, urine specimens were tested for pH, glucose and protein. Each experiment continued until the animal died, usually from hemorrhage or respiratory failure, or until the perfused kidney showed functional deterioration. At the conclusion of an experiment, the perfused kidney was inspected for signs of ureteral obstruction, arterial occlusion and infraction. In 11 experiments, both kidneys were weighed and sectioned for histologic study.

The technical features of these experiments are shown in Table I. Means excision time was 13.9 minutes with a range of 5.3 to 22.0 minutes. Mean perfusion time was 33.2 hours with a range of 8.0 to 73.0 hours. Perfusion time was 24 hours or longer in 18 experiments. In half of these, perfusion time was 48 hours or longer. In 11 experiments in which kidney weights were obtained, weight of the perfused kidney did not differ significantly from weight of the in situ kidney. With the exception of dog number 8, plasma hemoglobin did not rise significantly. Most of the experiments were terminated by death of the donor animal but several were complicated by clotting towards the end of the experiment.

TABLE I.—EXTRACORPOREAL PERFUSION OF DOG KIDNEY

| Dog. No. | Excision Time (min.) | Perfusion Time (hrs.) | Kidney Weight (gms.) | | Blood Pressure (mm. Hg) | | Plasma Hb (mm. percent) | | Reason for Termination | Complications |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Perfused | Control | Initial | Final | Initial | Final | | |
| 1 | 7.0 | 13.5 | | | 135 | 20 | | | Hemorrhage | Tubing clot. |
| 2 | 7.8 | 8.0 | | | 90 | 60 | | | do | Venous occlusion. |
| 3 | 5.3 | 47.0 | | | 150 | 80 | | | Respiratory failure | Tubing clot. |
| 4 | 7.5 | 32.0 | | | 110 | 118 | | | do | Do. |
| 5 | 13.5 | 16.0 | | | 100 | 120 | 3.4 | 3.9 | Sacrificed | Arterial clot. |
| 6 | 22.0 | 15.0 | | | 136 | 40 | 3.9 | 1.9 | Embolus | |
| 7 | 16.4 | 17.0 | | | 120 | 76 | 0.7 | 0.3 | Hemorrhage | |
| 8 | 11.3 | 14.0 | | | 130 | 110 | 44.4 | 69.6 | Sacrificed | Kinked ureter. |
| 9 | 16.8 | 17.3 | | | 110 | 75 | 0.6 | 0.3 | Hemorrhage | Tubing clot. |
| 10 | 14.1 | 28.5 | | | 114 | 68 | 1.0 | 0.9 | Respiratory failure | Hemorrhage. |
| 11 | 18.3 | 39.0 | | | 150 | 66 | 1.3 | 1.7 | do | Tubing clots. |
| 12 | 13.8 | 38.0 | | | 124 | 50 | 0.1 | 1.9 | Hemorrhage | Do. |
| 13 | 13.3 | 26.5 | | | 130 | 41 | 4.2 | 6.4 | do | |
| 14 | 15.1 | 73.0 | 93.4 | 79.6 | 118 | 88 | 0.3 | 0.8 | Sacrificed | |
| 15 | 18.3 | 49.5 | 78.1 | 75.5 | 120 | 94 | 0.3 | 0.3 | do | Kinked ureter. |
| 16 | 17.3 | 48.5 | 71.0 | 65.5 | 124 | 60 | 5.2 | 5.9 | do | Tubing clot. |
| 17 | 14.8 | 60.3 | 76.8 | 72.2 | 128 | 78 | 1.1 | 0.9 | Respiratory failure | Kinked ureter. |
| 18 | 21.8 | 28.0 | 80.9 | 84.9 | 120 | 40 | 6.0 | 3.5 | Sacrificed | Hemorrhage. |
| 19 | 22.0 | 33.5 | | | 120 | 90 | 0.7 | 3.6 | do | Tubing clot. |
| 20 | 13.5 | 23.0 | 56.0 | 57.7 | 140 | 40 | 9.9 | 2.0 | Respiratory failure | |
| 21 | 13.0 | 12.3 | | | 100 | 60 | 3.6 | 2.5 | Hemorrhage | Do. |
| 22 | 13.9 | 20.0 | | | 110 | 58 | 3.8 | 1.3 | do | |
| 23 | 12.9 | 17.0 | 69.8 | 69.6 | 100 | 34 | 1.4 | 0.6 | Respiratory failure | |
| 24 | 9.0 | 49.0 | 92.5 | 85.7 | 110 | 80 | 0.8 | 0.4 | Hemorrhage | |
| 25 | 12.1 | 50.0 | 58.7 | 58.2 | 120 | 30 | 4.6 | 5.0 | do | Venous occlusion. |
| 26 | 11.8 | 58.3 | | | 140 | 110 | 0.8 | 1.5 | Sacrificed | |
| 27 | 14.1 | 27.1 | 59.2 | 56.2 | 116 | 80 | 1.4 | 6.0 | do | Hemorrhage. |
| 28 | 12.1 | 68.1 | 44.2 | 45.9 | 110 | 44 | 0.4 | 3.0 | Hemorrhage | Tubing clots. |
| Mean | 13.9 (5.3–22.0) | 33.2 (8.0–73.0) | 71.0 | 68.3 | | | 4.2 | 5.2 | | |

