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HELD AT
WASHINGTON, D. C.

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Mi n u t e s.

The ninth triennial session of the Congress of American Physicians and Surgeons was held in the Assembly Room of the New Willard Hotel in Washington, D. C., on May 6th and 7th, 1913, according to the programme as ordered by the Executive Committee.

The first meeting was called to order at 2.30 p. m., Tuesday, May 6th, by the President, Dr. William C. Gorgas of Ancon, Canal Zone, who announced the subject for discussion to be “On the Study of Renal Function,” and stated that the first paper would be by Dr. Henry A. Christian of Boston. He was followed by Dr. Leonard G. Rowntree of Baltimore and by Dr. Theodore C. Janeway of New York City. These papers were followed by discussions by Dr. Hugh Cabot of Boston, Dr. George Dock of St. Louis, Dr. John T. Geraghty of Baltimore, and Dr. William S. Thayer of Baltimore.

At 8.00 p. m. the Congress assembled in the Assembly Room to listen to the address of the President. The meeting was called to order by the first Vice-President. Dr. Gorgas then delivered his address on “Sanitation at Panama as it Relates to Sanitation in the Tropics Generally.”

On the following day the meeting was called to order at 3.00 p. m. by the President, Dr. William C. Gorgas. The subject to be considered was “On the Development of Tissues in Vitro.” Papers were read by Dr. Ross G. Harrison of Yale University, New Haven, on “The Life of Tissues Outside the Organism from the Embryological Standpoint”; by Dr. Montrose T. Burrows of Cornell University Medical College, New York, on “The Life Tissues Outside the Organism from the Physiological Standpoint,” and by Dr. Robert A. Lambert of the College of Physicians and Surgeons, Columbia University, New York, on “The Life of Tissues Outside the Organism from the Pathological Standpoint.” These papers were discussed by Dr. Leo Loeb of St. Louis, and by Dr. Warren H. Lewis of Baltimore.

Adjournment.
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By Invitation of the Executive Committee.

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Dr. Edward M. Talbot, Washington, D. C.
Dr. James E. Tally, Philadelphia, Pennsylvania.
Dr. Henry Bascom Thomas, Chicago, Illinois.
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Dr. Parker Symns, Fall River, Massachusetts.
Dr. Martin J. Symnott, Riverside, California.
Dr. Edward M. Talbot, Ashville, North Carolina.
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Dr. James E. Tally, Wilkes-Barre, Pennsylvania.
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Dr. Edward M. Talbot, Baltimore, Maryland.
RECAPITULATION.

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Total membership of Congress .......... 2069
Guests and Visitors ................... 216

Total attendance ..................... 1071
ON THE STUDY OF RENAL FUNCTION: THE RELATION OF FUNCTIONAL TESTS TO PATHOLOGICAL DIAGNOSIS.

HENRY A. CHRISTIAN, M.D.,
Boston, Massachusetts.

The topic selected for discussion this afternoon, renal function, is one of interest to both physician and surgeon, for it deals with the means of measuring an excretory activity, necessary to life, of an organ subject to pathological changes in character diffuse, requiring medical management, or focal, demanding surgical operation. In either event, it is important to know, how well do the kidneys, combined or singly, function, and what has been the effect on function of remedial measures, for on this depends the prospects of continued life, or the risk of surgical treatment.

The problem of renal function has been one long under discussion and observation. The kidneys pouring their excretion, the urine, quite directly into the external world lend themselves readily to certain forms of study of their function, namely observation of changes occurring in the urine affecting the color, the reaction, the concentration, the character and quantity of various normal constituents, and the presence, qualitative and quantitative, of substances not found normally in the urine. At first crudely observed, these observations decade by decade have been made with increasing refinements of method.

Medical men in one way or another have long noted urinary variations, and from them have drawn inferences as to the health of the individual as well as inferences as to morphological changes in the kidneys. Much of the earlier work has concerned itself in the attempt to correlate urinary findings with renal morphology, to infer on the part of the clinician what lesions the kidney will reveal to the pathologist. Refinement of urinary analysis led to classification of variations in the urine, which in conjunction with observation of the patient's condition seemed to justify the diagnosis of different renal lesions. The pathologists, with improvements in technical methods, divided and subdivided renal lesions until a
very considerable knowledge of renal pathology was at hand for
correlation with clinical conditions. Much was discovered by these
methods, but the clinician, though able frequently to infer correctly
the anatomical condition of the kidney, realized that there was often
a considerable discrepancy between expected findings and observed
conditions of the kidney; the clinician, though often correct in his
diagnosis, too often failed and was confronted at autopsy by unex-
pected renal lesions. Even though the clinicians, for example,
simplified the pathologist's morphological classification of types of
nephritis to three groups, acute nephritis, chronic parenchymatous
nephritis, and chronic interstitial nephritis, still mistakes in diagnosis
were all too frequent and knowledge of that very important toxic
manifestation of nephritis, uremia, has remained disappointingly
slight, while prognosis in these cases was still more baffling. The
pathologist investigated the end result in most cases; the clinician
sought to harmonize a diagnosis of an end result with disturbances
in function due to a lesion progressing at an unknown rate to this
end result. Is it any reason for surprise that under these circum-
stances discrepancies between clinical and pathological diagnoses
occurred?

