RENAL COUNTERBALANCE

By FRANK HINMAN,* M. D., *San Francisco*

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Renal atrophy has been almost universally regarded by pathologists as degenerative in type and due to bacterial, chemical or other toxins, producing the well-recognized pathologic condition of cloudy, swelling, and fatty amyloid and hyaline degeneration. But there is also a well-recognized type of atrophy, which may be termed biologic, due to inanition, pressure or inactivity, and it is possible experimentally to produce what would seem to be an inactivity renal atrophy.

For clinical purposes, one may distinguish four groups of renal tissue relative to the adjustments that may follow surgery or disease.

Readjustments between these four types of tissue lead to four types of counterbalance. The normal renal tissue may show a complete unilateral counterbalance. Readjustments among portions which have an equal qualitative ability to respond instance a co-operative type of counterbalance, whereas readjustments between portions of unequal qualitative ability, irrespective of quantity mass, result in a competitive type of counterbalance.

DISCUSSION *by T. Addis, San Francisco; Walter V. Brem, Los Angeles.*

THERE are two facts which form the basis of renal counterbalance. These are that the renal mass is divided into two equal portions, a right and left kidney, and that injury or disease is usually circumscribed and rarely diffuse and uniform, even when bilateral, and the majority of renal injuries are unilateral. By counterbalance is meant an attempt on the part of the less injured or uninjured portion to take over the work of the more injured portion.

EXPERIMENTAL CONSIDERATION

In the experimental study of renal counterbalance there are four conditions for study: First, renal reserve; second, renal hypertrophy; third, renal atrophy; and, fourth, renal counterbalance.

Renal Reserve—There has been some confusion as to what constitutes renal reserve, and it is a popular conception that the remaining kidney, if normal, is able to immediately take over the extra burden occasioned by removal of its mate. Upon closer consideration this is found to be only partially true, and renal reserve is seen to be largely potential and to have an anatomic and functional correlation. It is a fact that the renal mass of different species of animals is proportional to the body weight. Small animals have small kidneys and large animals have relatively large kidneys. This is the anatomic reserve. But it has been definitely determined by a great many different observers that, by partial resections, the normal renal mass may be reduced by one-third, or even one-quarter, and the animal survive. This constitutes the minimal amount of renal mass compatible with life, but this one-third or one-quarter portion has undergone remarkable hypertrophic changes. The functional reserve, on the other hand, has been experimentally tested in a way by a study of the function of the remaining healthy kidney after unilateral nephrectomy. We have found that this kidney is at first unable to completely make good the loss of its mate, and during the first five or six days there is a relative renal insufficiency. This initial insufficiency can be demonstrated also by results following ligature of one branch of the renal artery. However, these insufficiencies are not proportional to the amount of renal mass thrown out of action, and in either case the insufficiency is very quickly removed by an anatomical hypertrophy of the renal mass remaining. Renal reserve is thus seen to be of two types—the native reserve, which is the normal physiologic response to stimulation as possessed by all glands and organs, and an acquired reserve, which is the repair of growth or compensation, in response to overstimulation.

Renal Hypertrophy—When one attempts to consider the changes incidental to renal hypertrophy or repair, a thorough understanding of the structure of the kidney is necessary, and it is at once also necessary to distinguish between renal hypertrophy and renal hyperplasia. Studies of structure have shown that growth by hyperplasia or new tissue formation may occur in young animals and man for considerable periods after birth; in human kidneys, up to the fifth or sixth year. And it is also necessary to distinguish, in a consideration of renal hypertrophy between natural growth and compensatory growth. Obviously, the kidney of a child is not as large as after full growth has been reached, nor are the glomeruli and tubules that make up such a kidney relatively as large. All experimental studies on animals must, therefore, take into consideration these two facts. In an adult animal's kidney it has been found, by careful measurements, that growth concerns two structures of the kidney particularly, namely, the glomerulus and the proximal convoluted tubular area, and it has also been estimated that from twenty to thirty days usually are required for the major amount of this growth to occur. When one attempts to apply these anatomic considerations to studies of compensatory repair, this distinction of hypertrophy and hyperplasia has its clinical counterpart. The congenital types of renal compensation, as instanced in the solitary and infantile kidney, are examples of renal hyperplasia, whereas in the clinically acquired types in which repair is due to hypertrophy there are two groups distinguishable—in one the change is by a diffuse mass hypertrophy, in the other by a circumscribed or group hypertrophy.

As an example of mass hypertrophy, is the commonly observed unilateral growth of one kidney following removal or loss of its mate. Some interesting experiments have demonstrated that this mass type of hypertrophy may be bilateral. A typical bilateral mass hypertrophy has been produced by the author by transplantation of one ureter into the duodenum, which throws out, so far as actual excretion is con-

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cerned, the work of one kidney, but, in view of the fact that this kidney continues to receive the same blood supply, it is found to undergo a compensatory hypertrophy hand in hand with that of its mate which actually does all of the renal work. As seen below, however, this initial hypertrophy is not permanent.

