The Effects of Experimental Chronic Passive Congestion on Renal Function

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THE EFFECTS OF EXPERIMENTAL CHRONIC PASSIVE CONGESTION ON RENAL FUNCTION*

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By experimental methods, the production of varying grades of chronic passive congestion of the kidney has been attempted in order to determine its effect on the urinary and clinical findings, on the excretory capacity of the kidney as revealed by certain functional studies and on the histological structure of the kidney.

In every cardiorenal case which he encounters the physician confronts problems which he is called on to solve. Is the heart or kidney chiefly involved in this case? Which is more responsible for the clinical picture here exhibited? Do permanent and irreparable organic changes exist in the kidneys which preclude the hope of reestablishing a condition of relatively good health, or will the decreased renal function return to normal with the improvement in the cardiovascular system consequent on the enforced confinement to bed? Can chronic passive congestion alone be responsible for the clinical findings? Shall the treatment be directed chiefly to the heart or to the kidneys? Can chronic passive congestion itself interfere to any considerable degree with the excreting capacity of the kidney or can it *per se* institute pathological processes which result in organic and irreparable changes which decrease the capability of the kidney to carry on its work?

By correlating the data obtained from this study with those obtained by utilizing clinically these identical functional tests in a rather extensive series of cardiac, cardiorenal and renal cases, we have attempted to devise some means whereby these problems can be successfully attacked.

HISTORICAL

The effect of partial or complete obstruction to the venous return from the kidney on the urinary picture and the histology of the kidney has been already investigated. Robinson[1] (1843) showed that complete or partial tying off of the renal vein resulted in the appearance of albumin

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1. Robinson: Med. Chir. Tr., 1843, xxvi, 51.

or blood, or both, in the urine, and in the enlargement of the kidney itself. He also performed a one-sided nephrectomy and showed that albumin sometimes appeared in the urine following such an operation, but that by tying the aorta below the level of the renal arteries, together with the above mentioned operation, the appearance of albumin in the urine was more likely to occur. None of Robinson's animals lived more than four and one-half days.

Robinson's work, as well as that of several other investigators, Meyer[2] (1844), Frerichs[3] (1851), Goll[4] (1854), Ludwig[5] (1856), Munk[6] (1864), Erythropel[7] (1865), Stockvis[8] (1867), Weissgerber and Perls[9] (1877), Litten[10] (1879), Posner[11] (1880), Cohnheim[12] (1882), and Heidenhain[13] (1883), has unquestionably established three facts in relation to complete or partial obstruction of the venous return from the kidney for periods varying from hours to a few days.

1. Albuminuria is produced.

2. Hematuria results, particularly if the lumen of the vein be greatly narrowed.

3. Numerous epithelial cells, singly, in groups, or as epithelial casts, appear in the urine.

There is not the same unity of opinion concerning the occurrence of casts in the urine under these conditions; Munk, for example, stating that fibrous and gelatinous casts *(Faserstoff und Gallert)* are never encountered except where nephritis coexists. Burkart[14] also states that following ligation of the renal vein he obtained infarction of the kidney, but no casts in the urine. The consensus of opinion, however, is that casts do occur when the venous return is interfered with, having been described by Frerichs, Erythropel, Weissgerber and Perls, Runeberg[15] and Litten.

Another phase, the effect of obstruction of venous outflow on the quantity of urine excreted, has also been investigated. Paneth[16] (1886) in cleverly devised experiments on anesthetized animals in which known weights were allowed to make traction on a thread, the loop of which

2. Meyer: Arch. f. phys. Heilkunde, 1844, iii, 116.
3. Frerichs: Die Bright'sche Nierenkrankheit und deren Behandlung, 1851, p. 276.
4. Goll: Ztschr. f. rat. Med., iv, 78.
5. Ludwig: Physiologie, ii, 416.
6. Munk: Berl. klin. Wchnschr., 1864, i, 333.
7. Erythropel: Ztschr. f. rat. Med., 1865, xxiv, 217.
8. Stockvis: J. de méd., chir. et pharm., 1867, xlv, 22.
9. Weissgerber and Perls: Arch. f. Pathol. u. Pharmakol., 1877, vi, 116.
10. Litten: Untersuchungen über den hemorrhagischen Infarct, 1879, p. 3.
11. Posner: Virchow's Arch. f. path. Anat., 1880, lxxix, 311.
12. Cohnheim: Allg. Pathol., 1882, ii, 314.
13. Heidenhain: Herrmann's Handbuch der Physiologie, 1883, v, 324.
14. Burkart: Die Harncylinder, Berlin, 1874, p. 46.
15. Runeberg: Deutsch. Arch. f. klin. Med., 1879, xxiii, 225.
16. Paneth: Pflüger's Arch. f. d. ges. Physiol., 1886, xxxix, 515.

was placed about the inferior vena cava above the entrance of the renal vein, or about the renal vein itself, showed that venous congestion *always* caused a decrease in the urinary output. Even the mildest grades of congestion were never associated with a normal or increased amount of urine. Similar conclusions had been drawn by Munk[6] (1864).

Schwarz[17] (1900) states that partial obstruction of the renal vein of one side resulted in a relative polyuria on that side. This he claimed could be obtained with more certainty when the blood was first defibrinated.

De Souza[18] (1900) repeated this work with exactly opposite results even when the blood was defibrinated. He sharply criticized the work of Schwarz, pointing out that the flow of urine from either side, in Schwarz's experiments, was exceedingly small. He concluded that any interference with the return flow of blood from the kidney resulted in lessened urinary output.

Ignatowski[19] (1905) determined the effect on the renal function of ligating one renal vein, the other kidney being left untouched. He showed that the urine for the next twenty-four hours was scanty in amount, poor in chlorid and in urea, contained albumin and blood. He later tied the remaining renal vein, death occurring within a few days.

The work of these various investigators has dealt essentially with the immediate effect (hours to four days) of partial or complete obstruction of the venous return from the kidney on the amount of urine, the presence of albumin, blood and casts in it, and on the histological picture.

The problems with which we deal are: the effects of varying grades of permanent chronic passive congestion (partial obstruction to venous return) on the urinary picture, on the functional capacity of the kidney as revealed by functional studies, on the kidney histologically, and on the general condition of the organism elsewhere.

METHODS

The method utilized for the production of chronic passive congestion of the kidney consisted briefly of the application of constricting bands about the renal veins or about the vena cava above the entrance of the renal veins. The bands were obtained by cutting sections approximately 1 cm. in length from ordinary Coudé catheters which were sterilized by boiling for a period of two or three minutes.

The dog's abdomen was opened aseptically. The vessel about which the band was to be placed was isolated and thoroughly freed from the surrounding tissue. The section of catheter was slit longitudinally, opened, flattened out, and grasped between the blades of an artery forceps in such a manner as to prevent it from curling back into its original shape.

17. Schwarz: Arch. f. Physiol. u. Pathol., 1900, xliii, 15.
18. De Souza: Jour. Physiol., 1900, xxvi, 139.
19. Ignatowski: Compt. rend. Soc. de biol., 1905, lviii, 130.

The band was slipped under the isolated vessel and grasped on the other side with forceps. By careful manipulation it was allowed to curl back into its original shape, enclosing the vessel within its lumen. Heavy silk ligatures were then tied about it, in the center and at either end, holding it firmly in place. The degree of congestion produced was controlled by the caliber of the band utilized, by one-sided nephrectomy, and by ligating or leaving untouched the vessels concerned in the collateral circulation of the kidney. The dog was then allowed to recover from the anesthesia and was placed in an appropriate metabolism cage for immediate observation.

After a series of functional studies the animal was turned loose until such a time as another series was wanted. Repeated observations at periods of days or weeks were made on the urine and on the renal functional capacity. Finally the dogs were killed and the kidneys studied from a pathological point of view.

We have in this manner attempted to create conditions simulating as nearly as possible those existing in cases of cardiac decompensation. In clinical cases there is stasis which undoubtedly interferes with the free flow of blood from the kidney. Since the heart action in cases of decompensation is weakened, there must exist a disproportion between the driving force on the arterial side and the outflow on the venous side. And while our experiments have been conducted on animals with normal hearts, the constriction of the vein leads here also to a disproportion between the inflow and the outflow. Therefore, we may assume that the conditions of our experiments actually resemble the conditions encountered clinically[20] as closely as experiments with animals with normal hearts will permit.

