TRANSPLANTATION IN MASS OF THE KIDNEYS.¹

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I. DEFINITION.

This operation consists of extirpating from a first animal both kidneys, their vessels and the corresponding segments of the aorta and vena cava, their nerves and nervous ganglia, their ureters and the corresponding part of the bladder (Plate XI); of placing this anatomical specimen into the abdominal cavity of a second animal whose normal kidneys have been previously resected and the aorta and vena cava cut transversely (Plate XII); and of suturing the vascular segments between the ends of the aorta and vena cava, and of grafting the flap of bladder onto the bladder of the host (Plate XIII).

II. INTRODUCTION.

The purpose of the transplantation in mass of the kidneys is to reconstruct, as safely and perfectly as possible, the urinary system, when it has been suppressed by a double nephrectomy, and to study the functions of the new kidneys. It would be important to know whether kidneys extirpated from an animal and transplanted on another animal after a suspension of life of some duration, can resume efficiently their functions. No therapeutic value can be expected from the graft of kidneys unless the secretion of the new organs should be practically normal. In order to ascertain whether or not transplanted kidneys functionate in a normal way, the crucial test is certainly the grafting on one animal, having undergone previously a double nephrectomy, of both kidneys extirpated from another animal. The efficiency of the transplanted organs would be absolutely demonstrated if the host lived in good health and secreted normal urine.

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The physiology of transplanted kidneys is not known, the main purpose of the experimenters having been until now to reëstablish the circulation through the organ, and not to study its functions. When gangrene did not occur and the kidney secreted a little urine, the operation was considered a success. As the normal kidneys of the host were not resected, it was not possible to appreciate the degree of usefulness of the transplanted organ. All these experiments were made by a method that may be called simple transplantation. It consists of dissecting the kidney and cutting its vessels, extirpating and transplanting it onto some other part of the body of the same or another animal and suturing the renal vessels to other vessels, such as the jugular vein and common carotid artery, or iliac vessels, or even renal vessels.

In 1902 the first attempt of transplanting a kidney was made by Ullmann. He removed a dog's kidney and transplanted it into the neck, the renal artery being united to the carotid artery and the renal vein to the external jugular vein by means of Payr's prosthesis. The end of the ureter was sutured to the skin and fluid flowed from the ureter, but no analysis of it seems to have been made. Three months after this communication Ullmann reported having transplanted the kidney of one dog into another, and the kidney of a dog into a goat. On macroscopical examination of the kidney transplanted into the neck several necrotic areas were seen. No analysis of the urine was published.

The same year, I performed on dogs several transplantations of the kidneys, at the University of Lyons. The carotid and jugular of a dog were dissected and prepared for anastomosis. The right kidney, having been extirpated, with its vessels and its ureter, was put into the cervical wound. End to end anastomoses by continuous sutures of the renal artery to the carotid, and of the renal vein to the jugular, were performed. The end of the ureter was united to a small opening of the skin a little above the sternum. After reëstablishment of the circulation a clear fluid began flowing from the ureter. Septic complications occurred in every case, and permanent results were not observed. No analysis of the urine was made. In 1902 Decastello also reported experiments on the transplantation of the kidneys. He extirpated the kidney of a large dog and transplanted a kidney from another dog into its place, uniting the vessels by means of protheses. The animal lived forty hours, during which time 1,200 cubic centimeters of urine, containing a great deal of albumin and many casts, were secreted. In 1903 Carl Beck of Chicago performed a transplantation of the kidney by using Murphy's method of anastomosing blood-vessels.

* Ullmann, ibid., 707.
* Carrel, Lyon méd., 1902, xcvi, 859.
* Beck, verbal communication.
Transplantation in Mass of the Kidneys.

In 1905 Floresco performed the transplantation of the kidney into the cervical and the inguinal regions, and in every case gangrene occurred. Then he grafted the kidney in the lumbar region; a kidney was extirpated from a dog and transplanted on another dog which had undergone the resection of one kidney, the renal vessels being united to the renal vessels of the host by continuous suturing and the ureter to the skin or to the ureter of the host. These experiments gave few facts about the functions of the kidneys. In one case a sample of fluid flowing from the ureter five days after the operation was examined and presented the character of urea. But on the tenth day the organ was found necrosed. Floresco transplanted the kidney five times into the lumbar region. In three cases necroses occurred. In two cases the animal is reported to have lived in good health. Definitive results were not published. No analysis of urine secreted by the transplanted kidney was made.

In 1905 Guthrie and P examined the functions of a transplanted kidney. The operation was performed in the Physiological Department of the University of Chicago. The kidney of a small dog was transplanted into the neck, the renal artery being sutured to the carotid artery, the renal vein to the external jugular vein and the ureter to the cesophagus. When examined three days later, the kidney was somewhat larger and its hue darker than normal. The pulsations of the renal artery were strong. The secretion of urine by the transplanted kidney was about five times more rapid than by the normal one. The intravenous injection of normal saline solution caused no change in the rate of secretion in the normal kidney, but markedly increased the rate of secretion in the transplanted organ. The constituents of the urines were similar, but the chlorides appeared more abundant in the urine from the transplanted kidney, while the organic sulphate, pigments and urea were more abundant in the urine from the normal organ.

This experiment showed that the secretion of a transplanted kidney need not be very different from the normal. However, the kidney was in an unfavorable condition. The denervation alone could not be responsible for the exaggeration of the circulation of the organ. In the neck or in the inguinal region the blood pressure is different from the pressure to which the kidney is used. Besides, its vessels, the renal vein especially, are exposed to many causes of compression and disturbance. Therefore, we gave up the idea of transplanting the kidney in a region other than the lumbar region, as Floresco did.

In 1907 Stich published the results of a transplantation of the kidney in the lower abdominal region. This experiment was performed at the surgical clinic of Garre in Breslau. The kidney was transplanted into the iliac region, the renal vessels being anastomosed, end to end, to the iliac vessels, and the end of the ureter being grafted into the bladder. The normal kidneys of the animal were not removed, and consequently, the usefulness of the transplanted organ could not be determined. The circulation remained excellent and the macroscopic and microscopic examinations showed that the organ was practically normal. The iliac region is certainly much better than the cervical region, but

1 Floresco, Jour. de Physiol. et de Path. generale, 1905, vii, 27, 47.
2 Carrel and Guthrie, Science, 1905, xxii, 473; Comp. rend. de la Societé de biologie, 1905, ii, 669.
it is probable that perfect functional results can be obtained more easily by putting the kidneys in their normal location in the lumbar region.

In 1906 I made with Guthrie a few transplantations of the kidney into the lumbar region. The renal artery and vein were implanted on the wall of the aorta and vena cava by the patching method. By this method occurrence of gangrene is almost impossible, for the wall of the renal vessels is respected and the suture is made between the edges of the arterial and venous patches and the openings of the aorta and vena cava of the host. The circulation was excellent. Nevertheless there were almost always some small changes in the direction, or the situation, and in the length of the vessels, or some twisting of the vein around the artery, or a little sclerosis of the connective tissue which produced a slight obstruction of the venous circulation, chronic congestion, and after a few weeks, marked lesions of the kidney. Such an organ is not proper for the study of the functions of a transplanted kidney, for its secretion is abnormal. Its lesions and troubles of function are not due to the fact of its having been transplanted, but merely of its having been transplanted with an imperfect technique.

For studying the functions of transplanted kidneys, the transplantation in mass appeared to be the ideal method. It permits an almost perfect reconstruction of the urinary apparatus, and prevents the occurrence of gangrene and, in a large measure, of secondary lesions of the parenchyma, since the renal vessels themselves are not disturbed and the ureters not severed. It may preserve a part of the nervous system of the organs, and places the organs in a condition as near as possible to normal.

The first transplantation in mass of the kidneys was performed in 1906 by Guthrie and myself in the Physiological Laboratory of the University of Chicago.

Both kidneys and the upper part of the ureters of a dog, together with their vessels, nerves, nervous ganglia, the surrounding connective tissue, the suprarenal glands, the peritoneum and the corresponding segments of the aorta and vena cava were removed. The mass was then placed in a vessel of isotonic sodium chloride solution. The aorta and vena cava of a bitch were cut a little

10 Carrel and Guthrie, Jour. of Amer. Med. Assoc., 1906, xlvi, 1648.
11 Carrel and Guthrie, Science, 1906, xxiii, 394; Comp. rend. de la Societé de biologie, 1906, i, 465.
Transplantation in Mass of the Kidneys.

above the mouth of the ovarian vessels. The kidneys of the first animal were then removed from the salt solution and put into the abdominal cavity of the second, and the segments of the aorta and vena cava were interposed, by bilateral transplantation, between the cut ends of the aorta and vena cava. The circulation was reestablished, after having been interrupted for one hour and a half. The kidneys immediately became red and turgid, as after a simple transplantation, but about half an hour later the state of the circulation became normal. Clear urine flowed abundantly from the transplanted ureters, which were united to the normal ones.

Both normal kidneys were then removed. Two hours after the operation the animal walked about her cage. In the afternoon she drank and urinated copiously. The following day and subsequently, up to the eighth day, her diet consisted largely of meat, which she took hungrily. In general her condition was normal. During this period the urine remained clear, showing no evidence of blood. The total amount appeared to be somewhat increased. In the seventh and eighth days several samples were collected and analyzed, the results of which showed a slight variation in composition, but entirely within normal limits. The only abnormal constituent detected was coagulable proteid, the largest amount present in any of the samples being less than 0.25 per cent.

On the ninth day she vomited. A diagnosis of stenosis of the bowels by adhesions was made. On the tenth day the urine was analyzed and its composition was practically the same as before. As the animal was vomiting almost continuously, she was etherized and a laparotomy performed. We found localized peritonitis on the right side of the abdomen, with kinking of several loops of intestines, the mass being very strongly bound down by adhesions. The circulation of both kidneys was found to be perfect. There was an enormous hydronephrosis on one side.

Afterwards a few other transplantations on dogs and cats were performed without obtaining better results. The animals died rapidly from intestinal, peritoneal or ureteral complications.

In 1907 at the Rockefeller Institute, I modified and improved the technique in order to suppress, as much as possible, the occurrence of complications. A few operations were made on dogs and on cats and it appeared soon that, in spite of the difficulties due to the smallness of the vessels, cats are better adapted from an anatomical standpoint for this operation than dogs. When the details of the operation had been worked out fourteen experiments were performed from February to October, 1907. Progressively the technique was improved and the cause of the complications which occurred ascertained, and as far as possible suppressed. The actual technique, however, must not be considered as a definitive one. It will be modified in many respects, as greater experience in performing it is obtained.
III. TECHNIQUE.

The transplantation in mass of the kidneys can be described as consisting of four stages: (a) preparation of the kidneys; (b) perfusion and extirpation of the kidneys; (c) preparation of the host; and (d) graft of the kidneys into the abdomen of the host.

It is evident that all resources of modern surgery must be used to prevent infection and shock after such an operation, which necessitates a large transverse incision of the abdominal wall, the evisceration of the intestines and the spleen, a double nephrectomy, the stopping of the aortic and caval circulations, the section of the aorta and vena cava, and the opening of the bladder. The animal is handled and operated on with the same rigid asepsis and care used for a human patient in a well-equipped hospital.