This condition of affairs has led in recent years to renewed
investigation, and the introduction of many new methods of
determining renal function with the hope of correlating more
satisfactorily functional disturbances with pathological lesions. It
is primarily with these functional tests that we are concerned to-day,
but by way of introduction it seems desirable to speak first of
certain relations of these tests to the diagnosis of pathological
lesions, and to leave to my colleagues the discussion of the relation
of tests of renal function to prognosis and treatment.

In the present period of renal study the experimental work of
Schlager and his associates in the medical clinic of Professor
Romberg at Tübingen has been of great importance. They pro-
duced in rabbits acute renal lesions by injecting various substances
known to cause injury to the kidneys. Instead of merely observing
the morphological changes so produced at different intervals follow-
ing the injections or in relation to doses of varying size, they
investigated the effect of these substances on renal function.

They recognized the close relation existing between renal blood
supply and general circulation, and the mutual effects of these on
blood pressure. They did not lose sight of the interrelation between
vascular phenomena and function of renal epithelium with the
dependence of diuresis on all of these factors. Consequently in
their animals they observed general blood pressure, renal volume,
diuresis, urinary variations, and renal histology. Instead of study-
ing merely the changes produced in these factors by the renal
irritants used, for this would have involved the uncertainty arising
from an inability to measure several of these factors both before
the renal irritant was given and again at the proper interval after
its use, they compared the response of the kidney and circulation to
various forms of stimuli. This involved the previous determination
of the response in normal animals to such stimuli as tobacco smoke
in the nostrils (sensory stimulus) and the effects of injections of
adrenalin, salt, caffèin and phloridzin. Having, so to speak, stand-
ardized these responses, they sought by them, in addition to the
methods of the direct observation of the urine mentioned above,
to measure the disturbance produced by various toxic substances,
chromium, uranium, mercuric chloride, cantharidin, arsenic, and
diphtheria toxin.

The morphological effects of these substances had already been
studied quite extensively by pathologists, and it was known that
some produced very striking degenerative lesions of renal epithel-
ium, while others had very much less effect on renal epithelium, and
yet all led to the appearance of albumen and casts, not infrequently
blood in the urine. With regard to renal function, Schlayer and
his associates found that these toxic substances produced quite
different effects. Some of them, as chromium and mercuric chloride,
affecting primarily the renal tubules and had little effect on the
vascular apparatus (tubular nephritis), while others, such as can-
tharidin and arsenic, primarily caused vascular disturbances with
little effect on the renal tubules (vascular nephritis). In the case
of other toxic substances such as diphtheria toxin and uranium
there was a condition produced at certain stages resembling in part
tubular nephritis, in part a vascular nephritis, with in general
the tubular type in the early stages and a more marked vascular
disturbance in the later stages. In the case of uranium there is a
stage in which, though the renal vessels still react to stimuli, there
is a sudden cessation of diuresis. It is particularly interesting
that uranium, thus differing as shown by functional tests from other
toxic substances, is the one substance which in animals frequently
produces cædema, thus more closely simulating human nephritis.
In experimental toxic nephritis it was shown by Schlayer and his associates that the albumen may be excreted by either glomeruli or tubules; that cast formation occurs only in the tubules and that severe vascular disturbance causes decreased diuresis, though the reverse may not be true. Of the various observations made on rabbits, all may be applied in modified form to man except those on the volume changes in the kidney. However, vascular response is a very important factor in distinguishing functional types of nephritis, and so it became necessary to determine whether the excretion of different substances might not be used as a measure of the efficiency of the vascular or tubular apparatus to replace observations on renal volume which could not be made in man.

Though there was and still is considerable difference of opinion as to the physiological activity of various portions of the complicated renal structure, it is generally believed that certain normal constituents of the urine are the result of activity of definite portions of the renal structure. If this be true, then a defective elimination of one of these constituents indicates functional inefficiency of a certain portion of the renal structure, and so determines the localization of a functional, if not anatomical lesion. In the same way certain substances not normal constituents of the body were known to be excreted by the kidney without producing renal damage. Selective excretory activity of renal structures for certain foreign substances then might be utilized as further localizing tests of functional activity.