The functional tests used in this connection were essentially five, e. g., phenolsulphonephthalein, lactose, salt, potassium iodid and water. In our earlier studies the excretion of certain other dye substances was studied in certain cases as was also the glycosuria following the injection of phloridzin. It became apparent early that nothing was to be gained from the continued use of indigo carmin and carbol fuchsin (rosanilin) in this connection,[21] inasmuch as they were excreted roughly in propor-

20. We are aware that in certain respects differences do exist. Although the pressure exerted a similar relative disproportion exists in the two conditions, naturally where the *vis a tergo* is normal the absolute pressure may be greater. Furthermore, there is a possibility that the insufficient oxygenation of blood generally, in broken compensation, plays a rôle in determining renal function. We do not think so much in this connection about the diminished oxygen supply to the kidney as of the possible toxicity of the waste products of other organs which suffer from lack of oxygen, affecting renal function.

21. Personal observations to be published later. For discussion of these tests, see also publication of Rowntree and Geraghty, Jour. Pharm. and Exper. Therap., 1910, i, 579.

tions paralleling the excretion of phthalein. The use of the indigo carmin was discarded, since its colorimetric properties are not well adapted to accurate quantitative work. Both drugs are excreted much more slowly than is the phthalein. The glycosuria following the administration of phloridzin seems to bear some relation to the excretion of lactose under similar conditions; e. g., glycosuria is prolonged. Phloridzin glycosuria, however, is exceedingly variable under any conditions and it was considered more advantagous to use only lactose, on which greater reliance can be placed.

In some of our later experiments observations were made on the urea and nitrogen content of the blood, which has been considered by Prevost and Dumas[22] (1821), Christison[23] (1834), Bright[24] (1836), Frerichs[25] (1851), Ascoli[26] (1901), Strauss[27] (1902), Müller[28] (1904), Obermeyer and Popper[29] (1911), Hohlweg[30] (1911), Widal[31] (1911), von Noorden[32] (1907), to be materially augmented wherever marked decrease in the excretory capacity of the kidney exists.

A brief description of these various tests, together with the technic, follows:

The Phthalein Test was used according to the original technic described by Rowntree and Geraghty.[33] One cubic centimeter of a phenolsulphonephthalein solution containing accurately 6 mg. was injected under antiseptic precautions into the lumbar muscles of the dogs, which were then placed in metabolism cages. A catheter was passed at the expiration of an hour and ten minutes and the total urine for this period collected. The urine was made distinctly alkaline, diluted to 1 liter, and the amount of drug present determined by the use of our[34] modification of the Autenrieth-Königsberger colorimeter. In our previous work with this test we have already determined that the output for normal dogs is 50 per cent., or more, for this period.

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22. Prevost and Dumas: 1821. Cited by Schöndorff, Pflüger's Arch. f. d. ges. Physiol., 1899, lxxiv, 307.

23. Christison: On Granular Degeneration of the Kidney, 1834.

24. Bright: Guy's Hosp. Rep., 1836, i, 358.

25. Frerichs: Die Bright'sche, etc., 1851.

26. Ascoli: Pflüger's Arch. f. d. ges. Physiol., 1901, lxxxvii, 103.

27. Strauss: Die chronischen Nierentzündungen in ihrer Einwirkung auf die Blutflüssigkeit und deren Behandlung, 1902.

28. Möller: Verhandl. d. Deutsch. path. Gesellsch., 1904-5, vii-ix, completing No. 80.

29. Obermeyer and Popper: Ztschr. f. klin. Med., 1911, lxxii, 332.

30. Hohlweg: Deutsch. Arch. f. klin. Med., 1911, civ, 216.

31. Widal: Bull. et mém. Soc. méd. d. hôp., Paris, 1911, Series 3, xxxii, 627.

32. Von Noorden: Metabolism and Practical Medicine, 1907, ii, 486.

33. Rowntree and Geraghty: Jour. of Pharm. and Exper. Therap., 1910, i, 579.

34. Rowntree and Geraghty: The Archives Int. Med., 1912, ix, 284.

The lactose, potassium iodid, salt and water tests, which have received a thorough study at the hands of Schlayer[35] and his coworkers in relation to the renal function in experimental acute toxic and vascular nephritides, and also in relation to nephritis as it exists clinically, were applied to this study of the renal function in chronic passive congestion. Schlayer's technic was adhered to as closely as possible.

Lactose was shown by Voit[36] to be excreted quantitatively by the kidneys following subcutaneous or intravenous administration. De Bonis[37] showed that lactose was excreted by the glomeruli. Schlayer therefore adopted it as a means of determining the functional capacity of the glomeruli in various forms of experimental nephritis and in the nephritides encountered clinically. He admits that its excretion is delayed in passive congestion, and therefore in his clinical studies he avoided cases which exhibited cardiac inefficiency. He considered delay in lactose excretion to be evidence of functional derangement of the vascular system. Since it is a substance foreign to the body and consequently not subjected to the many extrarenal factors which influence the excretion of water, he places his chief reliance on this test for information concerning the vascular functional capacity. Schlayer worked with rabbits and administered the lactose intravenously. We have worked with dogs, injecting it into the lumbar muscles.

Since De Bonis does not claim that lactose is not excreted by way of the tubules but merely that it is well excreted by the glomeruli, we thought that the frog's kidneys might furnish valuable information in regard to the mechanism of the excretion of lactose. Nussbaum[38] showed that the tubules in the frog's kidney are supplied by the renal-portal system which is entirely separate and independent of the arterial supply of the glomeruli. This work has been confirmed by Beddard,[39] Cullis,[40] and Rowntree and Geraghty.[33] An attempt was, therefore, made to see if the frog's kidney could excrete lactose in the absence of the glomerular system.

Large male frogs, *Rana catesbiana*, weighing about 300 gm., were pithed, their abdomens opened by long incisions on each side of and parallel to the anterior abdominal vein. The left kidney was exposed and all the arterial connections severed by means of the Paquelin cautery

35. Schlayer and Takayasu: Deutsch. Arch. f. klin. Med., 1910, xcviii, 17; 1911, ci, 333; and Schlayer, 1911, cii, 311.

36. Voit: Deutsch. Arch. f. klin. Med., 1897, lviii, 545.

37. DeBonis: Giorn Internat. d. sc. med., 1907, xix, 446, 451.

38. Nussbaum: Pflüger's Arch. f. d. ges. Physiol., 1878, xvi, 179; xvii, 580.

39. Beddard: Jour. Physiol., 1902, xviii, 20; see also Bambridge and Beddard: Jour. Physiol., 1906, xxiv; Proc. of Physiol. Soc. p. ix, and Biochem Jour., 1906, i, 255.

40. Cullis: Jour. Physiol., 1906, xxxiv, 250.

as suggested by Beddard. A cannula was then inserted into the anterior abdominal vein and a small glass cannula inserted into the left ureter. Protocols will indicate the course of the experiment and the results obtained.

PROTOCOLS OF EXPERIMENT

I. Ringer's solution was perfused from a Mariotte flask through the renal-portal system under a pressure of 35 cm. of water. Perfusion for fifteen seconds every three minutes was begun at 12:30 and continued until 12:50, no urine being secreted. At this time sufficient sulphonephthalein to make a 1 per cent. solution was added to the Ringer's solution and perfusion continued until 1:30 p. m., still no urine being excreted. Sufficient urea and lactose were then added to make a 1 per cent. solution of the former and an 8 per cent. solution of the latter and the perfusion continued. At 1:45 the urinary flow started, phthalein making its appearance but lactose being absent. At 2 p. m. sugar was recovered from the urine excreted.

II. Ringer's solution was perfused from a Mariotte flask through the renal portal system under a pressure of 35 cm. of water. Perfusion for fifteen seconds every three minutes was continued from 3:30 p. m. to 4 p. m. without any flow of urine. At 4 p. m., sufficient lactose to make a 0.5 per cent. solution was added to the perfusing fluid. Urinary flow started at 4:15 p. m. A trace of sugar was in the urine at 4:45 p. m. Phthalein (6 mg.) and sufficient urea to make a 2 per cent. solution were added to the perfused fluid at 5 p. m. At 5:30 p. m. the urine contained sugar and phthalein.

The kidney was perfused at 5 p. m. with a saturated solution of Prussian blue, immediately removed and placed in absolute alcohol. Serial sections were made but no blue found in the glomeruli.