Table II summarizes histologic changes in 11 experients. Interstitial nephritis was present bilaterally in 50% of dogs. Tubular changes were observed with equal frequency in both kidneys. The only abnormality attributable to perfusion was arterial thrombi with focal cortical necrosis. Arterial clots usually formed terminally when shock and decreased renal blood flow occurred.

TABLE II.—HISTOPATHOLOGY OF PERFUSED KIDNEYS

| Lesion | Number with Lesion | |
|---|---|---|
| | Perfused | In Situ |
| Interstitial Nephritis | 6 | 6 |
| Tubular Degeneration | 6 | 6 |
| Tubular Necrosis | 3 | 2 |
| Tubular Dilation | 2 | 3 |
| Thrombotic Occlusion and Focal Cortical Necrosis | 5 | 0 |

Table III summarizes functional data for all 28 experients. The ratio, perfused to in situ kidney, was calculated for each function in each period for each experiment. The means ratio of each function was then calculated for each experiment. The means for each dog is shown. Although there was individual variation, mean ratios of GFR and RPF for the series approximated unity. Excretion of water, sodium and potassium was generally higher in the preferred than in the in situ kidney. In 13 experiments, GFR and RPF in the perfused kidney were 90 percent or more of the values in the in situ kidney. They were at least 60 percent in 7 additional experiments.

Neither proteinuria for glycosuria was observed. Urine pH of the two kidneys was the same, usually 7.0 to 7.4. Hemoglobinuria did not occur. Hematuria occasionally appeared in one or both kidneys.

TABLE III.—FUNCTION OF EXTRACORPOREALLY PERFUSED DOG KIDNEY

| Dog. No. | Ratio of Perfused to in situ Kidney * | | | | | |
|---|---|---|---|---|---|---|
| | GRF | RPF | FF | $E_{H_2O}$ | $E_{Na}$ | $S_K$ |
| 1 | 1.1 | | | 1.2 | 4.2 | 1.1 |
| 2 | 1.9 | 1.7 | 1.1 | 1.2 | .7 | 1.8 |
| 3 | .7 | .8 | .9 | 1.3 | 1.6 | 1.3 |
| 4 | .3 | .3 | 1.0 | .7 | 1.4 | .5 |
| 5 | .3 | .3 | .8 | .3 | .4 | .3 |
| 6 | 1.1 | 1.0 | 1.1 | 2.0 | 4.0 | 1.5 |
| 7 | .2 | .3 | .7 | .4 | .5 | .5 |
| 8 | .2 | .3 | .8 | .3 | .2 | .3 |
| 9 | 1.0 | .9 | 1.1 | 1.1 | 3.1 | 1.7 |
| 10 | 2.1 | 2.4 | 1.0 | 1.2 | 4.3 | 5 |
| 11 | .3 | .4 | .7 | 1.3 | 1.5 | .8 |
| 12 | .7 | .6 | 1.0 | .6 | .4 | .7 |
| 13 | .9 | .9 | 1.0 | 1.4 | 2.7 | 1.2 |
| 14 | .6 | + 7 | .9 | .5 | .4 | .9 |
| 15 | .7 | .8 | .9 | 1.0 | 1.7 | 1.5 |
| 16 | .2 | .2 | .8 | .6 | .3 | .6 |
| 17 | .9 | .8 | 1.1 | 1.5 | 2.8 | 1.3 |
| 18 | 1.5 | 1.4 | 1.1 | 1.3 | 1.3 | 4.0 |
| 19 | .6 | .8 | .8 | 1.4 | 2.1 | 1.1 |
| 20 | .8 | .8 | .9 | .9 | 1.7 | .9 |
| 21 | .7 | .8 | .9 | 1.3 | 3.3 | .9 |
| 22 | .5 | .6 | 1.0 | .7 | .9 | .5 |
| 23 | 1.8 | 1.5 | 1.2 | 1.6 | 2.8 | 3.5 |
| 24 | .4 | .4 | .9 | .7 | 2.4 | .7 |
| 25 | .9 | .9 | 1.0 | 1.3 | 1.7 | 1.3 |
| 26 | .9 | .8 | 1.0 | 1.1 | 3.7 | 1.1 |
| 27 | 1.2 | 1.1 | 1.0 | 2.2 | .83 | 2.1 |
| 28 | 2.2 | 2.0 | 1.1 | 4.6 | 11.6 | 3.9 |
| Mean | .9 | .9 | 1.0 | 1.2 | 2.5 | 1.3 |