With the methods already used as functional tests of renal activity and the knowledge at hand of the types of functional disturbances produced by various toxic substances, variations in excretion of substances both natural and foreign to the body might be tested in relation to vascular and tubular types of toxic nephritis. This Schlayer and his associates did, using the excretion of water and lactose as a measure of glomerular activity and sodium chloride and potassium iodide as a measure of tubular activity. They found in experimental toxic nephritis in rabbits a close agreement between the excretion of these substances and the respective types of nephritis as determined by their earlier observations, thus confirming their views as to the place of excretion of these substances. This will serve to illustrate the method of using the selective excretory activity of portions of the kidney as a measure of forms of renal lesion and this method is not difficult of application to man.
RELATION OF FUNCTIONAL TESTS TO PATHOLOGICAL DIAGNOSIS.

However, as will be shown later, the place of excretion of these various substances as given by Schlayer is not accepted by all.

Does the utilization of the method of testing renal function by measuring the excretory activity of the kidney for different substances throw much light on renal pathology in man? In relation to diagnosis of pathological lesions functional tests of the kidney might be expected to yield information on two points; first, are the kidneys diseased; second, what type of pathological lesion do they show? Do the functional tests yield these results?

Schlayer and his associates found in acute nephritis predominantly of the vascular type, a delayed excretion of lactose and a normal elimination of potassium iodide, a disturbance of water excretion and a normal salt elimination. They point out that oliguria does not necessarily occur in a vascular nephritis; in fact polyuria is more common but indicates a less marked vascular disturbance. Low concentration of the urine may be the result of tubular insufficiency, a failure to excrete salts (tubular hyposthenuria), or the result of increased glomerular excretion of water, vascular hypersensitiveness causing vascular hyposthenuria. Increased water elimination may exist with decreased lactose excretion, indicating a selective, excretory activity within the glomerulus. According to them vascular hypersensitiveness is a valuable index of vascular disturbance, and its persistence indicates a failure of the process to heal. In chronic vascular nephritis, in which they include the atrophied kidney of chronic interstitial nephritis, they find the same excretory relations of water, lactose, salt and potassium iodide. In the chronic forms, as in the acute, polyuria or oliguria may exist, depending on increased or decreased vascular sensitiveness. In neither acute nor chronic types is the amount of urine any measure of the kidneys' functional capacity.

They claim by these methods to be able to distinguish definitely certain types of acute and chronic nephritis (tubular nephritis, vascular nephritis), and to find their distinguishing characteristics to be quite sharply demarcated. If this claim is sustained, a definite advance in our knowledge of human renal lesions has been made. Of the cases studied by Schlayer and his associates, but one died and had a post-mortem examination. Consequently it cannot be said that their cases have added any definite information that will help in anticipating during life what the microscopic study of the kidney will reveal after death. Still, if these methods give a sharply
outlined functional diagnosis, even without leading to a satisfactory anatomical diagnosis, a distinct gain has been made. What has been the experience of other observers using these tests?

Von Monakow, working in Müller's clinic in Munich, found, contrary to the observations of Schlayer, a delayed potassium iodide excretion with no disturbance of salt excretion. Furthermore, duration of potassium iodide excretion did not seem closely related to severity of renal disturbance. In four patients histological examination of the kidneys was made; here von Monakow, in agreement with Schlayer, found salt excretion to be normal or delayed according to whether the tubular epithelium showed no degenerative lesions or was definitely degenerated. Potassium iodide excretion was most delayed in the two cases in which a glomerular lesion was most prominent, which was not in agreement with Schlayer's claims. Nitrogen elimination, tested by giving weighed amounts of urea, von Monakow found delayed in cases with glomerular lesions. Contrary to Schlayer, von Monakow considers disturbance of water excretion dependent on tubular degeneration.

On the other hand in a group of cases studied by Conzen at Köln, five came to autopsy. These were cases of chronic interstitial nephritis with heart hypertrophy and in them Conzen found the functional tests of Schlayer in agreement with the histological findings, for they indicated a vascular lesion and extensive glomerular changes were found.

Rowntree and Fitz consider that lactose is an index of the vascular function of the kidney, thus agreeing with Schlayer, though in another paper they show that in the frog, at least, lactose may be excreted by the tubules. On the other hand potassium iodide, which Schlayer believes to be retarded in excretion by tubular lesions, they find retarded also in simple chronic passive congestion and so of no value in distinguishing renal from cardio-renal cases.