From this it is seen that the frog's urinary tubules are capable of excreting lactose. We feel, therefore, that sufficient proof has not been presented that lactose is excreted by the glomerular system entirely.

From a repetition of Schlayer's work on acute toxic nephritis and our own, as well as his experience with its use as a functional test clinically, and from the evidence presented in this study, we feel that the mechanism of its excretion differs essentially from that of phthalein, salt, indigo carmin, etc. Throughout this investigation we have used it as Schlayer did as an index of the condition of the vascular function of the kidney, admitting, however, that we need much more information concerning the manner and significance of its excretion.

TECHNIC

Our technic was as follows: 3 gm. of lactose in 15 c.c. of distilled water was injected into the lumbar muscles under aseptic precautions. The animals were placed in metabolism cages, catheterized at the end of four hours, and thereafter every half hour up to eight and nine hours. The total amount of lactose excreted in four hours was determined polarimetrically in a great many instances by the Schmidt and Haenisch instrument, but since the time necessary for total elimination is considered by Schlayer to be of greater importance, we have studied this more particularly. The presence of lactose in the urine has been determined by means of the Fehling and Nylander tests. The total time necessary for complete excretion of lactose under such conditions normally does not exceed six hours.

Potassium Iodid Test.—Potassium iodid was one of the first substances to be utilized in connection with functional renal studies, being introduced by Duckworth[41] in 1867. It appears quickly in the urine following its administration by mouth, Quetsch[42] stating that it appears in nine to eighteen minutes after a 2 gm. dose, Roux[43] thirteen minutes after a 3 gm. dose, and Studeni[44] thirteen to eighteen minutes after a 1 gm. dose. The time required for complete elimination, as stated by different authors, varies markedly. According to Geisler,[45] 6 gm. require twenty-five hours; Roux, 5 gm. require thirty hours; Studeni, 1 gm. requires thirty to thirty-six hours; Anten,[46] 0.5 gm. requires forty hours; Schlayer and Takayasu[47] and Monokow,[48] 0.5 gm. requires forty-eight hours. Schlayer, in his studies, however, did not consider anything less than sixty hours to be a delayed excretion time following 0.5 gm. by mouth.

According to the studies of Schlayer, potassium iodid is excreted by the tubules of the kidney and on it he has placed most dependence in determining tubular functional capacity. Anten[46] showed that the excretion is not hastened by the occurrence of diuresis. It has been claimed by Schlayer and Takayasu[47] that its excretion is not influenced by chronic passive congestion and that it is not delayed in cases of cardiac decomposition, characteristics which, if true, would make it of tremendous importance in differentiating cases of pure passive congestion of the kidney from passive congestion associated with nephritis.

In our studies 0.5 gm. of potassium iodid was administered by stomach tube and its presence in the urine determined by Sandow's[49] test. This amount we have found normally to be excreted within forty-eight hours, but, like Schlayer, we have considered a delayed excretion only that which continues for more than sixty hours.

In certain instances, on account of vomiting, the drug was given directly into the blood by means of an intracardiac injection. Following such administration it is entirely eliminated normally within twenty-four hours.

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41. Duckworth: St. Barth. Hosp. Rep., iii, 216.

42. Quetsch: Berl. klin. Wchnschr., 1884, xxi, 353.

43. Roux: Thèse de Paris, 1890, No. 248. Expériences sur l'élimination des jodures par l'urine.

44. Studeni: Untersuchungen über die physiologische Ausscheidung der Jodpreparate durch den menschlichen Harn. Zürich, 1897.

45. Geisler: Cited by Anten (Note 46).

46. Anten: Arch. f. Path. u. Pharm., 1902, xlviii, 331.

47. Schlayer and Takayasu: Deutsch. Arch. f. klin. Med., 1911, ci, 354.

48. Monokow: Deutsch. Arch. f. klin. Med., 1911, cii, 309.

49. Sandow's method consists of adding 1 c.c. of 2 per cent. sodium nitrite solution and 1 c.c. of 10 per cent. H_2SO_4 to from 10 c.c. to 30 c.c. of urine, followed by the addition of a small amount of chloroform. This is shaken together and allowed to separate into layers, the presence of the iodid being indicated by a purplish-red or violet color in the chloroform.

The Salt and Water Tests.—The excretion of salt following its administration in amounts greatly in excess of that ordinarily taken with the food, is accomplished by the tubules, according to Schlayer. Normally a large amount of salt is excreted by one of two methods. If it is given without extra water it is almost entirely excreted within twenty-four hours, without diuresis, by increased salt concentration in the urine; if given with an excess of water it is excreted partially through increased concentration in the urine and partially through diuresis.

Where vascular injury to the kidney exists we may have the simple administration of salt followed by a marked diuresis, all of the salt being smoothly excreted in twenty-four hours without its percentage content in the urine being at all increased. This is usually associated with a somewhat low and fixed specific gravity and the syndrome is spoken of as "vascular hyposthenuria." Here the inability to concentrate is not due to any incapacity of the tubules to excrete salt, but on hypersensitive vessels which respond to the salt administration with a diuresis. In more severe vascular injury the vessels do not act in the same way, oliguria characterizing the urinary picture. In severe tubular destruction, a urine of fixed low specific gravity is obtained, the quantity of which is not materially affected by the administration of salt and the salt content of which is not augmented by administration of extra amounts of salt because of the inability of the tubules to excrete it. Such a condition is known as "tubular hyposthenuria."

In this study the daily excretion of salt, both as to per cent. and total excretion, was first observed, the animal being kept on a constant diet. An extra 3 gm. of salt were given by mouth and the effect on the percentage content in the urine and on the total salt output for the following twenty-four hours determined. In certain instances, where administration of the salt by mouth produced vomiting, 1.5 to 2 gm. of salt were given intravenously or directly into the heart by an intracardiac injection. The Lütke-Martius[50] method was used throughout in the chlorid determinations.

VARIOUS METHODS OF PRODUCTION OF CHRONIC PASSIVE CONGESTION OF KIDNEYS

In order to obtain passive congestion of the kidneys, bands were placed, by the technic described above, on one or both renal veins, on the vena cava above the entrance of the renal veins, on the aorta below the origin of the renal arteries, while simultaneously vessels concerned in the establishing of collateral circulation were ligatured; the production of hyperemia was attempted by placing a band about the aorta below the

50. Sahli: Diagnostic Methods, 1911, 177.

level of the renal arteries. The urinary picture, functional renal capacity and pathological findings obtained following these various methods are indicated below.

A BAND ON THE VENA CAVA ABOVE ENTRANCE OF RENAL VEINS

The effect of placing a constricting band on the vena cava just above the entrance of the renal veins, without handling the kidneys or interfering in any way with their collateral circulation, is shown in the following protocols:

Hound Bitch I.—Weight 15 kg.

February 3. Was etherized. A band was placed about the inferior vena cava just above the entrance of the renal veins, constricting the cava to about one-third its normal size.

February 4. Animal is apparently feeling very well, eats and drinks normally and is playful.

February 5 and 6. Urine[51] shows a trace of albumin, a few hyaline and granular casts; no red blood-cells or pus. Phthalein output normal—70 per cent. in an hour. Lactose excretion delayed, 50 per cent. excreted in four hours; positive after eight hours.

February 14 and 15. Wound has healed perfectly. Dog apparently in normal condition.

Urine: Albumin a trace; negative for blood, pus or casts. Phthalein normal, 52 per cent. in an hour. Lactose excretion slightly delayed, 27 per cent. for four hours, still faintly positive at seven hours. Salt well concentrated.

February 27 and 28. Animal appears normal. Phthalein 65 per cent. Potassium iodid, forty-eight hours. Lactose, six hours. 3.7 gm. salt excreted on a 3 gm. intake. Salt concentrated good 1.2 per cent. The kidneys are therefore functionally normal.

April 22 to 24. Animal is normal apparently. Urine shows a trace of albumin, but sediment contains no abnormal elements. Phthalein 60 per cent. Potassium iodid 48 hours. Lactose slightly delayed—seven hours.

May 13. Animal is pregnant. Urine excreted in fair amounts. Specific gravity 1,040, slight trace of albumin. No casts or blood. Phthalein and salt normally excreted while potassium iodid requires sixty hours. Lactose more delayed than at last observation; still strong in urine after eight hours.