The order of the succession of the different stages of the operation is variable. We shall describe the simplest form, when the four stages are united in two: preparation and extirpation of the kidneys; preparation of the host and graft of the kidneys.

A. Preparation and Extirpation of the Kidneys.

A first animal is etherized. After shaving and sterilization of the abdominal and lumbar regions, the antero-lateral wall is cut transversely at the level of the umbilicus to about one half or three quarters of the circumference of the animal. The intestines are eviscerated and put on the left side of the body. Thus both kidneys and the lumbar region are largely exposed.

1. Dissection of the Kidneys.—The peritoneum is cut all around the kidneys in a rectangular shape, the short sides being along the external edge of the kidneys, the long sides uniting the ends of the organs and being perpendicular to the vena cava. Care must be taken not to wound the ureters and the vena cava. Through the peritoneum it is easy to see the point of implantation of the renal veins. At about one centimeter above the mouth of the right renal vein the vena cava is dissected and isolated from the lower end of the right suprarenal gland. On the left side of the vessel, just above the left renal vein, is often the mouth of the left suprarenal vein. This vein is ligated and cut, if the left suprarenal gland is not to be transplanted with the kidneys. Afterwards, the vena
cava is dissected on a point located at two or three centimeters below the mouth of the left renal vein. The left genital vein is ligated and cut. Then the aorta is dissected at two points located one and one half centimeters above and below the renal arteries. The kidneys are detached from the lumbar region by cutting the loose connective tissue which is interposed between them and the muscular plane. The posterior part of the aorta and vena cava is dissected. The posterior collateral branches of these vessels are ligated and cut.

The ureters are dissected from the lower edge of the peritoneal flap to the bladder. Their vessels must be carefully respected. Afterwards the part of the bladder on which the ureters are implanted is dissected. The musculo-peritoneal layer of the bladder is cut by a circular incision located at about one centimeter from the mouth of the ureters. Then the mucous membrane is easily seen and cut, in such a way, with the scissors, that the mucous flap is larger than the muscular one. The ureters and the flap of bladder are still fixed by the rectum and the uterus. The uterus is cut, and the meso-colon severed as far as the cœcum. The small intestine is cut and through the solution of continuity the ureters and the fragment of bladder are removed. Great care is taken to prevent infection by the section of the intestines.

If the left suprarenal must be transplanted, its upper vessels are ligated and cut. The last connective tissue adhesions are severed. The anatomical specimen is yet adherent to the animal by the aorta and vena cava.

2. Stopping of the Circulation, Perfusion and Extirpation of the Kidneys.—The aorta is clamped below the diaphragm. A glass cannula is introduced through the lower part of the abdominal aorta and connected with an irrigator containing Locke's solution at the temperature of the laboratory, which was from 26° to 37° C. The vena cava is cut one centimeter above and two or three centimeters below the renal veins. Then the aorta is washed and the kidneys are perfused with Locke's solution. In the first experiments they were washed until their surface became yellowish white and the fluid flowing from the vena cava was perfectly clear. In the last experiments the perfusion was much less complete. It was stopped
as soon as the blood in the vena cava appeared to be greatly diluted, and when there was still a good deal of blood in the kidneys.

Next the aorta is cut one centimeter or one and a half centimeters above and about two centimeters below the renal arteries. The anatomical specimen is removed (Plate XI) and put into a jar of Locke's solution at the temperature of the laboratory.

B. Preparation of the Host, Double Nephrectomy and Graft of the New Kidneys.

A second animal of the same size or a little larger than the first one is etherized. The abdomen and the lumbar region are clipped, shaved and carefully sterilized. The abdominal wall is transversely cut at the level of the umbilicus from one lumbar region to the other. The intestine and the spleen are eviscerated and wrapped in a towel or in a greased silk pad, and put outside on the left side of the body. They are protected there by a small wool blanket, in order to prevent cold and the consequent shock. The aortico-renal region is then largely exposed. When the bladder is too distended by urine, it is put outside of the abdominal cavity and covered with greased pads.

1. Extirpation of the Kidneys (Plate XII).—The lumbar peritoneum is cut longitudinally on the middle line, its edges dissected at the level of the renal veins. The pedicles of the kidneys are dissected and a ligature is put on each structure, artery, vein and ureter. Afterwards through the longitudinal peritoneal incision, both kidneys are extirpated in such a manner that the constitution of the renal region is not disturbed at all. Both suprarenal glands are respected, their lower vessels being sometimes ligated. The left genital vein is ligated.

2. Preparation of the Vessels.—The vena cava and the aorta are prepared for anastomosis. The vena cava is dissected at the point of implantation of the renal and the left suprarenal veins. One or two lumbar collaterals, and sometimes the right genital vein are ligated. The temporary haemostasis is secured by serre fines especially modified for this purpose. A serre fine is put on the vena cava four centimeters below the renal veins, and another one as high as possible, about two centimeters above the right renal

Alexis Carrel.
Transplantation in Mass of the Kidneys.

vein. Then the region on which the renal veins are implanted is resected (Plate XII). Through the cut ends of the vessels a curved glass cannula is introduced, and the blood is washed out with Locke’s solution. A little vaseline is put into the lumen and on the external part of the vein. The aorta is generally dissected just below the renal arteries; the first two lumbar collaterals are ligated, a serre fine is put on the wall of the vessel just below the renal arteries, and another three centimeters lower. It is better, but involves greater risk, to dissect the aorta above the renal arteries, in order to place the serre fine higher and to make the anastomosis a few millimeters below the implantation of these vessels. The relations of the thoracic duct and of the aorta are so close at that point that the duct is exposed to injury while the aorta is being dissected. It is much safer to put the higher serre fine below the renal arteries. Generally the aorta is cut two centimeters below the renals, or sometimes a very short segment, with the implantation of the first two lumbar collaterals, is resected. The aorta being very elastic there is immediately a gap of two or three centimeters between the cut ends of the vessel (Plate XII). The external sheath is resected for a short distance. The blood is washed out from the lumen of the vessel with Locke’s solution. The lumbar region is carefully washed with Locke’s solution and dried with gauze in order to remove all traces of blood. Then the vessels are washed again, and covered with a thin layer of vaseline. Vaseline is also put on the surrounding anatomical structures.

3. Transplantation of the Kidneys.—The anatomical specimen is removed from its jar and put into the abdominal cavity. Each kidney is introduced through the incision of the lumbar peritoneum into the corresponding renal region. The new kidneys, being about the same size as the extirpated ones, fill exactly their place. The aortic and caval segments are interposed between the cut ends of the aorta and vena cava. The ends of the vascular segments are washed, if necessary, and greased with vaseline. Afterwards the small region of the vessels is circumscribed with black silk towels, for it is necessary to protect the threads from all contact with blood or with plasmase of the tissues.

4. Anastomoses of the Vessels and Reëstablishment of the Circu-
lation.—The ends of the aorta are united to the ends of the aortic segment by continuous suturing with straight needles, No. 16, and silk thread boiled in vaseline. Care is taken to express the vaseline from the lumen of the vessel before completing the suture. Afterwards the anastomoses of the ends of the venous segments to the ends of the vena cava are made. The wall of the vein is very thin, and it is necessary to apply intima to intima while suturing, that is, to make a slight eversion of the wall. It is the safest way to prevent inclusion of the external sheath into the line of sutures.

After completion of the anastomoses dry gauze is applied on the anastomoses and the serre fines are removed first from the vena cava and secondly from the aorta. For about two minutes a slight compression is made in the region of the anastomosis. Afterwards the gauze is removed and, if there is still a little leakage, one or two complementary stitches are added. It is necessary that no blood at all flow from the line of sutures. The haemostasis must be absolute.

As soon as the circulation is re-established through the aorta, the kidneys begin to be injected with blood, and generally after a few minutes, they assume their normal appearance. The duration of the interruption of the circulation is about one hour. Gauze with Locke's solution is put on the vessels.

5. Graft of the Flap of Bladder on the Bladder of the Host, and End of the Operation.—The ureters are extended on the free surface of the peritoneum along the right side of the rectum and along the right uterine horn. The bladder is isolated by pads from the peritoneal cavity. On the middle line of its posterior face a longitudinal incision is made. The flap of bladder is grafted into that opening by muco-mucous, and muscolo-muscular continuous sutures. Then the bladder is put back into the abdominal cavity.

The arterial and venous anastomoses are examined again, and if there is slight leakage, it is stopped. If a little blood flows from some small vessels of the connective tissue a ligature is applied, even if the haemorrhage is exceedingly small. The vaseline and the blood which may be present in the connective tissue around the vessels are washed out with warm Locke's solution.
The lumbar region is closed by suture of the longitudinal peritoneal incision. Thus both kidneys are fixed in their normal location. The intestines and the spleen are put back into the peritoneal cavity. If the intestines are a little cold about one hundred grams of warm Locke's solution are injected into the peritoneal cavity.

The peritoneum and the abdominal muscles are closed by two planes of continuous silk sutures. The skin is sutured with catgut. The dressing consists of talcum powder, gauze, cotton, bandage and a linen shirt.

After the operation the animal is put for two hours into a cage heated to about 30° C. and then into an ordinary cage with screen floor or saw dust. No special care is taken. The animal is given meat and milk one day after the operation. The dressing is removed after about six days. When the urine is to be examined, the animal is put into a metabolism cage with fine screen floor. Only incomplete analyses of urine have been made by using the ordinary clinical methods. In spite of their lack of accuracy they are sufficient to prove that the kidneys functionate. It is not intended, in this article, to analyse minutely the changes in the secretion of transplanted kidney, but merely to show that after transplantation they can resume their function efficiently. This is demonstrated as much by the general condition of the animal as by the physical and chemical characters of the urine secreted by the new kidneys.

IV. EXPERIMENTS.

Fourteen experiments have been performed. Two animals whose ureteral anastomoses were defective died soon after the operation. No excretion of urine was observed from the bladder, because it flowed into the retroperitoneal spaces. Three other animals, operated on under unfavorable condition died almost immediately of shock. These five experiments will not be reported. Thus nine cases only will be described.

Experiment 1. February 25, 1907.

Extrication of the Kidneys.—Middle-sized male cat. Etherization and semi-
transversal laparotomy. Evisceration. Dissection and isolation from the surrounding structures of both kidneys, the left suprarenal gland, their vessels and the corresponding segments of the aorta and vena cava, their nervous system, and the upper part of the ureters, which are cut about 6 centimeters below the hilus. Opening of the lower part of the abdominal aorta. Animal killed by hemorrhage and opening of the diaphragm. Section of the vena cava 1.5 centimeters above and 3 centimeters below the mouth of the renal veins. Introduction of a cannula through the abdominal aorta. Washing of the aorta and perfusion of the kidneys with very hot (by accident) Locke’s solution, until their color became yellowish-white and the fluid flowed perfectly clear from the vena cava. Then section of the aorta about 1.5 centimeters above and 1.5 centimeters below the mouth of the renal arteries. Anatomical specimen removed and put into Locke’s solution at the temperature of the laboratory (30° C.).