Rowntree and Fitz are unable to make the sharply marked distinctions between vascular, vasculo-tubular, tubulo-vascular, and tubular nephritis made by Schlayer and his associates on the basis of their functional tests. They agree with Schlayer that the mechanism of the excretion of lactose differs from that of salt and potassium iodide. Few of their cases came to autopsy and the kidneys were not studied with especial reference to correlating functional disturbances with pathological lesions.
Nonnenbruch studied the excretory relations of salt, water, lactose, and potassium iodide in passive congestion. He found these relations were often disturbed in passive congestion, but unlike cases of nephritis the disturbance was dependent on the excretion of water, and when this returned to normal the other substances were excreted normally. In this respect there was a distinct difference between function in passive congestion and nephritis.

The several investigations cited will serve as examples of this method of renal study. It is evident that different observers have not obtained constant results, and opinions as to locus of excretion of the several substances are not in accord. So far too few cases are recorded with these functional tests and subsequent histological examination of the kidneys to justify final conclusions, but such as are recorded do not seem to indicate that any very close correlation between function and anatomical lesion can be made on the basis of rate of excretion of such substances as lactose, potassium iodide, salt and water.

Perhaps this is not to be expected, for Schlayer and his associates pointed out that in experimental animals there was no anatomical lesion demonstrable in the kidneys to explain differences in vascular response to stimuli. Takayasu studied particularly the glomeruli and found but slight anatomical change to explain demonstrated disturbances in function. On the other hand we have found quite commonly in uranium nephritis in rabbits glomerular lesions which appear to have been overlooked by Schlayer and his associates. Still it is undoubtedly true that in the functional studies of experimental toxic nephritis anatomical lesions do not parallel closely functional disturbances and so from these studies it was to be anticipated that in man there would continue to be some discrepancies between clinical diagnosis, even though based on functional tests and demonstrable structural changes in the kidney. These particular functional tests have yielded valuable information, but so far they have failed to serve as an adequate basis of diagnosis of type of renal lesions. They have, however, given much aid in determining whether, in a given case, a nephritic lesion actually exists or not. When applied to our clinical work they will undoubtedly save us often from the mistake of not diagnosing a renal lesion when such exists, even though they do not tell us of what type that lesion is.
A slightly different method of studying renal function has been employed by Volhard in distinguishing during life four forms of atrophied kidney (Schrumpföföer) in correspondence with two groups described anatomically by Jores. This method consists in measuring the ability of the kidney to excrete large amounts of water in a relatively short time, and to excrete large amounts of solids with small amounts of water. The normal kidney can excrete 1½ litres of water in four hours, and on the other hand on a dry diet can concentrate the urine to a specific gravity of 1025-1030. By applying these methods along with observations of blood pressure and heart hypertrophy, and study of symptoms and other physical signs, Volhard distinguishes a red granular kidney or primary atrophic kidney, a secondarily atrophied kidney, a mixed form, and an atrophied kidney without heart hypertrophy.

Frey has reported from Gerhardt's clinic at Basel somewhat similar studies of 78 cases of chronic nephritis, 43 of which came to autopsy. In these cases he is able to make quite definite groupings according to clinical observations and functional tests which are similar to, though not identical with the groups made by Volhard. When these subdivisions, however, are put to the test of anatomical study of the kidney, the agreement is not very close, so that Frey is of the opinion that it is very difficult to make clinical subdivisions of the atrophied kidney which will correspond with anatomical subdivisions made on the basis of histological study of the kidney. A similar view had been taken by Krehl in discussing Volhard's original paper.

Phenolsulphonephthalein seems to play a similar rôle. It is a most valuable aid in determining any diminution in total renal function, but it does not seem to help much in diagnosing what type of nephritis exists. Rowntree and Geraghty found that in frogs phenolsulphonephthalein could be excreted by the tubules. The frog is used for these experiments because glomerular function can be excluded, owing to glomeruli having a vascular supply distinct from the tubules. Other observations indicated that in man phenolsulphonephthalein is mainly excreted by the tubules, but this localization of excretion does not seem to be selective enough for use in diagnosis of the type of pathological lesion in a case of nephritis.

In all the methods discussed up to now, renal function has been tested by measuring the ability of the kidney to excrete certain
substances which are supposed to be excreted by definite portions of the renal structure. In making anatomical studies of the human kidney to determine how far renal function may be correlated with the pathological lesion, it has not been possible to apply to the human kidney methods similar to the vital staining used in experimental animals. These vital stains have shown in animals a very great amount of differentiation in the epithelium lining the tubules and a very considerable degree of specificity of different toxic substances for these several kinds of renal epithelium. This limitation in method of studying the human kidney may explain some of the failure to correlate morphology with function.