June 1. The bitch gave birth to a litter of pups. Her condition was excellent. No functional studies were made.

Bitch II.—Weight 7.2 kg.

January 31. Band placed about inferior vena cava just above entrance of renal veins. Ether anesthesia lasting one hour.

February 1 and 2. Animal in excellent condition, behaves normally. Urine contains albumin ¼ to ½ per cent., shows a few granular casts and epithelial cells. Phthalein output is normal, 60 per cent. Phloridzin glycosuria persisted four hours. Lactose excretion delayed; urine strongly positive for sugar at end of eight hours.

February 5. Excreted 150 c.c. of urine on a 500 c.c. fluid intake. Intake of salt 5.4 gm. with only a trace excreted. Urine shows only a slight trace of albumin and a few hyaline and granular casts.

February 19 to 23. Animal apparently normal. Phthalein 60 per cent. for one hour. Lactose is delayed; urine reacting strongly at end of seven hours. Salt excreted in good concentration, 2 per cent.—4 gm. output on 5 gm. intake. Potassium iodid requires seventy-two hours for excretion.

March 8. Dog has developed distemper. Chloroformed.

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51. All urinalyses here recorded were made on catheter samples.

From these experiments it is evident that a moderate obstruction to the inferior vena cava above the level of the renal veins causes no serious change in the renal function. A persisting mild albuminuria is produced which is associated early with the presence of casts. The urinary output is fair in amount. The excretion of lactose is markedly delayed; salt excretion may be somewhat slow at first, but later is normal. The potassium iodid was delayed in one animal, normal in the other. The phthalein was absolutely normal throughout. That no serious injury to the renal function is produced is evidenced by the subsequent history of the animal. Eventually a practically normal functional picture is obtained, although slight albuminuria persists.

BANDS ON BOTH RENAL VEINS

Bitch III.—Weight 35 kg.

December 19. Moderately tight bands placed on both renal veins.

December 21 and 22. Urine small in amount, shows albumin and numerous red cells but no casts. The phthalein was excreted in a mere trace on the 21st, and 8 per cent. for one hour on the 22d. Only a trace of rosanilin excreted.

December 26. Animal is feeling badly; walks about but does not eat. Vomits after drinking small quantities of water. Wound is infected. Phthalein and rosanilin were injected but no trace of them could be found in urine at end of one hour. Urine is very scanty, containing albumin and blood.

December 28. Found dead. No careful study of the condition of the renal veins as to thrombosis or slipping of the band, etc., was made.

Bitch IV.—Weight 10 kg.

January 22. Bands placed about both renal veins causing marked congestion.

January 23. Animal is exceedingly playful. Phthalein output 52 per cent.

January 25 to 31. Animal in excellent condition. Urine is normal in amount and contains albumin ¼ to ¼ per cent. On some examinations the sediment contains a few hyaline and granular casts and a few red blood cells while at other examinations sediment is normal. The phthalein is excreted normally, 52 per cent. in one hour. Rosanilin is also well excreted. Potassium iodid is markedly delayed, 100 hours being required for total excretion. Lactose is markedly delayed, while salt is excreted normally—1.4 per cent. and absolute output 5 gm. on a 5.2 gm. intake. The glycosuria following phloridzin is very slightly prolonged.

February 14 and 15. Animal in excellent condition. Phthalein output 65 per cent. Salt excreted well 1.5 per cent. concentration and 6.5 gm. absolute on a 6 gm. intake. Potassium iodid excretion still delayed—eighty hours. Lactose slightly delayed—six to seven hours. Urine plentifully excreted, 500 c.c. on 600 c.c. intake of water. Sediment negative for pus, blood and casts.

February 20. The abdomen was again opened. Both kidneys were seen to be enlarged and markedly engorged. The capsular veins were strikingly enlarged and tortuous. The left kidney was removed for histological study. The band was found in place surrounded by fibrous tissue and the veins not thrombosed.

A BAND ON LEFT RENAL VEIN; RIGHT-SIDED NEPHRECTOMY

A more pronounced grade of congestion was attempted through a right-sided nephrectomy and a band about the vein of the remaining kidney. The effect of such a procedure on the renal function was studied on several dogs, the results appearing in Table 1.

TABLE 1.—EFFECT ON RENAL FUNCTION OF A RIGHT-SIDED NEPHRECTOMY WITH BAND ON LEFT VEIN

Dog	Wt., Kg.	Date 1912	Condition	H_2O, c.c.	Urine				Lactose, Hrs.	KI, Hrs.	Salt			Remarks
					Quantity, c.c.	Sediment	Albumin	Phthalein			In gms.	Out gms.	Per Cent.	
V	7.9	1/12	.....	...	...	.....	.....	.....	....	.....	...	....	.....	Operation; rt. kidney removed; wt. 30 gm. Moderately tight band on left renal vein. Phloridzin glycosuria 7° on 13th. Indigocarmin 5 per cent. in 1 hr. on 14th. Carbolfuchsin 11 per cent. in 3 hrs. on 15th. Animal chloroformed. Left kidney showed marked chronic passive congestion. Wt. 50 gm. No venous thrombosis. Peritonitis.
		13	Good	200	120	.....	++	26	....	.....	...	.25	.21	
		14	Depressed	300	270	Many R. B. C. Hyaline and granular casts	+	.....	....	.....	...	.18	.03	
		16	Depressed	...	...	Epith. cells and a few hyaline casts.	.....	6	8°+	24 Intracardiac	...	....	.....	
		17	Very sick	200	350	.....	.....	16	....	.....	...	Trace	Trace	
VI	5.4	1/12	.....	...	...	.....	.....	.....	....	.....	...	....	.....	Operation; rt. kidney removed. Moderately tight band on left renal vein. Phloridzin glycosuria 7° on Jan. 13. Carbolfuchsin 45 per cent. in 3 hrs. on 15. Phloridzin glycosuria 6° on Jan. 15. Indigocarmin 7 per cent. in 2 hrs. Jan. 17. Phloridzin glycosuria 5° on the 29. Carbol-fuchsin 40 per cent. in 3 hrs. on Jan. 29.
		13	Good	300	180	.....	+	25	....	72	...	.41	.23	
		14	Good	250	210	Occasional R. B. C.	+	.....	....	.....	...	.45	.22	
		15	Excellent	300	277	.. ..	.....	90 (2.5°)	8°+	.....	...	....	.....	
		17	Excellent	400	180	.....	.....	30	8°+	.....	...	Trace	Trace	
		1/23-26	Excellent	400	good	Occas. R. B. C. hyaline and gran. casts.	⅛ to ¼%+	.....	8°+	72	3.5	1.8	.5	Chloroformed. Kidney was found to have an accessory renal vein. No marked congestion was found.
		1/29-31	.....	...	...	Hyal. and cell. casts; R. B. C.	⅛ to ¼%	52	8°	72	5.2	3.4	1.3	
		2/9	Excellent	...	...	.....	.....	65	8 +	.....	...	....	.....	
		2/13	Distemper	...	..	.....	.....	.....	....	.....	...	....	.....	

IV	10.0	2/20	.....	...	...	.....	.....	.....	....	.....	...	....	.....	One month previously dog had had bands placed on both renal veins; 2/20/12 left kidney removed. May 24 animal very lively and playful. The right renal vein was tied and animal lived on the collateral venous return.*
		2/21	Good Thin	...	...	.....	.....	.....	....	.....	...	....	.....	
		3/18	.....	...	421	Few hyal. and gran. casts; epith. cells	++	40	8°+	66	4.2	1.6	.39	
		5/13	Excellent	300	300	Blood and pus cells; few red cells	+	55	....	.....	2.6	2.4	.8	
		5/24	Excellent	300	300	.....	+	56	8	60	3.0	2.4	.8	
VII	9.6	1/29	.....	...	...	.....	.....	.....	....	.....	...	....	.....	Two anesthesias as vagina was slit open 3 days previously. Left kidney wt. 34.5 gm. Tight band on right renal vein. Phloridzin glycosuria 4° on Feb. 1.
		2/1	.....	...	70	Few hyal. and cell. casts; few R. B. C.	¼ to ½%	54	8°+	.....	...	....	.....	
		5-6	Good	700 800	440 550	Numerous R. B. C. and W. B. C.; no casts; normal	+	50	....	....	5.4 5.0	1.6 1.2	.38 .20	
		3/21-22	Good	500	300	.....	0	75	....	.....	...	....	.....	
		3/30 4/1	Thin	...	...	.....	Trace	60	8°+	48	3.0	2.2	1.1	Injected vital stain. Killed animal. Kidney wt. 62 gm. Band in place; no thrombosis.
VIII	6.0	1/27	.....	...	...	.....	.....	.....	....	.....	...	....	.....	Left kidney removed; tight band on left renal vein. Carbol-fuchsin 35 per cent. after 3° on 29. Phloridzin glycosuria 5° on 30. May 15, renal vein tied. Animal lived on collateral venous return.*
		29	Excellent	...	...	.....	.....	.....	....	.....	...	....	.....	
		31	Good	300	400	.....	⅛ to ¼%	.....	8°+	100	5.2	3.0	.73	
		2/18-23	Good	300	100	.....	.....	80	7°+	.....	...	....	.....	
		4/22	.....			Normal	0	55	6°+	.....	...	....	.....	
		5/8	Good	500	370	.....	+	70	7°	.....	3.0	3.2	.87	

* Described in text.

