tors. To obstruct biologic science by a general prohibition of experiments on animals, or to obstruct any other science by proscribing approved methods, is to sin against the light and to turn back the hands of progress. No thoughtful person is likely seriously to commend such a course.

The question as to the moral effect of the practice of animal experimentation on persons who engage in it or observe it is difficult to dispose of effectively. Undoubtedly most persons feel a squeamishness about their first operation on an animal, which later on they lose, and the critic of the practice is likely to interpret this fact as meaning that the practitioner has become callous and indifferent to suffering. I see no reason to deny that this result may occasionally occur. But in every reputable laboratory the usages are as humane as the circumstances will permit, anesthesia is the universal practice, and it is perfectly certain that the total amount of suffering which the animals undergo is negligible in comparison with that which confronts most of them in a state of nature. Moreover, a loss of the original squeamishness is by no means synonymous with a loss of practical tender-heartedness. It may act simply to insure a steadier and prompter hand, with a corresponding decrease in the length of time occupied by the operation and an increased chance of a favorable outcome. It should be remembered, too, that the selfish interests of the operator almost inevitably and invariably make it to his advantage that the animal should suffer as little as possible, in order that its vigor and vitality may be at the maximum. It should also be added that, just as many surgeons are most tender-hearted, despite their apparent indifference to the suffering of their patients, so many men who do a large amount of operating on animals are keenly alive to the welfare of their animals. But even if all experimenters were hardened by their work into a disregard of animal pain, society might still pronounce the value of their results to outweigh this drawback. In the larger view which looks to the ultimate welfare of society as a whole, such men are among its most valuable humanitarian members, whatever their personal attitude toward the animals with which they work.

In conclusion, then, it may be said that we find no obstacle to the practice of animal experimentation in any intuitive moral convictions, nor in the traditional morality of our own race. When we try to estimate its justification in terms of its results, we find that it has precisely the same kind of warrant as that which attaches to all our great social enterprises, in each of which we are ready to sacrifice a lesser good for a greater good, and are willing to encounter a moderate evil in order to escape a greater evil. For the sentimentalist, to whom all thought of gratuitous suffering is abhorrent, probably no argument can ever avail to justify certain forms of experimental procedure. On the other hand, to the man familiar with the revolutionary advances in science and medicine which have originated in the experimental use of animals its condemnation seems the last word of a pernicious insanity. To the great public, representing the intermediary between these extremes, it is to be hoped that a calm and discriminating judgment may be vouchsafed, and one which takes into account all angles of the case. In the long run we have confidence in the integrity of our public judgments on moral issues. In a case so serious as this, we need the highest degree of deliberation, sobriety, and intelligence.

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THE FUNCTIONAL ACTIVITIES OF THE KIDNEYS *

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This article consists of a report of the amount of work which I have done, tending to show the value or the lack of value of the tests which are being used at the present time to show the permeability of the kidney.

My attention was originally called to the value of this work by Dr. Robert Holmes Greene, in 1904. The result of some of the work done by me at that time and for some time subsequent was published in his text-book.[1]

I need hardly mention the various procedures which have been attempted in the past and by which it has been sought to determine the functional activity of the kidney, such as the estimation of the amount of urea, phosphates, chlorides, quantity of urine, cryoscopy, or the presence or absence of casts and albumin.

OLDER TESTS OF RENAL FUNCTION

Thirty-three grams of urea was estimated to be excreted by a healthy individual in twenty-four hours, or about 2 per cent. of the quantity of urine passed, and this has been considered an index of the normal renal function. Urea in the urine is dependent largely on the proteid element of the diet. As is well known, meat diet will increase the elimination of urea and a non-proteid diet will diminish it, but at no time will a non-proteid diet result in the total absence of urea, as a certain quantity of urea is indirectly derived from tissue metabolism. Munzer and Kaufman in 1894 proved that urea was also formed in the liver and to a small extent in other organs. It also seems evident that renal disease may indirectly produce a variable output of urea by increasing or diminishing metabolism or interfering with assimilation. Fever in any renal disease will cause increased metabolism with a corresponding increase in the quantity of urea excreted. Licci[2] states that diminished quantity of urea in renal diseases is entirely due to disturbances of the nitrogenous metabolism, and that renal permeability to urea is increased rather than diminished. The same is corroborated by Maragliano.[3] From such observations as these it is evident that the quantity of urea which comes to the kidney for removal must be a variable one, depending on absorption, tissue metabolism, diet, hepatic and other glandular action, and any of these processes may be affected by disease. All this tends to show that we cannot rely on the inconstant supply of urea to the kidney for elimination in estimating its functional activity.