Transplantation of the Kidneys.—Male, young, black cat, good health. Etherization. Semi-circular transversal laparotomy. Evisceration of the intestine on the left side of the body. Longitudinal incision of the lumbar peritoneum in the middle line, through which both kidneys are dissected and extirpated. Dissection of the vena cava at the level of the renal veins. Ligation of two posterior collateral branches. Dissection of the aorta, which is isolated from the thoracic duct. Ligation of both first lumbar collateral branches. Temporary hemostasis of a segment of aorta by two serre fines put on the vessel just above and 4 centimeters below the renal arteries. Section of the aorta a little above the mouth of the first lumbar branches. Resection of a segment of aorta about 5 centimeters long. Temporary hemostasis of the vena cava by two serre fines placed just above the right renal vein and the right spermatic vein. Resection of the point of implantation of the renal veins. Washing of the ends of the vessels with Locke’s solution and greasing with vaseline.

The anatomical specimen is then removed from the jar and put into the abdominal cavity, each kidney being placed under the lumbar peritoneum in its normal location. Interposition of the aortic and caval segments between the cut ends of the aorta and vena cava. Anastomosis of the vessels by suture. No expression of the vaseline from the vessels before completion of the suture. The serre fines are taken out and the blood flows through the aorta and vena cava. Slight leakage from the venous anastomoses, which stops by compression. No leakage of the arterial anastomoses.

Very slow reestablishment of the circulation through the kidneys. Nevertheless, after a few minutes, the right kidney assumes a rosy color, without blue or white spots, while the left kidney remains paler. The lower end of the left kidney is white. Small incision made at this point. Slight hemorrhage of red blood mixed with vaseline. Progressive improvement of the circulation of the left kidney. After thirty minutes its color is rosy. Circulation almost normal.

Invagination of the end of the transplanted ureters into the upper end of the ureters of the host, and fixation of the invagination by three stitches. Closing of the lumbar peritoneal incision. Reintegration of the intestines into the abdominal cavity. Closing of the abdominal wall by three planes of catgut sutures. Gauze and cotton dressing, linen shirt.

February 25, 4 p. m. Cat in good condition. A little depressed.

February 26. Cat in good condition, walks about its cage, drinks water, but does not eat. Femoral pulse normal. A little urine.
February 27. Cat in good condition, drinks water and milk, walks, does not eat meat.—9 a. m. Urinates abundantly.—4 p. m. Urinates again. Yellowish urine, acid reaction, albumin present.


March 2. Same condition.


March 4. Animal very ill, coughs, diarrhoea, discharge through the nose. Urinates abundantly.


March 6. Animal in better condition. Diminution of the discharge through the nose and of the diarrhoea. Drinks milk. Walks about its cage and the room.


March 10. Animal very ill. Not able to jump from its cage to the floor. No vomiting, no dyspnoea, no shaking. Urinates. Pressure on the abdominal wall is painful. In one point dressing is wet.—11 a. m. Etherization. Section of the dressing. Several loops of intestines in the gauze, the abdominal wound being almost completely disunited: premature resorption of the catgut. The intestinal loops are partially protected by the omentum which is adherent to the lower edge of the abdominal wound. Comparatively little inflammation of the peritoneum. However, four intestinal loops are adherent to the gauze dressing and very much inflamed. Adhesions are detached and intestine washed. Direct examination of the kidneys: normal peritoneal covering, normal location, marked enlargement, almost normal consistency. They look like normal hydronephrotic kidneys. Washing of the abdominal cavity with warm water. Closing of the abdominal wound by silk suture. Shock. Afterwards respiration and pulse become progressively almost normal.—4 p. m. Animal able to walk.

March 11. Died in the morning.

**Autopsy.**—**General peritonitis.**

**Macroscopical Examination.**—Both kidneys in normal location, covered with transparent peritoneum. Normal hue, increased size. Normal consistency.

The specimen is not dissected, but preserved as demonstration specimen. Incision on the external edge of the left kidney. Urine under pressure flows from the incision. The surface of section is a little congested. No infarction. Dilatation of the pelvis and calices. It is a typical hydronephrotic kidney. Right kidney not opened, but a knife is introduced deeply into the renal substance, and urine escapes along the blade. Same hydronephrotic condition on the right side. Opening of the vena cava. Anastomoses perfect. No dissection of the aorta. No dissection of the ureters. Specimen preserved in formalin.
Microscopical Examination.—Fragment of the left kidney in Zenker's fluid stained in hematoxylin and eosin. Glomeruli well preserved. In some of them slight exudate between capillaries and the capsule. Secreting tubules slightly dilated. Epithelium in good condition; brush border well defined, nuclei normal. Excretory tubules very much dilated. Around some of them slight small-cell infiltration. A little dilatation of the blood-vessels. Appearance of an ordinary hydronephrotic kidney.

Experiment 2.—March 14, 1907.

Extirpation of the Kidneys.—Small pregnant cat etherized and killed by aortic hemorrhage. Dissection and isolation in one mass of the kidneys, their vessels, their nerves and the upper part of the ureters. Left suprarenal gland not extirpated. By an intra-aortic injection of Locke's solution both kidneys are washed out very thoroughly, until all blood is expelled and their color becomes pure yellowish-white. Anatomical specimen extirpated and put in Locke's solution at the temperature of the laboratory (30° C.).

Transplantation of the Kidneys.—Large, gray, young, male cat. Etherization. Semi-circular transversal laparotomy. Evisceration. Extirpation of both normal kidneys. Dissection of the aorta and vena cava. Ligature of the lower suprarenal vein and section. Ligation of the first lumbar collateral branches of the aorta. Temporary hemostasis of the aorta by tapes fixed by serre lines, and of the vena cava by serre lines put directly on the wall of the vessel. Resection of a narrow segment of aorta in which the first lumbar arteries are implanted. Resection of a long segment of vena cava where are implanted the inferior suprarenal vein and both renal veins.

The anatomical specimen is then put into the abdominal cavity, the kidneys being in their normal location and the vascular segments interposed between the cut ends of the aorta and vena cava. Arterial and venous anastomoses by the ordinary method. Reestablishment of the circulation through the vena cava. Leakage at one point of the lower anastomosis; hemorrhage controlled by one supplementary stitch.

Reestablishment of the circulation through the aorta. Hemorrhage of the upper anastomosis, which is controlled by two additional stitches. Slow reestablishment of the circulation through the kidneys. Appearance of both kidneys normal twenty minutes after the reestablishment of the arterial circulation.

Anastomoses of the ureters to the upper portion of the ureters of the host by invagination. Suture of the lumbar peritoneum. Reintegration of the intestines in the abdominal cavity. Closing of the abdominal wound by two planes of silk suture and one plane of catgut suture. Gauze and cotton dressing. Shirt.

March 15. Animal in good condition, drinks milk and eats raw meat. Large amount of clear urine. In the afternoon several fits of abdominal pain.

March 16, 9 a.m. Animal less well, refuses to eat, drinks a great deal of water and milk. Since yesterday at 6 p.m. 130 c.c. of urine. Urinates again at 10.30 a.m. yellow, clear, acid urine. A great many spermatozoa, no red blood corpuscles, a little albumin. In the afternoon, fits of abdominal pain, vomited once, no feces. In the evening animal very ill.

March 17. Animal died in the morning.

Autopsy.—A little reddish fluid in the peritoneal cavity. A loop of small intestine is found dilated and of dark color: volvulus. Both kidneys are normal in size, color and consistency. Arterial and venous anastomoses perfect.
Transplantation in Mass of the Kidneys.

Experiment 3.—June 13, 1907.

Exstirpation of the Kidneys.—Middle-sized male cat. 10.38 a.m. Etherization. Kidneys exposed and dissected the same as before. Dissection of the aorta and vena cava at two points about 1.5 centimeters above and 2 centimeters below the mouth of the renal vessels. Section of the ureters about 6 centimeters below the hilus. The animal is killed by chloroform at 11.15 a.m. Section of the vena cava. Perfusion of both kidneys through the aorta with Locke's solution at the temperature of the laboratory (30° C.). Complete washing. The fluid from the vena cava is clear, and the kidneys are yellowish-white. Section of the aorta 1 centimeter above and 2 centimeters below the renal arteries. Then the kidneys, the left suprarenal gland, the upper part of the ureters with their vessels and their nerves are removed and put in Locke's solution.

Transplantation of the Kidneys.—Large, yellow, male cat. Etherization. Semi-circular transversal laparotomy. Evisceration of the intestines and the spleen and extirpation of both kidneys. Ligature of the lower suprarenal vein, of two venous collaterals of the vena cava, and the first pair of aortic lumbar collaterals. Dissection of the aorta and vena cava and temporary hemostasis with serre fines. Transverse section of both vessels. The anatomical specimen is then put in the abdominal cavity, the new kidneys being in the same location as the kidneys of the host. Anastomosis of the aortic and caval segments. Re-establishment of the venous and arterial circulation at 1:2.20 p.m. No leakage of the anastomoses. Immediate re-establishment of the circulation through both kidneys. No blue or white spots. Normal color and consistency. No apparent vasodilation.

Anastomosis of the ureters by invagination. Suture of the lumbar peritoneum. The intestines and the spleen are replaced into the peritoneal cavity. A few cubic centimeters of Locke's solution are let into the peritoneum. Closing of the abdominal wound by two planes of silk sutures and one plane of catgut. Gauze and cotton dressing. Shirt. Animal is put in a metabolism cage.

June 13, 4 p.m. Animal in satisfactory condition, lays down, does not walk, drinks water.

June 14, 9 a.m. Animal in good condition, walks about his cage, and drinks milk. In the jar 290 c.c. of a mixture of urine, vomitus and a little milk.—0.30 a.m. Animal urinates, clear, slightly rosy urine, quantity 42 c.c., reaction acid, density 1.021, a great many blood corpuscles, a few spermatzoa, no casts.

June 15, 9 a.m. Animal in good condition, drinks milk. Urine 110 c.c. mixed with feces.—3.45 p.m. Clear, rosy urine, with many blood corpuscles.—4.35 p.m. Animal urinates again. Urine 38 c.c., clear, slightly rosy, acid reaction, density 1.018, urea 2.5 per 100 c.c., albumin less than 0.50 g. per 1000 c.c. Many red blood corpuscles, a few spermatzoa, no casts.

June 16, 9 a.m. Vomits a little milk. In the jar 205 c.c. urine and milk.

June 17. Animal in good condition, walks about the room, drinks water, but refuses milk and meat. Does not vomit. Urine mixed with feces.

June 18. Urine 125 c.c., yellowish, acid, density 1.016, urea 2.8 per 100 c.c., traces of albumin. Animal refuses to eat.

June 19. Animal grows emaciated, drinks a great deal of water. Urine 164 c.c., pale yellowish, clear, density 1.013, very little albumin, urea 2.3 per 100 c.c. urinates again 35 c.c. at 1 p.m.
Alexis Carrel.

June 20. During the night the animal has escaped from its cage, and urinated on the floor. He is emaciated and refuses to eat. — 10.30 a.m. Urinates again, urine 35 c.c., clear, density 1.013 with traces of albumin.

June 21, 7.30 a.m. Urine 115 c.c., alkaline reaction. Density 1.012, urea 2.6 per 100 c.c., no albumin.

June 22, 7.15 a.m. Urine 167 c.c., density 1.017, no albumin. Animal is much emaciated, and does not eat.