TABLE 2.—EFFECT ON RENAL FUNCTION OF LIGATING COLLATERAL AS WELL AS RENAL VEINS

Dog	Wt., Kg.	Date 1912	Condition	Sp. Gr.	H_2O, c.c.	Urine					Salt			Remarks
						Quantity, c.c.	Sediment	Albumin	Phthalein.	Lactose	KI, Hrs.	In, Gms.	Out, gms.	Per Cent.	
IX	6.0	3/5	.....	....	...	...	.....	....	....	....	.....	.....	....	.....	Right kidney removed. Wt. 28.5 gm. Moderately tight band on left renal vein; ovarian and lumbar veins ligated.
		6 & 7	Good	1018	700	500	No casts	++	54.0	8°+	48	3.0	3.0	.6	
		9 & 10	Distemper	1012	500	450	.....	....	12.0	....	.....	3.0	.63	.14	
		11	.....	....	...	...	Many red blood cells; no casts	....	Trace	8°+	.....	.....	....	.....	General infection. 12th — found dead. Thrombosis of renal vein. Large subcapsular hemorrhage. Kidney weight 50 gm.
X	6.5	3/18	.....	....	...	...	.....	....	....	....	.....	.....	....	....	Right kidney weighing 24 gm. removed. Moderately tight band about left renal vein; ovarian, lumbar and suprarenal veins tied. Animal killed—thrombosis of renal vein at site of band. Kidney wt. 40 gm. No peritonitis. Kidney markedly congested.
		19	Good	1032	...	...	Numerous hyaline and granular casts; no blood	+	47.0	7°+	72	.....	....	.....	
		21	Fair	1018	500	400	.....	....	9.0	....	.....	3.2	2.4	.61	
		22	.....	....	...	...	.....	....	7.5	....	.....	.....	....	.....	
		23	.....	1018	500	300	Blood, pus and epith., no casts.	++	11.5	....	.....	.....	....	.....	
		24	.....	....	...	...	.....	....	11.5	....	.....	.....	....	.....	
		25	Fair	....	...	...	.....	....	15.0	....	.....	.....	....	.....	
		26	.....	1016	500	670	.....	....	12.0	8°+	60	4.0	1.4	.16	
		28	Very sick	1018	...	...	.....	+	11.0	....	.....	.....	....	.....	
		29	.....	....	...	...	Blood, pus and casts	+	5.0	....	.....	.....	....	.....	

XI	6.0	3/20	.....	....	...	...	.....	....	....	....	.....	.....	. ..	.....	Right kidney removed. Wt. 24 gm. Moderately tight band on left renal vein. Ovarian, lumbar and suprarenal tied. 28th — found dead. Band in place. No thrombosis. Cause of death unknown. Heart and lungs negative. No peritonitis.
		21	Good	1047	...	...	Few epith. cells W. B. C.	++	32.0	....	.....	.....	....	.....	
		23	.....	1039	400	300	.....	....	50.0	....	.....	.....	....	.....	
		24	Excellent	....	...	...	.....	....	60.0	....	.....	.....	....	.....	
		28	Dead	....	...	...	.....	....	....	....	.....	.....	....	.....	
XV	8.0	4/19	.....	....	...	...	.....	....	....	....	.....	.....	....	.....	Right kidney removed. Left kidney banded fairly tight. Ovarian tied at entrance to renal. Typical bronchopneumonia; beginning thrombosis of left renal vein. Kidney showed marked congestion and some cloudy swelling.
		20	Fair	1024	...	400	Casts, hyaline and granular	++	....	7°+	48	2.0	....	Trace	
		22	Distemper	....	...	...	.....	....	60.0	6°	.....	.....	....	.....	
		26	.....	....	...	...	Occasional cast	0	36.0	....	.....	.....	....	.....	
		27	.....	....	...	...	. .....	....	48.0	....	.....	.....	....	.....	
		28	Dead	....	...	...	.....	....	....	....	.....	.....	....	.....	
XII	8.5	3/26	.....	....	...	...	.....	....	....	....	.....	.....	....	.....	Right kidney removed. Wt. 34 gm. Left renal vein tied. Chloroformed. Kidney 52.5 gm. Showed marked congestion.
		27	.....	....	few c.c. Anuria	few c.c.	Much blood; hyal., gran. and cellular casts	++	0.0	....	.....	.....	....	.....	
		28	Chloroformed	....	...	...	.....	....	....	....	.....	.....	....	.....	
XIII	9.5	4/4	.....	....	...	...	.....	....	...	....	.....	.....	....	.....	Right kidney removed, weighing 45 gm. Very tight band on left renal vein. All collaterals tied. Right renal vein thrombosed. Wt. 60 gm.
		5	Very sick	....	few c.c.	...	Full of blood	+	0.0	...	.....	.....	....	.....	
XIV	4.5	4/11	.....	....	...	...	Blood and casts	+	....	....	.....	.....	....	.....	Right kidney removed. Wt. 13.8 gm. Left kidney banded; access collaterals cut. Left kidney 28 gm. at autopsy. Veins thrombosed. Marked congestion.
		12	Very sick	1006	200	325	.....	....	1.5	8+	Intracardiac 24	Intracardiac 2.0	.75	.23	
		13	.....	....	...	...	.....	....	1.5	....	.....	.....	....	.....	
		14	Chloroformed	....	...	...	.....	....	....	...	.....	.....	....	.....	

From a study of this table it is at once evident that a kidney subjected to such usage does not suffer seriously over any great period of time. Even on the day following the operation the animal may appear normal. The urine is fair in amount, contains some albumin, red blood-cells, a few hyaline and granular casts, but the phthalein output in many instances is little, if any, reduced. The lactose, however, is invariably delayed markedly, the excretion of potassium iodid is usually considerably delayed and the salt not well excreted. As time progresses it becomes more apparent that the functional injury is slight—the phthalein output rapidly increasing to normal, if it has been at all reduced. Weeks or months after the operation the animal is normal to all appearances. A urinalysis, however, usually reveals a trace of albumin, in which microscopically a few granular and hyaline casts are seen. A functional study shows normal phthalein, iodid and salt excretion, while the lactose is slightly delayed.

The establishment of a good collateral circulation was thought to be probably responsible for the rapid return to normal of the kidney function.

The effect of ligating the vessels chiefly involved in collateral circulation of the kidney simultaneously with the operation described above was investigated. The band was placed about the renal vein at its entrance to the inferior vena cava. The ovarian vein, at its entrance to the renal, as well as one of its branches, a large vein which passes from the lower pole of the kidney to the ovary, was ligated. In some instances one of the lumbar veins and the suprarenal vein were also tied.

The results obtained from a study of this series of animals are shown in Table 2. These animals can be divided into two groups: Group I, including animals IX, X, XI and XV, in which the bands were of moderate tightness only, and Group II, in which the bands were made very tight. All four animals of Group I show a normal, or only slightly reduced, phthalein output at first. The quantity of urine excreted was large, contained albumin, but blood and casts were absent in two animals. The lactose was markedly delayed in all, salt excreted fairly well in two, and the iodid normally in two and delayed in another.