Neither can we determine the functional activity of the kidneys by the quantitative estimation of chlorids excreted by the kidneys, as it is a well-known fact that a constant content of sodium chlorid is maintained in the tissues and fluids of the body and that its principal supply comes from the food; but we also know that the absorption of sodium chlorid stimulates metabolism whether the kidneys are healthy or diseased. Chlorids are diminished in the urine in fevers to a large extent and increased in the urine when the temperature falls.

* Read before the American Urological Association, Atlantic City, June 7, 1909.

1. Greene, R. H., and Brooks, H.: Diseases of the Genitourinary Organs and the Kidney, Saunders, New York, 1908.
2. Licci: Policlinico, 1901, p. 400.
3. Maragliano: Clin. med. ital., 1902, p. 437.

Mohr[4] has demonstrated that there is an excess of chlorids in the urine in chronic nephritis and that there is a marked decrease of chlorid in acute nephritis. Researches of Albarran[5] tend to show that the quantity of chlorids passed in twenty-four hours does not furnish any indication of the functional activity of the kidney.

The amount of uric acid and phosphates in the urine does not give any reliable information as to the functional activity of the kidney.

When we consider how many factors influence it, the quantity of urine in itself would not be considered as a valuable index to kidney permeability. Work done by Albarran recently, however, has shown that studies of the renal function by the ingestion of large quantities of fluid may be, in certain cases, an index to kidney permeability. At some future time I hope to have the pleasure of presenting my own work recently carried on along this line. I do consider, however, for a rough test, the twenty-four-hour urine with the specific gravity in order to estimate the quantity of solids as of some value in determining chronic kidney disease.

Cryoscopy is determination of the molecular concentration of the urine. This method of von Karonyi is a very ingenious one of determining the functional activity of the kidneys, but von Karonyi himself says that large quantities of water consumed by patients will have a great effect on the freezing-point of the urine, even to diminish it to 1 per cent. or less. Also a very low molecular concentration of the urine will be found in the various forms of anemia. In order to get the best results from this method it is necessary to cryoscope blood and urine both, and, as it takes three drams of blood, it is a test which, while it can be carried out under certain conditions, it will be found impracticable for general use.

It is hardly necessary for me to point out how rapidly the older methods of urinary examinations are passing into disuse. While the presence or absence of casts and albumin may in certain cases bear some relation to the state of the kidney or kidneys, we feel that no such corelation exists at present, as was formerly the generally accepted opinion. That this is true has been very well demonstrated by the work of such able observers as Richard Cabot[6] of Boston, Kapsammer[7] and many others. To be sure, while such factors as albumin and casts may not always be indicative of a diseased state of the kidney, their constant presence in large amounts might indicate some abnormal state of the body.

TECHNIC AND RESULTS OF ELIMINATION TESTS

Having briefly mentioned some of the various methods of estimating the functional activity of the kidney, let us now consider some of those which are being used at the present time in connection with ureter catheterization, and with which I have been experimenting for more than five years. The principle of these methods consists in introducing foreign substances into the human body and noting the time of their elimination by the kidneys. The principle is by no means a new one, as Dr. Hahn in 1820 noticed the odor of violets in the urine after the ingestion of turpentine, and also the absence of the characteristic odor in the urine after eating asparagus in patients suffering from nephritis. My first experiments were with methylene blue and phloridzin; then, three years later, I used indigo carmine. The methylene blue test was introduced by Achard in 1893, in the diagnosis of kidney diseases. Klemperer[8] was the first to apply phloridzin in clinical medicine, in 1896. Achard and Delamere used phloridzin for testing renal function in 1899.