June 23. Urine 110 g. Animal is very weak, nevertheless he can walk about the room. The dressing is removed. Wound completely healed. Animal very much emaciated, kidneys a little enlarged. Does not vomit. — 11 a.m. Transfusion of blood by Crile's method through an anastomosis of the carotid artery of another cat to the external jugular vein. Blood is transfused until the second animal dies from hemorrhage.

The animal is now in better condition. Pulse much stronger. The mucous membrane of the mouth and the skin of the feet are red. A few minutes after the operation clonic convulsions of the jaws and the limbs. Afterwards tonic convulsions. Tetanus-like appearance. — 5 p.m. Died.

Autopsy. — Macroscopical Examination.

Opening of the abdomen a few minutes after death. Excellent healing of the abdominal wound. No adhesions of the intestines. In the gastric region long and narrow strand compressing the duodenum just below the pylorus, without, however, producing complete occlusion. Both kidneys are increased in size, their color, their location and their consistency are almost normal. Section of the right kidney: dilatation of the pelvis and calices, cortex and medulla apparently normal, although a little congested. Capsule normal. Upper part of the ureter greatly dilated. Incision of the right ureter: stenosis of the invaginated part; below this point the ureter normal. The left ureter too is very much dilated and sinuous above the point of anastomosis.

Bladder filled with 35 c.c. yellow, clear urine, density 1020, urea 2.9, no albumin.

Vessels of the kidneys normal. Aorta and vena cava dissected and incised. No thrombosis or stenosis, perfect anastomoses. No sclerosis of the perivascular connective tissue.

Microscopical Examination. — Piece of the right kidney fixed in Zenker's fluid, stained in hematoxylin and eosin. Glomeruli normal, secretory tubules slightly dilated, epithelial cells in good condition. Excretory tubules somewhat dilated. Very few light casts. No interstitial infiltration. At a few points a few mononuclear leucocytes around the tubules.

Experiment 4. — June 19, 1907.

Preparation of the Host. — Young, white and black male cat in very good health. Etherization. Semi-circular transversal laparotomy. Evisceration, dissection and extirpation of both normal kidneys, ligation of the lower suprarenal vein, of two collaterals of the vena cava and of the first lumbar pair. Temporary hemostasis. Section of the aorta about 2 centimeters below the renal arteries. Resection of the venous segment on which are implanted the renal veins. Washing and greasing of the vascular ends. Then gauze compresses with Locke's solution are put on the operative field and protected with a wool blanket.
Transplantation in Mass of the Kidneys.

Exirpation of the Kidneys.—Middle-aged, pregnant cat. Etherization. Opening of the abdomen by the ordinary method. Veins extremely dilated. When the anatomical specimen, both kidneys, and left suprarenal gland are almost completely isolated, the ureters are dissected as far as the bladder. Resection of a flap of the vesical wall around their mouths. Then section of the uterus, mesocolon and the small intestine near the cæcum. The ureters and the flap of the bladder are removed from the lower part of the abdomen and placed temporarily below the left kidney. Perfusion of both kidneys with Locke’s solution at the temperature of the laboratory (37° C.). The anatomical specimen is removed and placed immediately in the abdomen of the host.

Transplantation of the Kidneys.—Each kidney is placed under the peritoneum in its normal location. Anastomosis of the vessels and reestablishment of the circulation. No leakage. It is noticed that the lower end of the venous segment has been twisted and that it produces a very marked stenosis just above the lower anastomosis. It does not interfere with the circulation of the kidney, the color of which almost immediately becomes normal. The circulation has been interrupted for 42 minutes only. Immediate secretion of clear fluid.

The ureters are placed in the abdominal cavity on the right side of the rectum. Longitudinal opening of the bladder on its posterior face and on the middle line, and graft of the transplanted flap of bladder by mucous-mucous and muscular sutures. Closing of the lumbar peritoneum. Through the lower part of this line of suture a small opening is reserved to allow the ureters to pass from the retro-peritoneal space into the peritoneal cavity. Both ureters are twisted around each other, but, as there is no tension, it probably does not interfere with the flow of urine.

The intestines are put back into the abdominal cavity. Suture of the abdominal wall. Dressing. Shirt.

June 22. Animal apparently in very good health, climbs on roof.
June 23. Dressing is removed, wound completely healed. Animal eats meat and drinks a great deal of milk, urinates abundantly.
June 24. Animal looks well, but refuses to eat.
June 25. Animal in good condition, does not eat. Does not vomit. No feces. Clear, yellow urine, urea 2.2 per cent. A little albumin, less than 0.25 g. per 1000 c.c.
June 26. Animal in good condition, walks, climbs on a wall more than six feet high, but refuses to eat and to drink milk. Then a direct examination of the abdominal cavity is decided upon.

10 a. m. Etherization. Longitudinal laparotomy on the middle line. No intestinal adhesions to the abdominal wall. A few adhesions between the duodenum, the anterior face of the right kidney and the inferior face of the liver. They are loose and easily detached. The kidneys are covered by normal peritoneum and apparently in excellent condition. Size, color and consistency normal. The surface of both kidneys is rosy, there is no apparent vasodilatation. No sclerosis of the connective tissue between the kidneys. The renal veins and the transplanted segment of vena cava appear to be absolutely normal. Normal pulsations of the aorta and the renal arteries.
Then closing of the abdominal wound by four planes of sutures.

One hour after the operation, the animal walks and seems in good condition.

June 27, 8 a.m. Animal found dead in its cage. Body is still warm.

Autopsy.—9:15 a.m.

Macroscopical Examination.—Peritoneum normal, no fluid, no adhesions. Bladder filled with urine.

Both kidneys are in their normal location, covered with sound peritoneum, and normal in color, size, consistency and connections with surrounding structures. From a point corresponding to the lower end of the incision of the lumbar peritoneum, both ureters adherent to one another, penetrate into the peritoneal cavity and go down toward the bladder along the right side of the rectum. Excellent union of the transplanted flap of bladder to the bladder of the host (Plate XIII).

Incision of the peritoneum and dissection of the kidneys. Their appearance is normal. They are surrounded by their covering of connective tissue, which does not present any sclerosis. Dissection and incision of the aorta and vena cava. Anastomoses healed without any deposit of fibrin. Vena cava is obliterated 1 centimeter above the lower anastomosis at the point of the twisting of the transplanted venous segment. This point is much below the mouth of the renal veins and the obliteration did not interfere with the venous circulation of the kidneys. Both kidneys are opened. Capsules normal. No hydronephrosis. In section they have the appearance of normal kidneys. A piece of the right kidney is fixed in Zenker’s fluid.

Lungs, heart, liver, spleen apparently normal. No examination of the brain and medulla.

Microscopical Examination.—Glomeruli normal. No exudate in the glomerular space. Epithelial cells of the tubules generally well-preserved, brush border very apparent, regularly disposed and adherent to the basement membrane. In some places vacuolization of the protoplasm around the nucleus. Exudate in the lumen of the tubules. Epithelial cells of the excretory tubules normal. A few typical hyalin casts. No infiltration whatever of the interstitial tissue.

Experiment 5.—June 28, 1907. 7.30 a.m.

Preparation of the Kidneys of the First Animal.—Middle-sized female cat in good health. Etherization. Exposition and isolation of both kidneys, which are abnormally pale, the left suprarenal, the ureters and the corresponding part of the bladder by the ordinary method. The aorta and vena cava are dissected but not cut. The organs are covered with compresses of Locke’s solution.

Preparation of the Host.—Strong, slender, young, black cat. Etherization. Exposition and extirpation of both kidneys by the ordinary method. Dissection of the aorta and vena cava, and temporary hemostasis. Section of the aorta 2.5 centimeters below the mouth of the renal arteries, resection of the segment of vena cava on which the renal veins are implanted, washing and greasing of the vascular ends.

Extrpation of the Kidneys from the First Animal.—Washing of the kidneys by the ordinary method. Section of the vessels. The anatomical specimen is removed and placed in the abdominal cavity of the second animal. The first animal is killed by opening the diaphragm and clamping the heart.
Transplantation in Mass of the Kidneys.

Transplantation of the Kidneys.—The kidneys are put in their normal location and the vascular segments interposed between the ends of the aorta and vena cava. Anastomoses. Because the incision of the abdominal wall is too short, and consequently the operative field narrow and deep, the anastomoses are difficult and a dissecting forceps is frequently used in the handling of the vascular ends. Reestablishment of the circulation 45 minutes after clamping the aorta and interrupting the circulation through the kidneys. After a few minutes the kidneys assume their normal appearance; their surface is rosy without white or blue spots. Opening of the bladder and graft of the flap by two planes of sutures.

Suture of the lumbar peritoneum. Through the lower part of the line of suturing an opening is left for the ureters. The intestines are replaced in the abdominal cavity. End of the operation as usual.

June 30. Same condition.
July 1. Slight paresis of the posterior limbs.
July 2. Complete paralysis of the posterior limbs and the tail.
July 3. Animal died.

Autopsy.—Peritoneum, kidneys and all abdominal organs apparently normal. Excellent healing of the flap of the bladder. The bladder is distended with urine. Perfect healing of the anastomoses of the vena cava. The upper aortic anastomosis and the renal arteries are in excellent condition. At about 1 centimeter below the mouths of the renal arteries, the aorta is completely obliterated by a clot. This clot is not adherent to the wall of the transplanted segment or to the line of suture. It is fixed to a wound of the intima of the lower end of the aorta at 1 millimeter below the anastomosis. The wound has been caused almost certainly by the handling of the vessel with the dissecting forceps during the performance of the anastomosis.

As the autopsy was performed a long time after death and the temperature was high, the specimens of kidneys are so poorly preserved that no interpretation of the sections is possible.

Experiment 6. a—July 12, 1907, 8:15 a.m.

Extrpation of the Kidneys.—Black, pregnant cat, mangy and in bad health. Etherization, extirpation and dissection by the ordinary method, both kidneys, left suprarenal gland, ureters and a large flap of bladder. Clamping of the aorta below the diaphragm at 8.40 a.m. Washing of both kidneys with Locke’s solution at the temperature of the laboratory. The perfusion is stopped when there is still a good deal of blood in the kidneys and the veins are still filled with bloody fluid. Then the vessels are cut, the specimen removed and put into Locke’s solution.

Preparation of the Host and Transplantation of the Kidneys.—White and black, young female cat in excellent health. Bloody discharge from the vagina. Parturition two days before. Etherization difficult. Semi-circular transverse laparotomy. Evisceration of the intestines, spleen and bladder. Longitudinal incision of the lumbar peritoneum, extirpation of both kidneys, dissection of the
aorta and vena cava, and temporary hemostasis. Resection of the segment of vena cava where the renal veins are implanted. Section of the aorta 2 centimeters below the renal arteries. The anatomical specimen is put into the abdominal cavity, the kidneys in their normal location, and the vascular segment between the ends of the aorta and vena cava. Reestablishment of the circulation at 9.45 a.m. No leakage. In a few minutes the circulation of both kidneys is apparently normal. The ureters are put along the right side of the rectum through the basis of the right broad ligament. Incision of the bladder and implantation of the flap of bladder by two planes of sutures. Suture of the incision of the lumbar peritoneum. The intestines and the spleen are put back into the peritoneal cavity. Intestines cold, a little shock. Suture of the abdominal wall by the ordinary method. Gauze and cotton dressing. Shirt. Animal in a metabolism cage.