Dogs IX and X both showed a sudden marked drop in the phthalein output four or five days after the operation. The first subsequent examination of the urine showed large numbers of red blood-cells, probably indicating the occurrence of thrombosis in the renal vein, inasmuch as thrombosis was encountered at autopsy in each case. Dog X was particularly interesting, living for more than a week with a low phthalein output, the lactose, salt and iodid excretion being also very low. The urine was plentiful and of low specific gravity, contained much albumin, numerous red cells and a few casts. The dog throughout this period was

only in fair condition, at times playful and sprightly, but on the whole inclined to lie quietly and to sleep. Vomiting occurred at intervals.

Dog XV differed from the others of this group in that only one collateral channel was ligated, e. g., the ovarian vein just at its entrance to the renal vein. On the third day following operation the animal was only in fair condition. The urine was large in amount, containing considerable albumin and casts. The phthalein and iodid output were normal, while lactose was markedly delayed and salt excreted with great difficulty. At this time it became apparent that the dog was developing distemper. Later, on the seventh to the ninth days the albumin had disappeared and the only abnormal constituent present in the sediment was an occasional cast, the phthalein output being practically normal — 42 per cent. On the ninth day the animal died, the autopsy revealing a marked typical bronchopneumonia, no peritonitis, an immense left kidney with a tremendous amount of collateral circulation and beginning thrombosis, localized in the vein at the site of the band.

Group II is composed of two dogs, XIII and XIV. The bands placed on the renal veins of these dogs were very small. In Dog XIV the ovarian, and the veins at the lower pole which empty into the ovarian, lumbar and suprarenal veins were ligated. Both animals were exceedingly sick from the time of operation until death. Dog XIII excreted only a few cubic centimeters of urine after the operation. This was full of blood and no phthalein was recovered within an hour. The animal died after forty-eight hours. The kidney was found much enlarged, the band in place, with thrombosis of the vein. A tremendous subcapsular hemorrhage, the blood having partially dissected the capsule, was found. The kidney showed marked chronic passive congestion.

Dog XIV excreted 325 c.c. of urine on an intake of 200 c.c. of water on the day following operation. The urine contained albumin, blood and casts. The phthalein output was only 1.5 per cent., and the lactose markedly delayed. As the animal was vomiting repeatedly, the salt and iodid were administered by an intracardiac injection. The iodid was entirely excreted within twenty-four hours, but the salt was poorly excreted. Again on the following day only a trace of phthalein was recovered. The animal died on the fourth day. The kidney was double the normal size with the band in place. The vein was patent at the site of the band, but thrombosed distally. The capsular and ovarian veins were markedly engorged and a peculiar fleshy-like tissue (probably hemorrhage) was found between the layers of the capsule in the region of the pelvis of the kidney. The animal also showed some bronchopneumonia.

To show the similarity of Cases XIII and XIV, from the point of view of urinary and pathological findings, to the picture following a

sudden complete ligature of the renal vein after removal of the opposite kidney, the data relating to Dog XII is included in this table. On the day following operation the animal was very ill and only a few cubic centimeters of bloody urine could be obtained on catheterization. This contained casts of various kinds—hyaline, granular and blood. After this no urine was obtained. At autopsy the kidney was found to weigh 52.5 gm. (R. 34 gm.) and to be dark violet in color. Between the layers of the capsule and in the tissues just outside of the capsule about the renal and ovarian veins was a large hemorrhage with clots of dark blood of varying age. The glomeruli were very distinct and markedly congested—more so than in any other kidneys met with in this study.

COLLATERAL CIRCULATION OF THE KIDNEY FOLLOWING GRADUAL BUT COMPLETE OCCLUSION OF THE RENAL VEIN AND THE CONDITION OF RENAL FUNCTION UNDER THESE CIRCUMSTANCES

It has been suggested in the earlier part of this paper that great importance is to be attached to the development of collateral circulation following gradual and progressive occlusion of the renal vein. An effort has been made to ascertain just how important collateral circulation may become in determining the state of renal function under such conditions.

Following the application of the band to the renal vein in dogs the capsular, ovarian, lumbar, suprarenal and ureteral veins become markedly engorged and distended. These enlarged vessels present a striking vascular picture which has been previously described by Litten.

The extent and tremendous importance of this development of collateral circulation is indicated by the following protocols:

Dog VIII.—Weight 6 kg.; had the right kidney removed and a moderately tight band placed about the left renal vein on January 27. Three months later the renal function had returned to normal save for a slight albuminuria and a slight delay in lactose excretion. A second operation was performed May 16, at which time it was seen that a tremendous collateral circulation involving the capsular, ovarian, lumbar, and suprarenal veins, had been established and that the renal vein itself was relatively small. The renal vein was tied and the abdomen closed. The animal's venous circulation, therefore, was entirely collateral. On the day following the operation urine was secreted which contained a large amount of albumin, blood and casts, but the phthalein excretion was 50 per cent. for an hour. During the next two days the animal was in good condition. The lactose was delayed over eight hours, but salt and iodid were excreted normally. At the present time, two weeks later, albuminuria and delayed lactose excretion still persist; otherwise the animal seems perfectly normal.

Dog IV.—Weight 10 kg.; had bands placed about both renal veins on Jan. 22, 1912. In the course of a few weeks function had returned practically to normal. On February 20 a second operation was performed, the left kidney being removed. The animal made a perfect recovery and the functions quickly again returned to practically normal. On May 24 a third operation was performed. The right kidney was found to be greatly enlarged and associated with a tremendous collateral circulation. The renal vein was tied at its entrance to the vena cava, the

abdomen closed and the animal allowed to recover. On the following day the dog was in good condition with a fair urinary secretion (250 c.c.) containing albumin, blood and casts. The phthalein output was 40 per cent. Two days later the lactose was found to be delayed for more than eight hours. Salt and iodid were excreted normally. The animal was in excellent condition, but the wound was badly infected.

In two instances this remarkable condition has been seen, e. g., an animal living in apparently good health, secreting practically a normal urine and exhibiting an excellent condition of renal function with the renal vein tightly ligated. This affords striking evidence of the great importance of collateral circulation where gradual obstruction to the venous return from the kidney develops.

Although, owing to different anatomical conditions in humans, so great a development of collateral circulation may not be possible, it undoubtedly is a matter of extreme importance where gradual venous obstruction occurs.

To summarize, then, it is evident that, after a one-sided nephrectomy, the application of a moderately tight band about the other renal vein causes marked congestion of the remaining kidney. The congestion is associated at first with the production of a good quantity of urine which contains usually albumin and casts and sometimes blood. The excretory capacity of the kidney is not seriously injured, as evidenced by a good phthalein output. The excretion of lactose is always markedly delayed, as is usually also that of the iodid and salt. With the development of a good collateral circulation the congestion becomes less intense, the albumin, blood and casts become a less pronounced feature of the urinary picture. The phthalein, iodid and salt may all be normally excreted, but the lactose is still delayed. Two or three months after such an operation the most probable abnormalities will be a very slight trace of albumin and a delayed lactose excretion.

When a moderately tight band is applied and the collateral channels ligated, the same picture is encountered during the following two or three days as is seen when the collaterals are left open. Thrombosis of the renal vein is apt to develop, however, and its occurrence is associated with the appearance of a large amount of blood in the urine and a sudden marked fall in the phthalein excretion. Nausea and vomiting develop. The amount of urine at first may be large. All the excretory functions finally fail and death ensues.

When an excessively tight band is applied to the renal vein and the collateral channels are ligated, the effect is usually similar to that which would be encountered following complete ligature; e. g., large amounts of albumin and blood, together with the excretion of minimal traces of phthalein, lactose, iodid and salt. Thrombosis occurs and death results.

The magnitude and importance of the development of collateral circulation following gradual obstruction to the return venous flow is indicated by the demonstration of the possibility of animals living and exhibiting a good renal function where the occlusion of the renal vein has been gradual, but complete.

THE EFFECT OF PLACING A BAND ABOUT ONE RENAL VEIN; THE OTHER KIDNEY REMAINING UNDISTURBED. URETERAL CATHETERIZATION OF BITCHES

Experiments were also made for the purpose of determining the effect on the urinary picture and on the total renal function of applying a band to one renal vein, the other kidney being undisturbed. Simultaneously, a comparative study was made of the urine from a normal kidney and that from a kidney with chronic, passive congestion in the same animal. By such a method it is possible to determine the effect *per se* of congestion on function.