The following is the technic of the tests:

Methylene Blue.—Catheterization of both ureters and intramuscular injection into the gluteal region of 15 minims of a 5 per cent. solution.

Phloridzin.—Catheterization of ureters and subcutaneous injection of 15 minims (1 to 200) freshly prepared.

Indigo Carmine.—Catheterization of ureters and intramuscular injection of 20 c.c of 4 per cent. solution.

I began my experiments with phloridzin and methylene blue in twenty-five perfectly healthy subjects, the experiments being conducted very thoroughly, with the results that the phloridzin gave the sugar reaction in eighteen to twenty-two minutes and the methylene blue tinged the urine in twenty-six to thirty minutes after the injection. After having a standard time for the appearance of the blue and the sugar in the urine in healthy kidneys, I began to apply the same tests to diseased kidneys, and noted the variations in time. The following is a list of kidney diseases in which the tests were conducted:

Interstitial Nephritis.—Twenty-eight cases. Delayed excretion was noticed in twenty-three cases, the two kidneys being alike. In two cases there was a delay in the time limit on the right side; normal time limit on the left. In three cases there was a delay in the time limit on the left side, normal time limit on the right.

Parenchymatous Nephritis.—Nineteen cases. There was a time delay in both kidneys.

Tuberculous Kidneys.—Eight cases. In two there was delay on the right side; normal on the left. In six there was delay on both sides.

Malignant Nephritis.—Four cases. In three cases there was delay on the left side; normal on the right. In one there was delay on the right side; normal on the left.

Calculous Nephritis.—Twenty-one cases. In twelve there was unilateral delay; in nine, delay from both sides.

Hydronephrosis.—Five cases. In four there was a delay from left side and in one from the right kidney.

Pyonephrosis.—Nine cases. In six cases there was delay from the left side; right side normal. In three cases there was delay from the right side; left side normal.

Most of the above cases came with a clinical diagnosis from other physicians.

In applying these tests I found phloridzin to be the most reliable; the time delay of the glycosuria represented the degree of renal inactivity or the degree of structural changes in the kidney.

The methylene blue test, although good in most cases, failed to tinge the urine in three cases after four hours' observation and in two cases of parenchymatous nephritis it tinged the urine in twelve minutes after injection.

I continued my investigations in twenty cases of diseased kidney with indigo carmine and verified it with phloridzin, and while the phloridzin gave the sugar reaction in the proper time, the indigo carmine acted like methylene blue. The indigo carmine usually tinges the urine in about five minutes, which time I take as a standard in testing the functional activity of the kidney, but, as indigo carmine is decolorized by alkaline puru-

4. Mohr: Ztschr. klin. Med., 1904, p. 331.
5. Albarran: Exploration des fonctions rénales, 1905.
6. Cabot, Richard C.: Clinical Examination of Urine; A Critical Study of Common Methods, THE JOURNAL A. M. A., 1905, xliv, 837.
7. Kapsammer: Erkrankungen der Niere, Vienna and Leipsic, 1907, p. 28.
8. Klemperer: Verhandl. d. ver. f. inn. Med. zu Berlin, 1896.

lent urine, we may be misled in the application of this test.

I will not attempt to enumerate the above cases with their histories, but will say that most of them were under observation of skillful physicians who based their diagnosis on the clinical symptoms in connection with urine analysis made in the best laboratories.

Despite the diagnosis, I found by these tests nine subjects of supposed interstitial nephritis, who responded perfectly to the standard time limit of excretion of sugar and also the methylene blue test, and four subjects of supposed parenchymatous nephritis who showed perfect functional activity of the kidneys.

Autopsies were performed in five of the last named cases; ten microscopic sections of each kidney were made and studied carefully. No structural changes of the kidneys were evident, although three of the cases had been diagnosed as parenchymatous nephritis and two as interstitial nephritis during life.

All of the five cases showed by the phloridzin and methylene blue perfect renal activity, in spite of the clinical symptoms and urine analysis.

One of the three patients supposed to have parenchymatous nephritis died from large gumma in the fourth ventricle of the brain, one of pneumonia and one of tetanus.