Cat 6 looking at a piece of meat. Photograph taken on the twenty-first day after the operation.

July 12, 2 p.m. Animal a little shocked, lies down in its cage.

July 13. Animal lies down and refuses to eat. From time to time she gets up, turns around in the cage, and cries as though suffering abdominal pain. Does not vomit. After having urinated she is quiet and looks comfortable again. Urine 130 c.c.


July 16. Animal in normal condition, walks, jumps, climbs, eats a great deal of meat, drinks milk, and urinates abundantly.

July 17, 18. Same condition.
Transplantation in Mass of the Kidneys.

July 19. Animal in perfect health, is growing fat. The dressing is removed. Wound completely healed. Both kidneys normal in size and situation.
July 20, 21 and 22. Same condition.
July 23. Animal fat, and in good health. Eats a great deal of meat. Both kidneys are a little increased in size and less movable.
July 24. Same condition.
July 25. Animal is apparently normal, runs about the roof, climbs and jumps on the table, eats a great deal.

Analysis of Urine: Experiment 6.

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I am much indebted for this observation to Dr. Levene and Dr. Auer who, during August, had the kindness to analyze the urine of this animal and to examine her clinically.
July 26, 27, 28, and 29. Same condition.

July 30. Animal is apparently in excellent health. Nevertheless, both kidneys are enlarged and increased progressively in size and are completely fixed and adherent to the lumbar region. They are no longer movable in the abdominal cavity as normal kidneys are.

July 31 and August 1. Same condition.

August 2. A photograph is taken while the animal is eating. (See figure.)

August 3. Animal is apparently in good health, but the kidneys are enlarged and the urine contains more albumin.

From August 3 to August 10 the animal was in excellent condition, eating and acting as a normal cat. On August 11 she began to vomit and in a few hours became very ill. A great deal of albumin in the urine. Died on August 12.

Autopsy.—The body was opened by Mr. McClure. The peritoneum, the intestines, the lungs and the heart were found normal. The kidneys and the vessels were not examined, but the body was put in formalin, and the autopsy completed on October 4.

Macroscopical Examination.—Kidneys in their normal location and greatly enlarged. Normal cicatrisation of the flap of the bladder. Both kidneys are strongly adherent to the posterior abdominal wall and to each other. They are united by a growth developed under the peritoneum and passing as a bridge over the aorta and vena cava. This growth is developed outside of the capsule of the left kidney. It is adherent to and interposes itself between the renal vessels, the aorta and vena cava. The vena cava is compressed against the internal face of the right kidney. The right renal vein is also compressed between the tumor and the kidney, while the left renal vein is too much extended. This growth is composed of hard, white, apparently fibrous tissue, well-defined on its anterior side and more diffuse on its posterior side. It is intimately adherent to the transplanted suprarenal gland. Anastomoses excellent. Opening of the kidneys. No hydronephrosis. Congestion. Dilatation of the stellate veins.

Microscopical Examination.—Cadaveric changes of the epithelial cells are so marked that an interpretation of the epithelial lesions is not possible. Glomeruli well preserved, dilatation of the capillary loops which fill almost completely the capsules. Infiltration by plasma cells of the interstitial tissue. This lesion is more marked in the cortex than in the medulla. Focal disposition. Very marked dilatation of the blood-vessels. Appearance of acute interstitial nephritis. Section of the growth shows organized blood clot.

Experiment 7.—July 17, 1907.

Extirpation of the Kidneys.—Pregnant female cat. Etherization. Preparation by the ordinary method of both kidneys, left suprarenal gland, vessels, ureters and flap of bladder. Incomplete perfusion of the kidney as in the previous experiment. Extirpation of the anatomical specimen, which is put into Locke's solution at the temperature of the laboratory (22.2° C.).

Transplantation of the Kidneys.—Young, black, pregnant cat in excellent health. Abdomen considerably enlarged; near the end of pregnancy. Semi-circular transversal laparotomy. Evisceration of the intestines, the spleen, the bladder filled with urine, and the uterus, which is distended by several foetuses. Ligation of the left ovarian vein. Longitudinal incision of the lumbar peritoneum
Transplantation in Mass of the Kidneys.

in the middle line and extirpation of both kidneys. Dissection of the aorta and vena cava, and temporary haemostasis with serre fines. The anatomical specimen is placed in the abdominal cavity by the ordinary method. Reestablishment of the circulation 60 minutes after the interruption. No leakage. Excellent and quick reestablishment of the circulation through the kidneys which assume almost immediately a normal color. Incision of the bladder and graft of the flap of bladder by the ordinary method. After completion of the suture, it is observed that the ureters are twisted around each other. However, the transplanted ureters being very long there is no tension and it will not interfere, probably, with the flow of urine. The intestines, the spleen and the uterus are put back into the abdominal cavity, which is closed by the ordinary method. Gauze and cotton dressing. Shirt.


Autopsy.

Macroscopical Examination.—Large abscess of the pelvis, located on the left side, between the pelvis and the rectum, extending as far as the sub-peritoneal space, and opening to the skin near the anus, on the left side. Big and soft uterus. The left uterine horn is increased in size. On section reddish fluid and a part of a placenta is found. No peritonitis. Intestines normal. Both kidneys surrounded by loose connective tissue, normal in location, color and consistency. Anastomoses and vessels normal. Slight congestion of the pyramids. No dilatation of the ureters. Excellent healing of the bladder.

Microscopical Examination.—Glomeruli well preserved. No coagulated fluid between the capsules and the capillary loops. It is difficult to appreciate exactly the lesions of the epithelium of the tubules, for the fixation of the specimen is not good. It seems well enough preserved. Slight leucocytic infiltration between certain tubules. Slight dilatation of the blood-vessels.

Experiment 8.—July 19, 1907.

Extirpation of the Kidneys.—Middle-aged pregnant cat. Dissection of the anatomical specimen by the same method as in the preceding experiments. A small quantity of Locke's solution at the temperature of the laboratory (31° C.) is injected into the kidneys. The washing is stopped when the renal vein is still filled with bloody fluid. Anatomical specimen removed and put in Locke's solution at the temperature of the laboratory. Cat killed by hemorrhage.

Transplantation of the Kidneys.—Long, middle-aged male cat. Semi-circular transversal laparotomy. Evisceration of the intestines and the spleen. Extirpa-
Alexis Carrel.

Dissection of the aorta and vena cava, and temporary haemostasis. Section of the aorta below the renal arteries. Section of the vena cava between the openings of the renal veins. The kidneys are removed from their jar, put into the abdominal cavity and the vessels anastomosed by the ordinary method. Reestablishment of the circulation 1 hour and 5 minutes after the interruption. No leakage. Excellent circulation through the kidneys, which assume, after a few minutes, their normal appearance. Opening of the bladder and graft of the flap of bladder. Suture of the lumbar peritoneum. It is found that the right ureter goes behind the vena cava and produces a slight degree of compression of this vessel. The intestines are put back into the abdominal cavity. Closing of the abdominal wall by three planes of sutures. Gauche and cotton dressing. Shirt.

July 23. Animal apparently in normal condition, walks about the roof. The dressing is removed. Apparent healing of the wound.
July 24. Same condition.
July 26, 27 and 28. Animal in good condition, eats meat.
July 29. Animal is less well. An abscess has developed on the left side below the end of the abdominal suture.
July 30. Animal looks ill. However, he urinates as usual.
July 31. Animal refuses to eat, and looks very ill. The abscess is examined. It is found that it is an extensive and deep abscess of the wall itself, and not merely of the subcutaneous tissue. All the left part of the abdominal wall is involved. Large openings and drainage. In the evening the animal is worse.

August 1. Animal died in the morning.

Autopsy.

Macroscopical Examination.—Large abscess infiltrating the anterior and left parts of the abdominal wall. No peritonitis. Heart, lungs, liver, and spleen normal. Both kidneys are almost normal in size, color, and consistency, and surrounded by a layer of adipose tissue, which has become very abundant below the lower end of the kidneys. Their mobility is normal. Both ureters adherent to one another enter the peritoneal cavity at the level of the lower end of the incision of the peritoneum near the lower end of the left kidney. Perfect union of the transplanted flap to the bladder.

Opening of the bladder. On the posterior wall the flap is found limited by a linear and almost circular scar. The transplanted mucous membrane is normal. The mouth of each ureter presents its ordinary appearance.

Opening of the lumbar peritoneum and dissection of the vena cava. No perivascular sclerotic tissue. The right ureter is twisted around the vena cava. Renal veins almost horizontal, dense connective tissue around the left suprarenal gland. Opening of the vena cava, anastomoses perfectly smooth. A little clot around and in which a short piece of silk thread is found free in the lumen of the vein at 1 centimeter above the upper anastomosis. In a point of the upper anastomosis is a very small red spot where this clot was probably adherent. Dissection of the aorta. The lower anastomosis is almost invisible: at the level of the upper anastomosis, the aorta is adherent to the vena cava by
Transplantation in Mass of the Kidneys.

dense connective tissue. This tissue is removed and, corresponding to the point where it is mostly adherent to the wall of the aorta, a very small opening of the line of sutures between two stitches is observed. The aorta is opened; anastomoses smooth and glistening.

Longitudinal section of the kidneys: cortex and pyramids almost normal although a little congested. A small piece is fixed in Zenker's fluid.

Microscopical Examination.—Gomorini well preserved. Epithelium of the tubules without very marked lesions. Very few casts. Extensive foci of infiltration of the interstitial tissue by plasma cells; subacute interstitial nephritis. Slight dilatation of the blood-vessels.

Experiment 9.—October 14, 1907.

Dissection and Preparation of the Kidneys.—Middle-aged female cat. Etherization. Preparation of the anatomical specimen as usual. The lower suprarenal vein is ligated and the gland is not included in the specimen. Section of the uterus and the intestine. The specimen, of which the circulation is not interrupted, is protected by the omentum and towels.

Preparation of the Host.—Gray and white female cat, living in the laboratory several months; young and in good health. October 1. Urine examined—yellow, clear urine. Density 1.039. Urea 5.9 gr. per 100 c.c. No albumin. Etherization. Opening of the abdomen and evisceration as usual. The intestine are protected by Japanese silk towels sterilized in vaseline. Dissection and extirpation of both kidneys: Ligature of the ovarian veins, of the lower suprarenal vein and of two aortic collaterals.

Extirpation of the Kidneys.—Clamping of the aorta below the diaphragm at 11.25 a.m. Incomplete washing of the kidneys with Locke's solution. Section of the vessels and removal of the specimen.

Transplantation of the Kidneys.—The specimens are placed immediately in the abdominal cavity of the host. After temporary hemostasis with serre fines, the aorta is cut 3 centimeters below the renal arteries. Resection of the region of implantation of the renal veins. Washing and greasing of the vascular ends. Anastomosis of the vessels. Reestablishment of the circulation at 12.15 p.m. No leakage. Excellent circulation through the kidneys and the small vessels of the lower ends of the ureters. Nevertheless, the left kidney remains pale, while the right kidney is rosy and secretes urine. Opening of the bladder and graft of the flap by two planes of stitches. After the completion of this suture, a slight hemorrhage from the lower arterial anastomosis is noticed and controlled by one stitch.