Another important source of error may be in our failure to allow for variations in excretion not dependent on structural disturbances, hardly dependent on functional lesions, but due to variations in fatigue in the kidneys of different individuals, or of the same individual on different days. Amato and Flaggella have shown that in normal rabbits variations in excretion of those fed with salt and water are due to renal fatigue. Schlayer has pointed out that the injured kidney is abnormally easily fatigued. This fact opens to the above methods of testing renal function, the possibility of numerous errors in interpretation of results, even though fatigue itself may serve as a functional test of renal insufficiency.

The quantitative determination of the non-proteid nitrogen in the blood of nephritics has received more attention as a means of gaining knowledge of uremia than as a method of diagnosing the pathological lesion of the kidney. Strauss found that rest-nitrogen showed more variation in nephritis and uremia than did the molecular concentration of the blood as determined by measurements of the freezing point. Ascoli, Umber and others investigated phases of this problem with similar results. Recently Hohlweg has claimed that marked nitrogen retention was an index of renal insufficiency rather than a sign of uremia; if there was a high degree of nitrogen retention in the blood, it indicated a fatal issue with or without uremia; in the uremic stage nitrogen retention might not be excessive and then, according to Hohlweg, the prognosis was relatively good. Strauss in reply, points out that the term uremia is indefinite, and part of the difference between his views and those of Hohlweg are merely matters of terminology. Uremia, both agree, may occur without marked nitrogen retention. This is usually in cases with marked œdema or where the uremia is of the convulsive
or eclamptic type. In the former, hydremia reduces the amount of nitrogen in the blood, and in the latter the symptoms conceivably may be due to other factors than those producing the ordinary type of uremia.

Recently, Folin has devised methods of determining non-proteid nitrogen and other substances in blood and urine which require the use of only very small quantities, in the case of blood 2-5 cc. These methods make it possible to quantitate nitrogen bodies in the blood of patients with far greater ease and freedom than was possible by earlier methods that necessitated using relatively large quantities of blood. Folin and his associates have found, like the previous observers, a considerable nitrogen retention in cases of nephritis. Folin, Karsner and Denis in experimental acute nephritis produced in the cat by uranium, chromate and cantharidin, have found an accumulation of nitrogen in the blood. This is more marked in those forms of experimental nephritis of the vascular type than in the tubular type. Anatomical study shows distinct glomerular involvement in the cats with greatest retention. In the rabbit, Frothingham, Fitz, Folin and Denis have found a similar nitrogen retention in experimental uranium nephritis. They compared the nitrogen retention with the phthalein excretion and found the two methods of testing functional renal activity to give quite comparable results. As might be expected, phthalein excretion decreased quickly while a longer time was needed for nitrogen retention to take place. Similarly the nitrogen content of the blood remained high after phthalein excretion had risen toward the normal level. I have found, in conjunction with Folin, high figures for non-proteid nitrogen in rabbits with severe uranium nephritis and these are particularly high in rabbits that in addition have received diuretin. In other studies in our laboratory we have found that diuretin and other diuretic drugs exert an unfavorable influence on severe acute experimental nephritis expressed in the shortening of the life of the animals and the severity of the lesion found on histological study. It is especially in these animals with nephritis, to which diuretic drugs have been given, that marked glomerular lesions such as have been described by myself and O'Hare occur.

Most of these observers have found a greater average nitrogen retention in cases of interstitial nephritis than in cases of parenchymatous nephritis. As already pointed out, von Monakow found nitrogen elimination following doses of urea was delayed in cases
with glomerular lesions. Experimental work as cited above harmonizes with the observations of von Monakow, for nitrogen retention appears to be most marked in nephritis of the vascular and tubulo-vascular type of Schlayer's classification. However, in Hohlweg's cases the averages for interstitial and parenchymatous nephritis are not very different and individual cases may show no difference, so it cannot be claimed from this work that any great help has been given in the diagnosis of types of renal lesion. However, finding a distinct nitrogen retention is often of very great help in distinguishing cases in which the symptoms are chiefly of renal origin from cases in which they have other causes, the very frequent association of high degrees of nitrogen retention with uremic conditions may be of the greatest diagnostic help in patients in whom it is doubtful whether cerebral manifestations are of renal origin or not.

Wohlgemuth's method of determining variations in urinary diastase has not been applied in the observation of cases with any special view of diagnosis of the type of renal lesion. The estimation of the indican in the blood as suggested by Obermayer and Popper has been discussed as an indication of uremia rather than as a diagnostic test. Variations in urinary acidity have been observed too, more as a measure of certain functional disturbances brought about by nephritis but not dependent on any particular form of anatomical lesion.