* Each ratio shown is the mean of the ratios obtained in each collection period of each experiment.
FF=filtration fraction.

The above experiments were conducted prior to use of perfusion chamber **10** with a human, and the operative technique developed in excising the dog kidneys was applied to the human kidney. Although chamber **10** was designed for renal perfusion it should be suitable for perfusion of any organ with a solitary arterial blood supply. The principle of free lymphatic and venous drainage into container **12** should be of value in perfusion or organs such as the pancreas and liver.

It will be understood that the invention is not to be limited to the details given herein but that it may be modified within the scope of the appended claims.

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

**1.** A perfusion chamber, comprising:
a container having side walls and a bottom which are rounded so as to be free of any internal corners, said container having first, second and third orifices therein, the interior of said container being coated with graphite having absorbed thereon benzalkonium-heparin;
a top for said container removably sealed thereto, said top having the surface internal to said container coated with a silicone grease or graphite having benzalkonium-heparin absorbed thereon;
first and second housings sealingly fitted to said first and second orifices, respectivley, in said container and having an internal end flush with the internal wall of said container at the point where each housing fits into said container, each housing containing an aperture adapted to receive a cannula, said housings having a surface internal to the container coated with graphite having absorbed thereon, benzalkonium-heparin;
a first cannula extending through said aperture in said first housing and sealed to said housing, part of said cannula being inside said chamber and part of said cannula being outside said chamber;
a second cannula extending through said aperture in said second housing and sealed to said housing, part of said cannula being inside said chamber and part of said cannula being outside said chamber; and
a third cannula extending through said third orifice in said container and sealed to said container, part of said cannula being inside said chamber and part of said cannula being outside said chamber.

**2.** The perfusion chamber of claim **1** wherein the cannulae are coated with graphite having absorbed thereon benzalkonium-heparin.

**3.** The perfusion chamber of claim **2** wherein the container and top are acrylate resins.

**4.** The perfusion chamber of claim **2** wherein the container and top are methyl methacrylate and the cannulae are a polymer of trifluorochloroethylene.

**5.** The perfusion chamber of claim **1** wherein the first cannula is tubular in shape having: a flange therearound, square-cut ends with chamfered edges, a plurality of circumferential grooves therearound and at least a part of said cannula having thin walls, said flange being located inside said first housing and having a side of said flange facing the interior of said container sculptured so as to be free of any sharp corners.

**6.** The perfusion chamber of claim **1** wherein the third cannula is tubular in shape having a flange therearound, the part of said cannula outside of said chamber having: a square-cut end with a chamfered edge, a plurality of grooves therearound and thin walls, said flange being located outside said third orifice but in sealing relationship thereto, the part of said cannula inside said chamber having a closed end and a plurality of side ports therein.

**7.** The perfusion chamber of claim **1** wherein the second cannula is tubular in shape having a flange therearound, the part of said cannula inside said chamber having a square-cut end with a chamfered edge, a plurality of grooves therearound and thin walls, said flange being located inside said second housing and having a

side of said flange facing the interior of said container sculptured so as to be free of any sharp corners.


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