The appearance of the kidneys is now very much modified. The left kidney is vasodilated, and its vein carries red blood, while the right kidney has become pale and vasoconstricted, and its vein is filled with dark blood.

End of the operation as usual.

October 14, 4 p.m. No shock. Animal walks, drinks water, has urinated 9 c.c. of bloody urine, the blood depositing itself quickly at the bottom of the glass, urine clear on the top. Urea 4.9. Uretises again, much less blood.

October 15. Animal a little sick, drinks water, walks about the cage.—4 p.m. Since yesterday 25 c.c. urine only, dark yellow, with a little blood. Albumin. Density 1.051.
Alexis Carrel.


October 17. Good condition, drinks milk, is given very little meat.

October 18. Same condition.

October 19. Cat in excellent condition. He is given plenty of milk and very little meat.

October 20. Same condition.

October 21. Cat is completely recovered. He is a normal cat, in the same condition as before the operation.

October 22. Diet from now raw liver and milk.

October 23. Dressing is removed; wound completely healed.

October 24. Cat normal. By palpation the kidneys are found small and movable. They are apparently normal.


October 26. Cat normal, kidneys normal in size and movable.

October 27. Same condition.

October 28. Cat being normal is allowed to go out from the cage and to run freely through the room.

October 29. Cat is put into another room and spends all day climbing on and jumping off the furniture.

October 30. Normal general condition, kidneys a little enlarged and less movable.

October 31. Cat a little depressed. The kidneys are very much enlarged and fixed to the lumbar wall. Samples of urine are then examined—1 p. m. Pale yellow, clear urine. Urea 3.6. Marked quantity of albumin.—3 p. m. Heavy precipitate of albumin by nitric acid.—6 p. m. Albumin 6 gram per 1000 c.c.

November 1. Cat is a little depressed, but still in very good general condition. The kidneys are much enlarged. Very large amount of albumin.—10.30 a. m. Etherization. Semi-circular transversal laparotomy, just above the scar. A few adhesions of the omentum to the wall. Peritoneum and intestines normal. Both kidneys appear very much enlarged and covered with sound peritoneum. Their consistency is a little softer than normal. Incision and dissection of the lumbar peritoneum on the middle line. There is a little sclerosis of the sub-peritoneal connective tissue around the anterior side of the vena cava. It may possibly produce a slight degree of compression of the vessel. Nevertheless, the arterial and venous circulation appear to be normal. The connective tissue of the hilus is oedematous, clear fluid flows after incision. The wall of the ureter is also oedematous, without congestion. The small vessels are distinctly seen with red blood. The color of both kidneys is rosy and normal. There is no congestion. Incision of the capsule of the right kidney: clear fluid and red blood flow. The tissue of the kidney is incised: it is oedematous and not congested. Abundant haemorrhage. Suture of the capsule with Lyon's silk and needles, No. 16. Both renal veins of the right kidney are dissected. The circulation is normal. The peri-vascular connective tissue is not sclerotic but oedematous. During the dissection of the upper vein several blue, round spots are seen on the surface of the organ, and disappear after a few minutes. No suture of the incision of the lumbar peritoneum. Abdominal wound closed as usual.
Transplantation in Mass of the Kidneys.

6.30 p. m. Cat in good condition. Urine 18 c.c. Much less albumin, 2.75.
November 2, 8 a. m. Cat in good condition, but depressed. Walks about cage. Takes milk only, possibly a little meat.—10.30 a. m. Urine 19 c.c. Albumin 0.60.
November 3. Same condition. Diet consists only of milk. Cat depressed.
November 4. Better condition. 8 a. m. Urine 61 c.c., dark yellow, density 1.033. No albumin.
November 5. Same condition.
November 6. Albumin again 1.50.
November 7. Cat depressed, walks about its cage.
November 9. Cat in better condition, but very emaciated. Therefore, he is given rare liver and codfish and eats hungrily. Dressing removed. Wound healed. Both kidneys much diminished in size, but still abnormally large.
November 10. General condition improved.
November 11. Both kidneys diminish steadily in size. Cat eats codfish.
November 12. Cat eats meat and fish. From 9 a. m. to 6.30 p. m., urine 48 c.c., clear yellow. Density 1.021. Urea 3.2. Albumin 1 gr.
November 13. Cat in good condition. Albumin less than 1 gr.
November 14. Cat well in the morning. In the evening, looks ill. Discharge from the nose. Refuses to eat.
November 15. Abundant nasal discharge. Cat refuses to eat. Urine, yellow clear. Albumin less that 1 gr.
November 17. Animal very emaciated, weak, but still able to jump from his cage and walks about the room. Abundant nasal discharge. Refuses to eat.
November 18. Animal very weak.
November 19. 1 p. m. died. Post-mortem 2.15 p. m. Opening of the abdominal cavity. A loop of jejunum is adherent to the posterior abdominal wall. Sharp flexure without obstruction. Both kidneys normal in location, color, size and consistency. Ureters normal. Perfect healing of the transplanted flap of bladder. In the bladder, yellow clear urine 5 c.c., albumin. Longitudinal incision of the kidneys, which are apparently normal. However the cortex is pale. Medulla normal. Capsule normal. No dilatation of the stellate veins.
The main pathological change is a general and intense calcification of the arterial system. The arteries are as hard and friable as thin-walled glass tubes. These lesions have developed since the transplantation, for the cat was a young animal in excellent health and its abdominal aorta was perfectly normal.

V. RESULTS.
The results of the experiments will be examined from the clinical and anatomical standpoints.
A. Clinical Results.

In every case the reestablishment of the renal functions was observed. These functions were determined by the characters of the urines and the general condition of the animals.

The secretion of urine may begin as soon as the arterial circulation is reestablished. In several cases, clear urine flowed from the ureters while the flap of bladder was being grafted onto the host. More often, no urine was seen flowing from the ureters immediately after completion of the operation. But the secretion always began during the first twenty-four hours. It is difficult to ascertain exactly the amount of urine secreted during the first few hours, because of the vomitus and water which are often mixed with urine. However, Cat 6 did not vomit, and after the first twenty-four hours the jar contained 120 cubic centimeters of urine. On the other hand Cat 1 urinated very little on the first day. Cat 9 urinated only 25 cubic centimeters during the first twenty-four hours; the second day the amount of urine passed was only 16 cubic centimeters, this urine was highly concentrated and contained much urea. These differences in the immediate amount of urinary secretion are due probably to unknown conditions of the vasomotor nerves. It is generally supposed that denervation of the kidney produces the secretion of an abundant and diluted urine. In the simple transplantation of the kidney, when, for instance, an isolated organ is transplanted into the neck, these phenomena were observed. But in the case of transplantation in mass, immediate vasodilatation is not so marked. Sometimes there is vasoconstriction, but oftener the kidneys retain their normal appearance. Exceptionally, vasodilatation alternates with vasoconstriction. In Experiment 9 about ten minutes after the reestablishment of the circulation, the right kidney was rosy, its venous blood red, and some urine flowed from its ureter, while the left kidney was pale, and apparently did not secrete. About thirty minutes afterwards, when the suture of the bladder was completed, both kidneys were examined again. The conditions were now reversed: the right kidney had become pale, and its vein filled with dark blood, while the left kidney was rosy and its vein contained red blood. It seems
that following transplantation the renal ganglia begin to act and that variable conditions of the nervous system may be responsible for the differences in the immediate results observed.

In all the experiments, the urinary secretion went on as long as the animal lived. Every cat urinated abundantly every day. But the animals presented sooner or later some complication, which modified in some measure the renal functions. As is to be expected after an operation as complex as the transplantation in mass, various accidents occurred; hydronephrosis, intestinal compression by peritoneal adhesions, volvulus, phlegmon, puerperal infection, compression of the renal veins by organized hematoma of the connective tissue, which were the direct or indirect causes of death in these animals. It is well known that several of the complications, especially the compression of the renal veins, produce grave renal lesions of their own. Therefore, the results of our experiments must not be considered as expressing generally the normal condition of transplanted kidneys, but merely of transplanted kidneys when subjected to various complications, that is, of more or less abnormal transplanted kidneys. Actually, it is impossible to know exactly how a normal transplanted kidney would functionate, for we cannot as yet discriminate between the disorders produced by such a common complication as hydronephrosis or compression of the veins and the less defined ones which may be due to lesions produced by the transplantation itself. However, in Experiment 6 and 9, for instance, the functions of the kidneys seem to have been for a certain time almost completely normal.

The color of the urine was yellow, generally or often less dark than the normal urine of the cat. Its reaction was acid. Its quantity for twenty-four hours oscillated between 120 and 160 cubic centimeters. But it might be, exceptionally, 25 and even 15 cubic centimeters, or, in another case, 215 or 255 cubic centimeters for twenty-four hours. In this case there was congestion of the kidneys produced by venous compression. The density was very far from constant; generally it oscillated between 1.018 and 1.030, going sometimes as high as 1.035 and 1.031. In Experiment 6 there was little parallelism between the amount of urine and the
density. Once the kidneys secreted 170 cubic centimeters of urine with a density of 1.035.

In all cases the amount of urea bore a relation to the diet of the animal. In Cat 6, abundantly fed with raw meat, the amount of urea varied from 2.7 to 5.1 grams. Cat 9 passed through his own kidneys, fourteen days before the operation, 5.9 grams of urea for 100 cubic centimeters. Eleven days after the operation, he eliminated through his new kidneys 5.1 grams of urea for 100 cubic centimeters. The difference is explained by the diet which was less abundant after the operation than before.

Among the abnormal constituents of the urine, the presence of albumin only has been looked for. In Experiment 1 albumin was present during the fourteen days of the post-operative life of the animal. These kidneys were abnormal owing to the perfusion with too hot Locke's solution and to a developed hydronephrosis. In the other cases there was little albumin during the first days, ranging from 0.50 to 0.25 gram for 1000 cubic centimeters. This was probably due in part to the blood coming from the suture of the ureter or the bladder. The amount of albumin decreased progressively and disappeared about one week after the operation. In Experiment 6 albumin was again found on the thirteenth day after the operation, and its amount increased progressively to 1.50 grams and beyond. In Experiment 9 there was albumin in the urine one day after the operation. On the eleventh day no albumin at all was present. On the fifteenth and sixteenth days the animal was allowed to run and climb freely. On the seventeenth day albumin was found again in marked quantity and, at the same time, enlargement of the kidneys was distinctly detected by palpation.

The general condition of the animal can be used, in some measure, to indicate the perfection of the urinary elimination. As long as no complications were present, the animals lived as normal cats do, without presenting any symptoms which could be considered as produced by renal insufficiency. When general complications occurred the cats reacted against them in normal ways.

Cat 1 suffered from eventration, due to a premature resorption of the catgut in the abdominal suture. In two other animals sutured with the same catgut, the resorption and eventration
Transplantation in Mass of the Kidneys.

occurred on the fifth or on the seventh day after the operation. We may admit that in Experiment 1 the resorption took place at about the same time. However, in spite of the extrusion of intestine outside of the abdominal cavity in the gauze dressing, the animal lived several days, drank water and milk and ate a little meat, and urinated abundantly. When the reduction of the inflamed intestines into the abdominal cavity was performed, fourteen days after the operation, the animal was still able to overcome the operative shock, and to walk about the room a few hours later.