In order to determine the function of each individual kidney it was, of course, necessary to collect the urine separately from the two sides. This was done by means of ureteral catheterization and was accomplished without discomfort to the dog. The animal was tied down on its back with comfortable holding straps and the ureteral catheters introduced in the manner constantly employed in the clinic.

In order to use the ordinary instruments for ureteral catheterization, large bitches are necessary. It would be possible to use comparatively small bitches if a single-barrelled catheterizing instrument large enough to carry a single No. 6 F. catheter were employed. In order, however, to catheterize both ureters, and at the same time carry catheters large enough to obturate them effectively, an instrument of at least 24 F. must be employed. The ureteral orifices are readily recognized in the bitch, and as a rule but little difficulty is encountered in entering them. But, owing to the curved course of the ureter in the vesical portion, passing the catheter higher than 2 cm. frequently requires considerable manipulation.

The Brown-Buerger catheterizing cystoscope No. 24 F. and No. 6 flute-end catheters were used in all of our experiments. When the internal orifices cannot be recognized readily, an injection of indigo carmin intramuscularly will, within a few minutes, clearly indicate their positions.

Bitch XVI.—Weight 18 kg.; showed a normal renal function as determined by functional tests. On January 18, a moderately tight band was applied about the left renal vein. Five days later the phthalein output was practically normal.

On February 9, both ureters were catheterized without anesthesia by the technic described above. The urine was obtained for twenty minute periods as follows:

TABLE 3.—URINE FROM BITCH XVI WITH BAND ON LEFT RENAL VEIN

FIRST PERIOD

Amount, c.c.		Sulphonephthalein, Per Cent.		Indigo Carmin, Per Cent.		Sp. Gr.		Urea, Gm.	
Left	Right	Left	Right	Left	Right	Left	Right	Left	Right
1.9	*1.0	63.3	100	59.0	100	1.010	1.030	0.0145	0.015

SECOND PERIOD

2.1	1.3	64.7	100	64.1	100	1.005	1.014	0.015	0.021

*The urine from the side having the smaller amount was diluted to the quantity of the other and then the two urines compared in the Duboseq colorimeter. The diluted urine of the right side was much more intensely colored than that of the left. In these tables the relative amount of dye substance of the side containing the smaller amount is expressed as percentage of the other.

TABLE 4.—URINARY FINDINGS IN BITCH XVI AFTER 300 C.C. WATER BY STOMACH TUBE

FIRST PERIOD

Urine c.c.		Sp. Gr.		Sulphonephthalein, Per Cent.		Indigo Carmin, Per Cent.		Sodium Chlorid, Per Cent.	
Left	Right	Left	Right	Left	Right	Left	Right	Left	Right
6.7	5.0	1.010	1.017	79.0	100	78	100	....	....

SECOND PERIOD

6.0	7.0	1.010	1.019	73.2	100	67	100	0.20	0.26

THIRD PERIOD

4.3	6.9	1.010	1.010	....	....	..	....	....	....

February 16, 300 c.c. of water was given by stomach tube one-half hour before catheters were in place. The right ureter was catheterized and the urine of the left side collected transvesically. The leakage was practically zero—not more than 0.5 c.c. for any period of twenty minutes.

On March 19, a phthalein test was made in the usual way, showing an output of 70 per cent. in one hour.

On April 3, the animal was killed by bleeding, owing to severe septic infection from a wound in the leg. The kidneys were found to be of about equal weight, 48 gm. each. The band was in place, exerting but moderate pressure on the vein, which was patent and free from thrombosis. The cut surface of the kidney did not exhibit marked evidence of congestion. There was thinning of the cortex in two or three areas at the lower pole, over which areas the capsule was found to be adherent. The capsular veins of the left kidney were markedly engorged and there was considerable enlargement of the vessels concerned in the collateral circulation.

Bitch XXII.—Weight 8 kg.; was subjected to operation on May 10 and a moderately tight band placed about the left renal vein. Ten days later the animal was in excellent condition, the phthalein output normal. Chlorbutanol was administered by stomach tube, the lower abdominal wall opened in the median line and the bladder exposed. The urethra was tied and the bladder sewed down the middle from the urethra to the apex of the bladder, with a fine needle and fine silk. A glass bladder-cannula was then placed in each half of the bladder. In order to start urinary secretion it was found necessary to inject 40 c.c. of 5 per cent. NaCl solution intravenously. The urine was then collected from each side separately for one hour periods. The results of these studies are tabulated below:

Table 5.—Urinary Findings in Bitch XXII With Band Around Left Renal Vein

FIRST PERIOD

Urine, c.c.		Sp. Gr.		Sulphone-phthalein, Per Cent.		Urea, Mg. Per c.c.		Indigo Carmin, Per Cent.		Lactose, Gm.		Carbol-fuchsin, Per Cent.	
Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right
16.7	14.0	1.013	1.009	83	100	4	10	..	...	..	..	..	...

Total phthalein output 46 per cent. for one hour.

SECOND PERIOD

16.4	15.0	1.034	1.035	..	...	10	15	..	...	1-1	1-1	..	...

THIRD PERIOD

10.5	12.4	1.031	1.028	..	...	..	..	93	100	..	..	..	...

FOURTH PERIOD

10.8	11.2	1.015	1.007	..	...	..	..	..	...	..	..	60	100

Total N. from 10 c.c. of mixed urine from left side, 0.0536 gm.
Total N. from 10 c.c. of mixed urine from right side, 0.0658 gm.

On opening the abdomen the left kidney appeared considerably larger than the right and a good collateral circulation had developed. In order to demonstrate that there was no communication between the two halves of the bladder, water was slowly injected into one half, and recovered through the corresponding catheter, without any flow from the other side. The animal was killed by bleeding. The right kidney weighed 25 gm. and the left 25.5 gm.

These experiments are interesting and instructive from several points of view. A greater excretion of urine has been encountered on the side where the venous return was obstructed in several observations which, in one case, extended over a period of weeks. *This bears out the contention of Schwarz as to the possibility of encountering increased urinary output with obstruction to venous return, and directly disproves the claims of Paneth and de Souza.* It shows, further, that even in the presence of the relative polyuria on the congested side that the per cent. of solids, as indicated by the phthalein, indigo-carmin, lactose, urea and salt content, is greater from the normal than from the congested side. The experiments further suggest that the water goes by preference through the slightly congested kidney, whereas the excretion of solids is considerably interfered with. The uniform relative excretion of the same dye on different occasions, as well as the parallelism of the excretion of different dyes at the same observation, is exceedingly striking. The truth of Albarran's claim, i. e., that with forced fluid the extra demand for secretion is responded to by the normal kidney, is demonstrated by the greater output of water from the right kidney in the second and third period of the first experiment. The excess from the right kidney began at the proper period at which the polyuria should appear. The fact that the water only, and not the salt, lactose, carbol-fuchsin, the indigo-carmin and phthalein, are increased is also significant.

BANDS ON THE AORTA BELOW LEVEL OF RENAL ARTERIES

A greater quantity of blood was directed through the kidney by cutting off to a considerable degree its escape from the aorta below. Moderately tight bands, which constricted the aorta to approximately half its normal diameter, were applied just above its bifurcation. This experiment alone was performed on one animal, combined with a nephrectomy on a second, and with nephrectomy and a band on the renal vein on the third. The following protocols indicate the results:

Birch XVI.—Weight 5.5 kg., operated on February 12. A fairly tight band was placed on the aorta below the renal arteries so that the vessel was decidedly larger above and smaller but still pulsated below the band.

February 13-16. Dog in excellent condition. Normal quantity of urine containing a few hyaline and granular casts. Phthalein and salt excreted normally; iodid delayed to seventy hours. Lactose delayed to seven hours.

February 27-28. Phthalein, salt, iodid and lactose all excreted normally. Animal in good condition. Here we have an entirely normal renal function.

March 4. Animal developed distemper and died.

Autopsy: Bronchopneumonia. No peritonitis. The aortic band is in place buried in fibrous tissue. The aorta is patent, standing out well above band, but is much smaller below. The kidneys are probably slightly enlarged, and combined weight 50 gm.; are dark blue in color.

Hyperemia, therefore, caused the appearance of casts in the urine, together with a delayed lactose and iodid output, which rapidly returned to normal.