Early in this paper it was stated that in the diagnosis of pathologic lesions of the kidney functional tests might be expected to yield information on two points; first, are the kidneys diseased; second, what type of pathological lesion do they show? Review of the methods of testing renal function by measuring the excretion of salt, water, lactose, potassium iodide, and sulphonephthalein, by measuring the retention of non-proteid nitrogen in the blood, by the determination of diastase in the urine, by determining the presence of indican in the blood, or by estimating urinary acidity, show that very great aid is given in determining clinically whether the kidneys are diseased, but distinctly less help has come in answering the second query, what type of pathological lesion do the kidneys show. As in all forms of clinical diagnosis, not the single test but many yield the data on which diagnosis must be based. In this sense these functional tests have yielded new data and a discriminating evaluation of this new data along with a consideration of
data furnished by other methods of examining our patients already
long in use, justify us in making diagnoses of renal condition with
an increased certainty. We can expect fewer failures in renal
diagnosis than before we had these functional tests, but so long as
microscopic study fails to yield a demonstrable anatomical change
to correspond with all observed functional variations, so long will
we remain unable to make in advance an exact anatomical diagnosis
which in most cases will prove to be correct when the pathologist
examines the kidneys.

RELATION OF FUNCTIONAL TESTS TO PATHOLOGICAL DIAGNOSIS.


27. A Study of the Therapeutic Value of a Diuretic (Theobromine sodium salicylate or Diuretin) in Acute Experimental Nephritis. Christian and O'Hare, Archives of Int. Med., 1913, II, 517.


THE STUDY OF RENAL FUNCTION: ITS BEARING ON TREATMENT.

THEODORE C. JANEWAY, M.D.,
New York, N. Y.

No advance gained in the knowledge of any group of diseases can be without significance for treatment. This is particularly true when new methods of study increase our understanding of the complex functional disturbances and afford more precise means for their differentiation. On the other hand, the possible gain to practical therapeutics depends primarily upon the existence of means for favorably influencing disordered function. In the domain of chronic diseases of obscure causation, which make up so large a part of the subject matter of internal medicine, diagnostic skill, inadequate though it be, usually runs far ahead of remedial measures.

Of no diseases is this more true than of the medical diseases of the kidney. Rowntree has shown how the added precision in functional diagnosis, gained by such a measure as the sulphonephthalein test, has made the results of renal surgery more certain. From a broad standpoint, therefore, this functional test, and the less satisfactory ones which it has replaced, have contributed greatly to the effectiveness of treatment. But the medical diseases of the kidney, which we group under the contentious term nephritis, do not permit of so easy an attack after recognition. It is not conceivable that even the earliest discovery of functional disorder should lead to brilliant therapeutic results when the underlying lesions are essentially progressive, though we may hope to safeguard the damaged organ and retard to some extent the development of advanced anatomical changes. Only studies in the etiology of chronic disease and the discovery of means of prevention can ever make internal medicine as cheerful and therapeutically satisfying as surgery. At present, the internist cannot shift the responsibility for his "inoperable cases" to any other convenient shoulders.
Nevertheless, as the result of the recent studies of renal function, the internal treatment of renal disease has made definite progress along two lines:

(1) The study of experimental nephritis in animals has made clear the existence of isolated disturbances in the excretion of individual constituents of the urine, and the existence of definite types of abnormal reaction of the diseased kidney to stimuli. These have been found to have their counterparts in human nephritis.

(2) The accurate study of the salt and water exchanges in human nephritis and their relations to œdema, has resulted in a precise and scientific method of treatment which is highly effective in certain types of renal disease.

The study of disturbances in the excretion of individual urinary constituents in human nephritis as a guide to treatment is not of recent date. As early as 1881, Fleischer\(^1\) conducted elaborate observations. Von Noorden and his pupils have been especially active in this field, and as a result of the facts which they accumulated, von Noorden\(^2\) has formulated fairly definite rules for protective treatment in the various clinical types of nephritis. His most important practical contribution is the management of the water intake and his demonstration that the conventional milk diet for nephritis, while empirically successful, was irrational, because of excessive fluid volume and protein content. The diet which he has worked out for acute nephritis, with low protein content but ample fat and carbohydrate, of 1500 c.c. bulk, has been of great practical value.