Of the two patients with supposed interstitial nephritis, one died of pneumonia and the other of abscess of liver. From these facts we can see that we should not place too much reliance on the clinical symptoms and urine analysis in diagnosing kidney diseases.

I have had other cases in which albumin and casts were present in the urine. One very old man, who had been refused life insurance forty-two years before, was examined, with the result that both specimens of urine had the same specific gravity and the same amount of albumin and casts and both tests showed perfect functional activity of the kidneys. In these cases, however, outside the evidence furnished by the urine, there were no clinical manifestations of disease.

I have within the past four years, with the aid of my colleague, Dr. H. J. Friedman, examined 2,200 specimens of urine; the patients had not consulted me as to their kidney condition, but were being treated for various ailments, with the following results: Albumin was found in 85 cases; albumin and casts, in 62 cases; transient diabetes, in 12 cases, and true diabetes, in 9 cases.

Of these 85 patients having albumin only, I tested 40, 38 of whom showed perfect renal function and 2 imperfect. Of the 62 patients with albumin and casts, I tested 20, 12 showed perfect renal function; 8 imperfect.

Very curiously, in four cases of transient diabetes, on catheterization of both ureters I found sugar coming from one kidney, and when the temporary glycosuria had disappeared I tested the kidneys with indigo carmine and phloridzin and found imperfect renal function in the kidney which gave the glycosuria. The explanation of this curious phenomenon I am unable to give.

All nine patients with permanent diabetes were tested. Sugar was found coming from both kidneys and the functional activity of both kidneys was greatly diminished. In one case of permanent diabetes the indigo carmine tinged the urine in one hour and a quarter and the methylene blue in two hours and twelve minutes.

CONCLUSIONS

My studies lead me to the following conclusions:

1. They confirm the views of those who believe that little value can be placed in the presence of casts and albumin alone, as evidence of kidney disease, for my statistics show that one in every fifteen persons walking the streets has albumin or albumin and casts in the urine.

2. The most accurate test for permeability of the kidneys is phloridzin in connection with ureter catheterization, although it is sometimes a very tedious process. Next of importance is the indigo carmine, which is a very quick test, and last, methylene blue.

3. The relationship of transient glycosuria to impaired kidney function when found in one kidney is deserving of study and investigation.

4. These investigations tend to show that the diagnosis of kidney disease by chemical tests and clinical symptoms in most instances is not borne out by the examination with phloridzin, methylene blue and indigo carmine.

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ACQUIRED INTESTINAL DIVERTICULA

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Diverticula of the intestines are without doubt more frequent in occurrence and more important from a clinical standpoint than is generally realized. Although statistics on this matter do not exist to any extent, yet it is evident from the few figures available that this condition is by no means rare.

By diverticula are understood localized dilatations of the intestinal wall. These are naturally subdivided into two varieties, the congenital and the acquired, the former being particularly well recognized. Meckel's diverticulum and the appendix (if it be so regarded) have been studied for many years; their embryology, anatomy, physiology and pathology have been dealt with voluminously. Consequently they will not be discussed here.

It is the acquired variety, however, that is at present attracting much attention, its importance having been understood only within the past few years. This type is supposed to occur toward adult life, as it has not been described as having been found in childhood.

These acquired diverticula might again be subdivided into the true and false, according to whether or not all the layers of the intestinal wall are present. This division does not seem, however, to be of any special value. If any tissue is lacking it is that of the muscular coat, and, as will be shown, this is largely the result of mechanical conditions.

The diverticula are as a rule numerous, varying in number from three or four to several dozen. In size there are the greatest differences, from those of almost microscopic dimensions to others several centimeters in diameter. In the majority of instances they are flask-shaped, the opening into the intestine being less than the diameter of the expanded portion. This construction has a very distinct bearing on the clinical importance of the condition.

The favorite site is at the mesenteric attachment, the dilatation lying between the layers of the mesentery. They do not, however, always occur at that point, as cases have been reported in which they were found along the free border of the intestine.

Although found most commonly in and adjacent to the sigmoid flexure, yet they may occur anywhere along the alimentary tract, beginning with the duodenum.