The second group in which hypertrophy is circumscribed and not diffuse is of more clinical importance in a consideration of renal counterbalance, and this type of growth may be experimentally tested by comparison of results following various types of repair following relief of ureteral obstruction in hydronephrosis. In one group, in which after a period of complete ureteral block the ureter is transplanted to the bladder and at the same time the opposite kidney removed, it is found that the animal will survive only where the ureteral block has been for a period of two weeks or less.

Even more interesting, relative to counterbalance, are the results that follow transplantation of a completely blocked ureter to the bladder when the opposite kidney is undisturbed. If the ureteral block producing the hydronephrosis has been for a short period, say two weeks, the opposite kidney has not had sufficient time to undergo complete compensatory repair and good stimulation for repair of the hydronephrotic side will be present, whereas if the block has been for longer periods, say sixty days, the complete compensation of the opposite kidney removes any stimulus or need for repair on the hydronephrotic side. It is found, experimentally, that all of these repair hydronephroses, whether of two weeks or sixty days, when the opposite kidney is undisturbed, show early evidences of an attempt to repair. But the point of particular interest in these two types of experiments is that there is found to be a great difference between the condition of this repair, irrespective of short or long obstruction, if examined months or years after the ureteral transplantation. Even as short ureteral block as two weeks will have produced injury which is sufficient, in view of the healthy compensatory mate, to lead to its complete atrophy even after successful ureterocystoneostomy, upon examination one or two years later, and this leads up to the consideration of the third factor in renal counterbalance, namely, renal atrophy.

Renal Atrophy—Renal atrophy has been almost universally regarded by pathologists as degenerative in type and due to bacterial, chemical or other toxins, producing the well-recognized pathologic condition of cloudy swelling and fatty, amyloid and hyaline degeneration. But there is also a well-recognized type of atrophy, which may be termed biologic, due to inanition, pressure or inactivity, and it is possible experimentally to produce what would seem to be an inactivity renal atrophy. The late atrophy, for instance, of an earlier repair hydronephrosis, as has just been mentioned above, is a type of atrophy from insufficient stimulation. Another example of a disuse atrophy may be furnished by the experiment mentioned above of ureteroduodenostomy, in which it was shown that in the early period there was a complete compensatory hypertrophy of the kidney, whose ureter has been transplanted into the duodenum, if examined within a relatively short time after the transplantation, thirty to sixty days, but that, if the animal is allowed to survive before being sacrificed for a period of one and a half to two years, this initial hypertrophy has completely disappeared and the same kidney will be found to be a small, almost functionless, or completely atrophic kidney. The explanation of this late period atrophy of an early period hypertrophy after ureteroduodenostomy is not altogether clear, but it would seem reasonable that it results from a gradually diminishing stimulation or loss of work. In a successful experiment, infection has not occurred to produce atrophy, there has been no back pressure or ureteral obstruction to cause it, and it is doubtful if one might presuppose toxic injury from ascension of the contents of the duodenum into the pelvis of the kidney to cause it. On the other hand, it is a well-known fact that kidney activity is not continuous and there are periods of inhibition or lessened activity and, in this experiment, whenever the kidney, whose ureter is transplanted into the duodenum, takes a rest period this influences in no way the accumulation of waste substances in the blood, in view of the fact that the opposite kidney is always doing all the work of actual excretion. Therefore, such rest periods do not lead to any hyperactivity on its part subsequently. Any rest period of the compensatory kidney on the opposite side, however, must be paid for by it by an increase of activity later. This difference in burden of response and the greater predisposition of the transplanted kidney to inhibition would account for the gradual loss of stimulation on one side and its progressive and late atrophy, an example, therefore, of disuse atrophy.

Renal Counterbalance—Such experiments as outlined above, with respect to hypertrpohy and atrophy, give an indication of the process of renal equilibrium after renal injury, and the occurrence of this counterbalance is beautifully illustrated by the experiment referred to above, in which the opposite compensatory kidney is gradually injured by a partial ureteral obstruction so as to throw a gradually increasing stimulus and demand for work on the repair hydronephrotic side. It is found by such an experiment that an hydronephrosis of thirty or forty days complete ureteral block is capable, under this gradual stimulation, of a complete compensatory repair itself, so that in the course of one or two years, when its mate has undergone a complete hydronephrotic atrophy as a result of partial obstruction of its ureter, the thirty or forty-day hydronephrosis, whose ureter has been transplanted to the bladder, has taken over total renal work and maintains normally total function.