The recent studies of Schlayer\(^3\) and his co-workers, especially Hedinger and Takayasu, have approached the problems of the functions of the diseased kidney from a more fundamental standpoint. They have observed in animals with various types of

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experimental toxic nephritis, the disturbances in the excretion of water and sodium chloride among the normal urinary constituents, and of potassium iodide and lactose as foreign test substances. They have studied equally the changes in the general blood pressure and the responses of the kidney vessels to various stimuli, including substances producing diuresis and excretion. This work they have more recently extended to the study of selected cases of human nephritis. While the results in the main bear upon the underlying problems of the pathology of nephritis and the sub-division of diseased kidneys into functionally separable types, as Christian has already set forth, nevertheless, some of their results must now be reckoned with in the treatment of human nephritis. In the first place, they have shown that, both in animals and in man, polyuria is an evidence of slight or early disturbance of the kidney vessels, whereas oliguria represents a much more severe type of functional damage. The polyuria of vascular irritability will result in the excretion of a urine having low specific gravity and low sodium chloride concentration, even when the ability of the kidney to excrete salt is not itself disturbed, as determined by the response to added sodium chloride, as well as by the high concentration in portions of the daily urine. They name this "vascular hypos-thenuria," and it must be sharply differentiated from the hyposthenuria due to primary disturbance in the ability to excrete sodium chloride. This discrimination is of real importance in the management of clinical nephritis.

Closely allied to this state of irritability of the vessels is their susceptibility to fatigue. Schlayer, in his paper before the Kongress für innere Medizin in 1912\textsuperscript{4}, demonstrated how the excessive use of a common diuretic of our daily food, ordinary salt, which always leads to increased output of water in the normal kidney, in the diseased kidney may produce rapid diminution of diuresis. A sharp restriction in the salt intake may then be followed by increasing outputs, both of water and salt. He made similar observations with the purin diuretics. Mosenthal and Schlayer (personal communication) have subsequently studied this in detail in experimental toxic nephritis. Their results, which will appear shortly, make it clear that abnormal susceptibility to fatigue is highly characteristic of the vascular system of the diseased kidney. This fact, like

\textsuperscript{4} Schlayer, Ueber die Ermüdbarkeit der Nierenfunktion, xxix Kongress f. inn. Med., 1912.
Diuresis of four days' duration from a single dose of caffeine, gr. 1, in a patient with chronic nephritis and myocardial insufficiency. The solid black columns represent the intake of water, and the hatched columns the output of urine, each in c. c. for each 24 hours.
the allied phenomenon of vascular over-irritability, must never be neglected in treatment. It justifies the already established custom of Romberg's Tübingen clinic, where the caffein diuretics were never given continuously, but intermittently, and in comparatively small doses. Our practical experience with these drugs at the Presbyterian Hospital bears out Schlayer's thesis. It is sometimes possible to obtain diuresis persisting for forty-eight hours or more from so small a dose as a single grain of caffein. When a diuretic of this type is indicated, as a rule we use theocin, giving three doses of 3 grains each for a single day, and not repeating until the diuresis resulting therefrom has ceased. Failure to respond to these diuretics should always indicate the need for at first diminishing, rather than increasing, the dose. The initial dosage of these drugs should always be small, because of the possibility of constriction resulting, rather than the desired dilatation. The response of the kidney vessels to digitalis seems to follow somewhat the same laws. Gottlieb and Magnus, Jonescu and Loewi, Kasztan and Fahrenkamp have shown definite selective action for the digitalis bodies, the arterioles of the kidney being dilated, while those of the intestine are constricted by small doses. Increase in the dose leads to general vasoconstriction, in which the kidney shares. Hedinger has published some experiments which seem to indicate a diuretic effect from digitalis in human nephritis without the least associated cardiac insufficiency. He is inclined to view this as evidence of increased susceptibility of the kidney arterioles, similar to their over-response to water, salt, and the purin drugs. Digitalis then becomes a possible pure renal diuretic.

While perhaps wholly speculative as yet, it is of interest to recall the fact that, following the lead of Jores and of Aschoff, there has been a general return by pathologists to the old view of Gull and Sutton that the primary contracted kidney, that type of kidney


disease in which vascular irritability and the tendency to polyuria are most marked, is primarily a disease of the arterioles; that this disease of the arterioles is by no means limited to the kidney, but is widespread, the kidney participating in it now to a greater, now to a lesser extent. There is a tendency, which I have already discussed elsewhere, to consider the most characteristic symptom of this general arteriolar disease, high blood pressure, as associated with or dependent upon abnormal irritability of the diseased arterioles generally and especially in the splanchnic circulation. Inasmuch as such a drug as digitalis will produce dilatation of the kidney vessels and constriction of the remaining splanchnic vessels, it seems not impossible that polyuria and hypertension are in their fundamental pathogenesis identical; that both are exaggerations of the normal vascular response in the organs concerned, under the influence of a disease whose functional expression is vascular over-irritability and whose anatomical expression is the arteriolar lesion described by Jores.