In Experiment 6 the animal was in apparently normal condition four days after the operation. She walked about the room, played and ate a great deal of raw meat. Her condition remained excellent for several weeks. Twenty days after the operation she was in good health, had glossy hair, was very fat and ate with appetite all kinds of food. She ran about the room, played, jumped and climbed on the desks and tables as a normal cat does (see figure). There was, however, albumin in the urine, and slow and progressive enlargement of the kidneys took place, which showed that she was not in an entirely normal condition. Nevertheless, until the twenty-ninth day after the operation, she seemed to be in excellent health. Then gastro-intestinal symptoms appeared and death occurred on the thirty-first day after the operation. In Experiment 7 the animal operated on was a pregnant cat whose uterus contained several large foetuses. After the operation, she was immediately in good condition. Two days afterwards parturition occurred without any eclamptic fits or any abnormal symptoms. As the animal seemed to recover very easily and began eating meat one day afterwards, she was not observed very carefully. The dressing was removed and she was let alone. When she was examined again, eight days after the operation, she was found less well and feverish. Her condition grew worse and she died thirteen days after the operation. The autopsy showed puerperal infection with retention of a placenta and an enormous abscess of the pelvis.

Experiment 9 was a female cat which lived in the laboratory for several months. She was in excellent condition when she was operated on, and recovered very quickly from the operation. Her life went on just the same as before. The kidneys were movable
and small. She looked in excellent health and lived as a normal cat. On the eighteenth day after the transplantation a direct examination of the kidneys was made to ascertain the cause of the appearance of albumin. The general condition was little affected by the operation and the albumin disappeared on the twenty-first day, but reappeared again a little later. On the thirty-fifth day, the animal was very weak and emaciated. She died on the thirty-sixth day.

We can conclude from these results that the functions of the kidneys reestablish themselves after the transplantation. Since an animal, such, for instance, as Cat 6, can live in an apparently prosperous condition of health fifteen or twenty-five days, and more, after a double nephrectomy, and eliminate each twenty-four hours 120 and 160 cubic centimeters of urine through the new kidneys, it is certain that the functions of the transplanted organs are efficient. Even these functions during a part of the life of animals No. 6 and 9 can be considered as having practically been normal. When complications contingent or inherent to the actual method of transplantation occurred, the functions of the kidneys were modified and became abnormal according to the pathological changes suffered by the organs.

B. Anatomical Results.

The Blood Vessels.—The condition of the blood vessels was examined three times by laparotomy on the living animal and in the other cases at the autopsy.

The direction of the vena cava was almost always found normal. Once, however, the interposed segment was too long and bent. In Experiment 9 the position of the veins was modified considerably by an organized haematoma which had pushed the vena-cava against the right kidney. The right renal vein was compressed and the left one too much extended. This diminished the activity of the venous circulation and produced marked congestion of the kidneys. It is very important that the veins be given their normal situation and direction. On account of the low pressure and the thinness of the wall, they are not able to take care of themselves as arteries do. Every departure from the normal produces a diminution of
the caliber and consequently slight or marked congestion of the transplanted organ.

The relations of the veins with the surrounding structures, arteries and ureters were generally normal. It happened once that by mistake the right ureter was twisted around the lower part of the venous segment. It did not appear to cause any marked disturbance. The vessels were free in loose connective tissue, excepting in Experiment 6 where the vena cava and renal veins were compressed by an organized haematoma. When progressive compression of the veins had occurred it was expressed clinically by progressive enlargement of the kidney, and by reappearance of albumin in the urine on the thirteenth day after the operation, while the animal appeared otherwise in perfect health. In another case there was a little sclerosis of the perivascular connective tissue, which produced some retraction of the right kidney toward the middle line. The induration or sclerosis of the connective tissue may be a serious secondary complication. It occurs in the transplantation in mass but more often in simple transplantation, and oftenest in transplantation with implantation of the renal vessels on the aorta and vena cava. The induration has no influence on the arteries, but interferes with the venous circulation. As soon as the vein is no longer able to dilate freely in the loose connective tissue of the hilus, its circulation is slightly hampered and the result is a chronic congestion of the organ. This sclerosis may be brought about also by slight non-suppurative inflammation or perhaps by chemical irritation. It is probable that this condition is often due to a slight infiltration of blood into the connective tissue. Blood has an irritative influence on tissues. In Experiment 8 there were strong adhesions between the aorta and vena cava, at the level of the upper arterial anastomosis. The vessels were connected by a mass of dense connective tissue. The aorta was dissected, and the maximum of adhesion was found to be on the anastomosis itself and on this point there was a small gap between two stitches. The connective tissue was probably produced under the influence of the infiltration of blood through this opening. Many examples of this sclerotising influence of blood have been observed after transplantation of segments of vessels. It is well
known that extravasation of blood in joints, muscles, or in the
central nervous system produce hard connective tissue. Thus in-
jection of blood has been utilized by Bier and Schmieden\textsuperscript{14} for
inducing callous formation in cases of pseudarthrosis. The peri-
venous sclerosis, which is a dangerous secondary complication in
transplantation of organs, can be prevented probably by rigid hæmostasis and asepsis.

The venous anastomoses healed without thrombosis or stenosis. In one case there was an obliteration of the vena cava due to a
torsion of the vein. But this was quite independent of the anasto-
omosis. In Experiment 8 the venous anastomosis was normal. Nevertheless, a very small ovoid clot, which developed around a
fragment of silk thread, was found free in the lumen of the vein, about one centimeter above the upper anastomosis. On the anasto-
omosis itself by minute examination a little red spot was detected, which might have been the point where this clot was adherent. This is an absolutely exceptional complication.

The aorta and the transplanted aortic segment assumed in every
case a normal direction and appearance. The direction of the renal
arteries was the reverse of normal. This was due to the fact that
the transplanted segment was fixed on the aorta below the implantation of the normal renal arteries. A modification of direction has
no harmful influence on the arterial circulation. The thickness
of the wall and the high blood pressure allow the arteries to adapt
themselves to abnormal situations. Only one complication was
observed: in Experiment 5 there was a complete obliteration of the
lower part of the venous segment and the lower end of the aorta
by a thrombus. This thrombus was dissected and found adherent
to a wound of the intima, just below the lower anastomosis. The
wound was evidently produced by the dissecting forceps used in
this case for handling the vessel.

The anastomoses healed without thrombus or stenosis. The
intima of the transplanted segment was smooth and glistening. No
deposit of fibrin was observed, and consequently no embolus. In Experiment 1 a fatty embolus was noticed. A few minutes after
the réétablissement of the circulation, the right kidney assumed

\textsuperscript{14} Schmieden, \textit{Jour. of Amer. Med. Assoc.}, 1907, xlvi, 395.
a rosy and normal color, while the left kidney remained pale. The lower end especially was almost completely yellowish white. An incision through the capsule was made at this point. A small haemorrhage of red blood mixed with a good deal of vaseline followed, and stopped after a few moments. However, the circulation of the left kidney improved progressively and after thirty minutes was almost normal. It is probable that the vaseline under the progressive increase of temperature of the kidney became more fluid and flowed through the capillaries. The anatomical examination of the kidneys, fifteen days after the operation, showed no evidence of this embolus. The few accidents described could be almost completely prevented by operating on animals of a larger size.

The Nervous System.—The anatomical conditions of the nervous system of transplanted kidneys are not yet known. The attempt was made to preserve as completely as possible the circulatory apparatus of the nervous ganglia with the hope that they would resume their functions partially. It is not impossible to believe that sympathetic ganglia of which the vessels are respected and the circulation reestablished immediately after the transplantation do not degenerate completely. It has been shown, especially by the experiments of Morat,15 that sympathetic nerves have some of their trophic centers in the ganglia. A part of the vasoconstrictor nerves of the tongue, contained in the hypoglossus nerve, have a trophic center in the superior sympathetic ganglion. After section and degeneration of the sympathetic, stimulation of the hypoglossus still produces vasoconstriction of the tongue. After extirpation of this ganglion, stimulation of the hypoglossus becomes negative. After intra-cranial section of the facial nerve on a dog, almost all vasomotor fibres degenerate from six to twenty-six days after the operation. However, the stimulation of the chorda tympani produces a slight vasodilatation of the gland. Morat assumes that in this case the geniculatus ganglion must be considered as a trophic center for these fibers.

Even if it be admitted that nervous ganglia can, in some measure, functionate when severed from the central nervous system, it is

15 Morat, Comp. rend. de l'Acad. des sciences, 1897, cxxiv, 1389.
not certain that transplanted ganglia can recuperate their functions. The experiments of Stewart and Guthrie\textsuperscript{16} show that after an acute and complete anemia of the nervous centers for more than twenty minutes, the reëstablishment of their functions is not possible. The functional activity of the ganglia should necessitate also the re-establishment of a practically normal circulation. The experiments of Tuckett\textsuperscript{17} have demonstrated that if the vascular supply of the upper sympathetic ganglion is deranged, degeneration sets in forthwith. But, by preserving the connective tissue surrounding the pedicle of the kidneys and not cutting the small collateral branches of the aorta and vena cava, the vascular apparatus of the kidneys can possibly be kept in its integrity. In this condition, the ganglia may resume their functions, if it be physiologically possible.

_Ureters and Bladder._—Dilation of the ureters and hydronephrosis took place in the cases where anastomoses of the ureters were performed. In Experiment 3 the upper part of both ureters was very much dilated and the invaginated part stenosed. However, the urine flowed into the bladder satisfactorily, as is shown by the clinical history of the animal. The ureters of a cat are so small that the anastomosis is very difficult, and stenosis or disunion occurs. On small animals it seems proper to give up completely uretero-ureteral anastomoses.

The results of the graft on the bladder of the host of a fragment of bladder extirpated around the points of implantation of the ureters were excellent. The anatomical specimens showed that there was no distension of the upper part of the ureters or the kidneys. Both ureters, adherent to one another, entered the peritoneal cavity through the lower part of the incision of the lumbar peritoneum and went downward along the right side of the rectum. In one case they were twisted around one another; in another, the right ureter was twisted around the vena cava. In spite of these faults of technique the functional and anatomical results were very satisfactory.

In every case, the union of the flap of the bladder of the host took place. After opening the bladder, the transplanted flap ap-

\textsuperscript{17} Tuckett, \textit{Jour. of Physiol.}, 1905, xxxiii, 77.
Transplantation in Mass of the Kidneys.

peared congested and swollen, or entirely normal with the same color and appearance as the surrounding mucosa from which it was separated by a linear scar. On the surface of the transplanted mucosa both openings of the ureters were distinctly seen, normal in size and appearance.

The Kidneys.—The kidneys were examined three times only on living animals. During the operations performed on Cats 1 and 9, fourteen and eighteen days after transplantation, the kidneys were seen covered with sound peritoneum and as regards their color, situation and general appearance, they looked just like ordinary hydronephrotic or oedematous kidneys. In other cases, the anatomical examination was performed after the autopsy. For this part of the work, I am very much indebted to Dr. Simon Flexner, who had the kindness to look over the specimens and histological sections and to give me the invaluable help of his advice.