Bitch IX.—Weight 7 kg.; had a right-sided nephrectomy and a tight band about the aorta just above its bifurcation, on February 17. On the following three days the animal was in poor condition, showing evidences of peritonitis. The urine output was rather small in amount, the phthalein and iodid normal, lactose delayed and salt poorly excreted. On the 23rd the animal was chloroformed. The autopsy revealed peritonitis and retroperitoneal abscesses. The band was found in place, the aorta enlarged above it. The kidney was dark, purplish-red in color, deeply engorged and weighed 45 gm. The capsule strips readily.

Dog XVIII.—Weight 9 kg.; March 4 had a right-sided nephrectomy performed, the kidney weighing 38.5 gm. A band was placed on the aorta just above its bifurcation, causing marked constriction, and a second band of moderate size was placed about the renal vein at its entrance into the vena cava.

March 5. Animal in good condition exhibiting a polyuria—1,000 c.c. output on 700 c.c. water intake. Urine contains a trace of albumin and a few hyaline casts, but no blood cells. The phthalein output is reduced to 29 per cent. Lactose delayed to seven hours; iodid normal. The salt is excreted poorly in low concentration, .09 per cent., yielding a total of .9 gm. on a 3 gm. intake.

March 6. Polyuria persists—900 c.c. urine on 700 c.c. water intake. Salt concentration low—0.11 per cent.

March 7. Phthalein output normal, 50 per cent. Polyuria 750 c.c. on 700 c.c. intake. Salt concentration is low—0.12 per cent.

March 8. Phthalein normal, lactose delayed—eight hours; iodid seventy-two hours. The fluid excretion was not noted.

March 11. Phthalein normal, 60 per cent. Animal shows signs of distemper developing. Urine contains a trace of albumin, but no casts or blood.

March 13. Animal died with symptoms of distemper. At autopsy the kidney was found intensely congested. Weight 60 gm. Both bands were in place and both vessels patent. An abscess containing about 5 c.c. of pus was found in the region of the aortic band. Some fibrinous peritonitis was also found.

This experiment is of peculiar interest on account of the occurrence of a definite persisting polyuria associated with venous obstruction, which coexists with an excessive amount of blood flowing into the kidney.

CONTROLS

It was considered desirable to see what effect on the renal function was produced by simple unilateral nephrectomy. The first dog, in addition to a right-sided nephrectomy, had the left renal vein isolated from the surrounding tissue just as is done in each of the experiments when the band is applied.

Dog XX.—Weight 6.9 kg.; nephrectomy performed on February 26.

February 27. Phthalein 57 per cent. Iodid eighty hours. Lactose eight hours +. Sodium chlorid excreted in good concentration.

March 18 and 19. Urine normal in quantity. No albumin or blood, an occasional hyaline cast. The phthalein output was normal, as was also the salt. The lactose was very slightly delayed—6½ hours; but the iodid was not excreted in less than seventy-two hours.

April 14. The phthalein, salt, iodid and lactose were absolutely normally excreted, and the urine itself was entirely normal.

Dog XXI.—Weight 5 kg., April 24. Right kidney removed; weight 17.8 gm.

April 25. Phthalein 38 per cent.; slightest trace of albumin, an occasional cast seen in centrifugalized specimen.

April 27. Phthalein normal—55 per cent. Lactose delayed seven hours, salt excretion somewhat delayed.

May 3 to 9. The salt, lactose and phthalein excretions are all normal, the only abnormal urinary feature being a very faint trace of albumin.

Simple one-sided nephrectomy in a healthy dog, therefore, causes but slight change in the renal function which is of short duration.

INCOAGULABLE NITROGEN OF THE BLOOD IN CHRONIC PASSIVE CONGESTION

In five cases of animals with a moderate degree of chronic passive congestion, and with relatively normal renal function, and in one with marked congestion, the incoagulable nitrogen of the blood was estimated. The technic employed was as follows: 10 c.c. of blood was withdrawn from the heart and placed in 115 c.c. of 95 per cent. alcohol to precipitate the albumin. This was filtered, and 100 c.c. of the filtrate evaporated to dryness. The total nitrogen of this residue, representing 8 c.c. of blood, was estimated by Kjeldahl's method. In the five nearly normal cases, the nitrogen was not increased above 0.50 gm. per liter of blood. In the dog with advanced congestion, the nitrogen was increased to 0.60 gm. per liter.

It can be concluded, therefore, that mild experimental chronic passive congestion in dogs does not produce an accumulation of incoagulable nitrogen in the blood.

HISTOLOGICAL STUDY

The histological study[52] of the kidneys removed at autopsy was made as follows: The kidneys were fixed in formaldehyd solution or Zenker's fluid, cut and stained with hematoxylin and eosin. The microscopic study in all cases revealed varying degrees of chronic passive congestion of all the vessels and capillaries. In certain of the cases there were foci of leukocytes or small abscesses. In one case there was considerable increase in connective tissue suggesting a chronic nephritis. Whether this was due or not to the congestion cannot be stated. On the whole, histologically, it seems that by this method, chronic passive congestion of varying intensity is produced without an accompanying chronic nephritis.

52. A further study of the histological changes following more prolonged chronic passive congestion is intended.

CONCLUSIONS

1. By the technic described it is possible to produce over short periods any grade of chronic passive congestion desired.

2. Slight experimental chronic passive congestion of the kidney is characterized by (a) a normal quantity of urine which contains a trace of albumin, intermittently a few hyaline and granular casts and occasionally a few red blood-cells; (b) the functional capacity varies but little from normal, since phthalein, salt and potassium iodid may be all normally excreted, while lactose excretion is but slightly delayed.

3. Moderate experimental passive congestion of the kidneys is characterized by (a) a fair amount of urine containing albumin, casts and frequently red blood-cells; (b) a total excretory capacity which is apparently not markedly decreased, since the phthalein excretion is usually normal. The excretion of salt is usually somewhat decreased, that of potassium iodid variable, that of lactose invariably delayed.

4. Marked experimental chronic passive congestion of the kidneys is characterized by (a) very scanty amounts of urine containing a large amount of albumin, casts and red blood-cells; (b) a much reduced functional capacity, since the phthalein, salt and lactose excretions are markedly delayed, as is also frequently that of iodid.

5. Albuminuria is almost a constant accompaniment of experimental passive congestion, casts are usually present, and red blood-cells appear if the congestion is of any considerable degree.

6. Lactose excretion is the first to become affected by increasing grades of chronic passive congestion; then the excretion of salt and iodid, and lastly, that of phthalein.

7. The phthalein test gives the most reliable information concerning the degree of renal insufficiency in experimental chronic passive congestion. Marked delay in the excretion of lactose, iodid and salt has, indeed, been encountered in animals showing a normal phthalein output. These animals were, however, apparently in good general condition, while subsequent events showed that they remained in good condition. On the other hand, a marked decrease in phthalein excretion has invariably been associated with the development of clinical manifestations, indicating renal inadequacy and followed by death. The phthalein test is, therefore, the test of greatest prognostic importance in chronic passive congestion.

8. Lactose, while of least value in revealing the degree of involvement of renal function in experimental chronic passive congestion of the kidney, is of the greatest value in detecting its existence. It is, therefore, of these tests that of greatest diagnostic, but of least prognostic value.

9. The excretion of potassium iodid is usually prolonged in experimental chronic passive congestion of the kidney. The time of elimination of this drug is, however, so variable that the test proves practically valueless in this connection.

10. The excretion of sodium chlorid is usually decreased where moderate or marked experimental passive congestion is present.

11. Partial obstruction to venous return through the renal vein is not invariably associated with decreased urinary secretion. In an apparently normal unanesthetized or anesthetized (chlorbutanol) animal which has partial occlusion of one renal vein only, more urine is sometimes excreted from the congested kidney, while the solids are excreted in greater concentration from the normal side.

12. Where gradual progressive obstruction to the renal vein occurs, the development of a collateral circulation is of great importance in maintaining the functional capacity of the kidney since an efficient renal function may be encountered when the venous return from the kidney is entirely collateral. On the other hand, ligation of collateral vessels, simultaneously with a moderate degree of obstruction to the renal vein, usually results in renal inefficiency and death.

13. An excessive flow of blood through the kidney simultaneously with an obstruction to its outflow may be followed by polyuria.

14. Mild grades of experimental chronic passive congestion are not associated with the accumulation of incoagulable nitrogen in the blood.

15. Varying degrees of chronic passive congestion which are unassociated with nephritis are produced by the above-described procedures.