CLINICAL CONSIDERATION

In the application of these experimental considerations, the clinical problem is made difficult and uncertain because of our continued ignorance of the mechanism of renal activity and because of the deficiency in our tests of renal function. All tests of function are purely empirical and they have the added defect of indicating renal work for the period of the test and that period only. They give no indi-

cation of what the kidney has done or will do. They are also an extremely uncertain guide as to anatomic conditions and, because of the incidence of inhibition and hyperpermeability, are frequently inaccurate. Renal inhibition is of frequent occurrence and may be reflex, chemical or the result of some type of back pressure. From a clinical standpoint, one speaks of total function and relative function, and tests of excretion are particularly of value as indication of relative function when controlled for factors of inhibition, hyperpermeability and the technical errors of leakage, etc. Better and more reliable tests, as well as specific tests of renal function, are very much to be desired, but not until the mechanism of renal activity itself is better understood will these tests be forthcoming.

Clinical consideration of co-operative and competitive types of counterbalance, as outlined above in the experimental consideration, is particularly of value preliminary to all renal surgery, and such a consideration is worth much more than that of relative function alone because it takes into account the anatomic conditions at the time and the probable anatomic conditions that may be expected to result afterwards. Consideration of counterbalance is valuable in unilateral disease because, when taken in conjunction with surgical risk, it renders renal surgery for unilateral disease much more conservative and under much better control. There are not apt to be so many disappointments after attempts to preserve the unilaterally injured kidney, and the application of consideration of counterbalance is of even greater value preliminary to surgery in bilateral renal disease in which conservation is always indicated.

For clinical purposes one may distinguish four groups of renal tissue relative to the adjustments that may follow surgery or disease. In the first group is normal renal tissue which is known to have a good reserve power and good repair ability so that, with any demand for more work placed on it, an hypertrophy will occur, except under some unusual conditions of inhibition. In the second group is renal tissue which has already undergone hypertrophic changes but which may be expected, under proper stimulation, to undergo additional hypertrophy. In the third group is the diseased or injured renal portion which has a lowered reserve and a diminished ability to repair but which, with relief of injury and proper stimulation, may show considerable repair; and, finally, in the fourth group is the type of renal tissue, called hypoplastic, which has no reserve power or ability to grow, as instanced by the infantile type of kidney.

Readjustments between these four types of tissue lead to four types of counterbalance. The normal renal tissue may show (1) a complete unilateral counterbalance. Readjustments among portions which have an equal qualitative ability to respond instance (2) a co-operative type of counterbalance, whereas readjustments between portions of unequal qualititative ability, irrespective of quantity of mass, result in (3) a competitive type of counterbalance. Failure of response may give (4) renal decompensation.

DISCUSSION

T. ADDIS, M. D. (Stanford Medical School, San Francisco)—This paper is a brief and incomplete summary of work which has extended over many years. It is an investigation which represents the first persistent and systematic attempt to determine the relation of the process of compensatory hypertrophy to the special problems of the genito-urinary surgeon. This is in itself a significant fact. For a long time operations have been performed without a knowledge of the principles which these experiments reveal, and as a consequence many mistakes have been made, each one of them a commentary on the slow and painful growth of knowledge in the hands of so-called "practical" men. As is the case with all really fundamental clinical work, it is based on a fresh first-hand study of anatomy and physiology and leaves us with fresh problems to solve.

WALTER V. BREM, M. D. (Pacific Mutual Building, Los Angeles)—A discussion of a paper reporting original research is always difficult and usually gratuitous. However, one cannot refrain from commending the spirit that urges one to seek further knowledge, and it is especially inspiring to know that research can be done even by a doctor in the midst of a large and busy practice such as that of Dr. Hinman. Time and again I have heard this feature of Hinman's work spoken of with admiration.

Hinman, in this research, is attempting to clear up the fundamental principles of kidney damage, repair and compensation, and it will go far toward aiding in rational treatment of kidney disease.

BILHARZIA DISEASE—ITS CURE BY TARTAR EMETIC

By W. B. PALAMOUNTAIN,* M. D., *Oakland*

INTRODUCTORY EDITORIAL NOTE

Doctor Palamountain's report forms another link in the chain of evidence tending to prove that a specific cure for another important disease has been found. It is an important disease, from which millions of people constantly suffer. They are for the most part residents of the tropics, but the rapid increase in travel is making a knowledge of so-called tropical medicine an essential of every physician's education everywhere.

As Doctor Palamountain says, his patient's condition would have been promptly diagnosed by any educated physician practicing in countries where such infections are common.

Every physician everywhere should always make a low amplification microscopic examination of every specimen of urine. There are many useful lessons to be learned from such a routine.—EDITOR.

DISCUSSION *by Herbert Gunn, San Francisco; John V. Barrow, Los Angeles; Marshall Chipman Cheney, San Francisco.*

IN FEBRUARY, 1916, I was consulted by an Englishman, age 34, who complained of frequent and painful urination, blood and pus in the urine, and blood at stools.

His health as a child had been good, and when 19 years old he entered the South African Constabulary, where he served three years and was never sick. At the age of 23 he first noticed an irritation in the bladder region which he described as a desire to scratch. At 25 he first noticed a tinge of blood in his urine for a short time. Occasionally, during the next six years he noticed some blood in the urine, but was never troubled much by it.

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