Macroscopical Examination.—In the experiments where there was no hydronephrosis or venous compression, the size of the kidneys was normal. Hydronephrotic and congested kidneys had their ordinary appearances. Their location was always normal. They remained at the place where they were put during the operation and maintained by the suture of the lumbar peritoneum. As a rule, they were not as movable as the cat's kidneys are normally. However, in Experiments 6 and 7 for instance, their mobility was practically normal. The kidneys of Cat 6 were strongly united to each other and to the lumbar wall by hard connective tissue. In the cases where no hydronephrosis or congestion took place, the consistency of the organ was normal. The external and internal appearance of the organs presented no special characters. They looked like congested, hydronephrotic, or almost normal kidneys. The kidneys of Cat 6 were very much congested. The capsule was slightly adherent to the parenchyma. The stellate veins were very much dilated and the medulla and cortex much increased in size.

In Experiments 1 and 3 the urine flowed from the organs when opened, the calices and pelves were dilated, and the surface of the parenchyma congested. The kidneys were ordinary hydronephrotic
organs. In the other experiments, the kidneys assumed the appearance of normal or slightly congested organs.

Microscopical Examination.—The specimens were generally fixed in Zenker's fluid and stained in haematoxylin and eosin. Some of them were taken from the animal several hours after death. In Experiments 6 and 7, the body was simply opened and put in a jar of formalin, while the pieces for histological examination were cut from the kidneys two months after. These faults of technique explain why in several cases the specimens were so badly hardened and why there were such cadaveric changes, especially in the epithelium of the tubuli contorti that an interpretation of the pathological lesions was difficult. It was found that the kidneys presented some lesions, very slight in some cases and more marked in others. In Experiment 4, for instance, the glomeruli and the epithelia of the tubules were very well preserved. There was no interstitial infiltration, and a few casts only were observed. The lesions of these kidneys were very slight.

The lesions noticed in the other experiments belong to two classes; hydronephrosis and nephritis. Hydronephrotic lesions were observed in Experiments 1 and 3. The excretory tubes were very much dilated. There was, too, some dilatation of the tubules of which the epithelium was flattened. In a few places between the tubes slight interstitial infiltration was present. In Experiment 3 the glomeruli were normal. In Experiment 1 some coagulated fluid was seen between Bowman's capsule and the capillary loops. The changes of the epithelium of the tubules were slight. The cells were regularly disposed inside the basement membrane, and the brush border was distinctly seen. The lumen contained some fluid exudate, but very few casts were observed. All these lesions may be explained by the presence of hydronephrosis.

Inflammatory lesions were present in three cases; very slight in Experiment 7, but more marked in Experiments 6 and 8. The epithelial degeneration was not extensive in Experiment 8. It seemed more marked in the other cases, but the cadaveric changes were so pronounced that no accurate interpretation was possible. The characteristic lesion met with in these three cases was the infiltration of the interstitial tissues between the tubules. The most
Transplantation in Mass of the Kidneys.

marked case was Experiment 8, in which the foci of infiltration were extensive. The infiltration was composed of cells having the characters of the plasma cells described by Councilman in acute interstitial nephritis, so-called.

This subacute interstitial nephritis is not a necessary complication of the transplantation, since it was absent from the first cases. It is due probably to secondary causes, physical or chemical conditions of the fluid used in the perfusion, congestion of the organ, diet, general condition of the animal, etc. Many factors may come into play during and after the transplantation for injuring the kidneys. The interstitial and epithelial lesions are due doubtless to some of these. It was regarded as surprising that comparatively few changes were found in the renal structure considering that the organs had been exposed to the rough handling of the transplantation. The cells of the secretory epithelium of the kidney are extremely delicate and sensitive to the modifications of the circulation, etc. It is well known that temporary ligature of the renal vein produces extensive degeneration of the epithelial cells. The simple suspension of the circulation has a harmful influence on the epithelium. The cadaveric disintegration of the cells of the tubules begins very early. One hour after death, the brush border has almost always disappeared.

In the transplantation, the renal tissue is not only deprived of circulation for one hour at least, but is also subjected to a perfusion with a fluid which exerts probably its own harmful influence. The perfusion of the organs seems necessary for preventing the formation of clots and the occurrence of thrombosis of the vessels or infarcts of the kidneys. The solution employed is the ordinary Locke's solution. It has been chosen because it is a physiologically balanced fluid. Pure sodium chloride solutions have injurious effects on the tissues. Ringer has shown that minute amounts of calcium and potassium salts antagonize the effects of the pure sodium salt. Loeb and his pupils have laid special emphasis on the poisonous effects of pure sodium chloride solution. Fundulus eggs put in a pure sodium chloride solution of the same concentration as sea


Loeb, *Amer. Jour. of Physiol.*, 1899-1900, iii, 327.
water cannot live, but they can live if a definite proportion of calcium chloride be added. Howell$^{20}$ and Harvey Cushing$^{21}$ also showed the injurious effects on the heart and muscles of the pure sodium chloride solution. In their experiments on tumors, Flexner and Jobling$^{22}$ found that the percentage of successful transplantations is much higher when the fragments of tumor have been preserved in Ringer's instead of salt solution. Therefore, in the perfusion or washing of delicate anatomical structures, physiologically balanced solutions must always be used. But even such a solution is harmful if it has not the same osmotic tension as the tissues. It is very probable that the osmotic tension of Locke's solution is not exactly suited to the cat's kidney. Rathery$^{23}$ has shown that slight variations of the cryoscopic point of the solution in which a fragment of the kidney is preserved is able to modify in a large measure the morphology of the cells. For the rabbit's kidney, the best solution has a cryoscopic point of $-0.78 \, ^\circ\text{C}$. All other solutions are nephrolytic. If, for instance, a solution which freezes at $-0.90 \, ^\circ\text{C}$ is used, the cells are found retracted and as having expelled into the lumen of the tubules a great many of their nuclear granulations. In order to prevent the osmotic disturbances that Locke's solution probably produces in some measure on the cat's kidney, it would be necessary to determine accurately the cryoscopic point of the solution isotonic for the cat's kidney, and to use then a balanced solution of this same tension.

Nevertheless, even an iso-osmotic, physiologically balanced solution would not be able to keep the kidney in its normal condition. Salkowski$^{24}$ has shown that organs kept at body temperature under conditions which prevent bacterial growth undergo self-digestion. The autolysis of liver and kidneys, etc., is due to proteolytic enzymes which are contained in the cells and come into play as soon as the circulation is stopped. Opie$^{25}$ succeeded in isolating two proteolytic enzymes.
ferments from the leucocytes and the lymphocytes, leucoprotease and lymphoprotease, and discovered that these enzymes are held in check by an antibody present in the serum. He was able also to isolate this antibody and to show that in a relatively small quantity it can neutralize the action of the autolytic ferments.

The researches of Opie explain why a mineral solution is not able to preserve tissues in normal condition, since autolysis soon occurs. To hold in check the activity of the proteolytic ferments set free by the suppression of the circulation, it is necessary to use a fluid containing in some proportion the antibody of the serum. The simplest method would be to use normal serum for perfusing the kidney. Another method consists of cooling immediately the organ to +1°C. a temperature at which the enzymatic activity is almost completely suppressed.

In the first experiments, the kidneys were thoroughly perfused with Locke's solution. In the last ones, the perfusion was very incomplete, a great deal of blood being still mixed with Locke's solution. This change was made with a view of leaving in the vessels of the kidney a little normal serum and contained anti-enzymotic bodies. But the amount was probably insufficient to prevent autolysis.

After the circulation has been re-established, the kidneys are not, however, in normal condition, and their cells are still exposed to many causes of injury.

The blood pressure of the host may differ from that to which the kidneys were accustomed. Possibly, the serum of the host is injurious, in some cases, to the new organs. Generally, however, the serum of an animal has no cytolysic action on the cells of another animal of the same species. Nevertheless, Ehrlich has shown that isocytolysins exist. Consequently, it may happen that the cells of the transplanted kidneys are injured by the serum of the host, even of the same species. This is probably an exceptional complication.

The isolation of the nervous apparatus of the kidneys from the central nervous system may be the cause, direct or indirect, of anatomical lesions. The denervation appeared as a grave objection to the possible efficiency of the transplanted kidneys.
physiological evidence of the existence of secretory renal nerves. However, denervation of the kidney produces, according to Bindo de Vecchi, degenerative lesions of the epithelial cells of the tubules. Marked disorders of the renal functions followed the section of the nerves in the experiments of Krimer, Brachet, Muller and Peipers. The urine, very abundant and diluted, contained albumin and even blood corpuscles. It is, of course, impossible to ascertain whether these changes are due to the section of the hypothetical secretory nerves or merely of the vaso-motor nerves or, perhaps, to other secondary causes. But, even if the denervation alone be able to bring about these results, it need not be considered as especially dangerous. An animal can live in good health after section of the renal nerves. Floresco dissected and cut out the nerves of the left kidney of a dog. Fifteen days afterwards, he resected the right kidney. The animal remained in good health. Last year, an experiment still more complete and conclusive was performed by me at the Rockefeller Institute. In the same operation, the right kidney of a bitch was extirpated and the left kidney isolated and left united to the body only by its ureter and vessels which were dissected as closely as possible. Practically all the nerves were severed. Nevertheless, five days after the operation, the amount of urine voided was 130 cubic centimeters. There was no albumin and the animal was in a normal condition. After one month the animal was found secreting from 90 cubic centimeters to 124 cubic centimeters of urine with high specific gravity and without albumin in the twenty-four hours. Eight months after the operation, he was in excellent health. This demonstrates that the denervation of the kidneys is of little importance for the general health of the dog. It is probable, however, that the kidneys, being deprived of the powerful protection of their nervous system, are more sensitive to pathological insults than the normal kidneys are. Had the animal been allowed to live as street dogs do instead of being kept quietly in a cage at an even temperature, with good food and without muscular exertion, perhaps pathological changes would have ensued.

*de Vecchi, Arch. di farmacol. sperimentale e scienze affini, 1906, v, 433, 479.

*Floresco, loc. cit.
CONCLUSION.

Among so many etiological factors, it is impossible to discriminate which are responsible for the complications which took place in our experiments. An attempt to explain the occurrence of nephritis, edema or calcification of the arterial system, for instance, will not be made, but the technique of the operations will be modified in order to suppress as much as possible the causes which may originate these secondary changes. The purpose of this article was not to analyze minutely the physiological or pathological character of the functions of transplanted kidneys, but merely to ascertain whether these functions are efficiently re-established.

It is to be concluded that an animal which has undergone a double nephrectomy and the grafting of both kidneys from another animal can secrete almost normal urine with his new organs, and live in good health at least for a few weeks. This demonstrates that it is possible to re-establish efficiently the functions of transplanted kidneys.

EXPLANATION OF PLATES.

PLATE XI.

Anatomical specimen extirpated from the first animal and ready for transplantation to the second animal (host).

PLATE XII.

The host ready for the reception of the anatomical specimen of Plate I.

PLATE XIII.

Specimen taken from Cat 7, showing the transplanted kidneys, and cicatrized vascular anastomoses and flap of bladder.