In the treatment of chronic nephritis of this type, von Noorden has always insisted upon the danger of abusing water. He urged this precaution in order to safeguard the heart from the bad effects of overfilling the blood vessels. Schlayer's work at least suggests that the constant overstimulation of the kidney by so apparently harmless a diuretic as water may entail danger to the integrity of its local vascular functions.

The overuse of salt clearly falls into this category\(^1\) and the French observers have insisted on the reality of increase in blood pressure and in uraemic symptoms from this cause, with corresponding improvement on a salt-poor regimen. In a number of cases I have convinced myself that, even in non-oedematous patients, restriction of the salt intake was one factor in the lowering of the blood pressure brought about by hospital treatment. In such patients, however, I have seen oliguria result from too protracted salt starvation.

In these vascular types of nephritis, caution in the use of the common beverages, coffee and tea, is likewise suggested. Hedinger\(^8\) has advised testing out individual nephritics with reference to their

\(^1\) See Widal and Javal, p. 41, La Cure de Déchloruration, Paris, 1906, J. B. Baillière et fils.

functional response to the various diuretic substances contained in ordinary diets. He uses kidney test meals and collects the urine at two-hour intervals throughout the test day. The observation of water output, specific gravity, the total output of sodium chloride and its percentage concentration, with comparison of the day and the night urines, gave interesting differences in the cases he studied. Normal persons responded in a typical way to the diuretic influence of the meal. Some patients with nephritis evidenced a striking over-response, while others of an advanced grade did not respond at all. The latter patients showed nocturnal polyuria. This method seems especially fitted to guide us in the intelligent dietetic treatment of patients with chronic nephritis.

Von Monakow has studied the response to water by means of a water test day, on which the patient took double the quantity of water contained in the regular diet. Such water tests are most important guides to treatment, especially in the convalescent stage of acute nephritis, but it scarcely seems necessary to make them very schematic, provided the intake and output are always definitely known. I should like here to call attention to the necessity for absolute uniformity in the salt intake when testing the excretion of water, and similarly the need for careful study of the relation between water and sodium chloride in making salt tests.

The study of the excretion of nitrogenous substances has also been carried on by von Monakow, who used urea in twenty gram doses added to a fixed diet, by Widal, who compared the blood urea with the protein intake, and by many others. The results in this field it is scarcely necessary to discuss from the therapeutic standpoint, apart from the obvious precaution of enforcing physiological economy of protein on general principles, as our means for combating nitrogen retention are conspicuous by their absence. I am convinced that the observation of the uncoagulable nitrogen of the blood, even by such simple methods as used by Widal in the estimation of the blood urea, is of great importance prognostically, but does not yet help us to make the outlook any less grave. In the same way, the sulphonephthalein test, while of the greatest prognostic value, cannot serve in any way as a guide to treatment. In chronic passive congestion of the kidney, however, it may frequently afford a most useful measure of the degree of improvement.

in kidney function during treatment. The same considerations hold good for Wohlgemuth’s diastase tests. Geylein’s observations in my wards have shown, as a rule, a considerable parallelism between it and the phthalein output.

The treatment of oedema in nephritis is much more satisfactory. The functional studies which have resulted thus happily have been of a somewhat different order from the foregoing. The observations of Widal and of Achard, brought together in the admirable little monograph of Widal and Javal, La Cure de Déchloruration, have put a simple and usually effective weapon against renal dropsy into the hands of every practitioner. The salt-poor diet is the result primarily of Widal’s observations on the strict parallelism between ingested NaCl and body weight in a nephritic with obstinate oedema. By reducing the sodium chloride of the diet to one and one-half grams a day he was able to free his patient completely from oedema. On then adding salt, he brought about first a gain in weight without evident oedema; then, if the salt were continued, the reappearance of oedema, which in turn was promptly absorbed when the salt intake was again reduced to a minimum. Subsequently this method of “demineralization” was extended to the treatment of other types of oedema, sometimes with success, and to other forms of renal disturbance in which its rationale is not so clear. In the treatment of the oedematous types of subacute and chronic nephritis, however, it remains the most effective measure.

Schlayer and Takayasu’s studies of salt excretion indicate that this occurs predominantly through the tubular epithelium. Von Monakow’s studies of human nephritis confirm this. Extreme diminution of sodium chloride excretion may exist with slight damage to the other functions of the kidney, except the secretion of water. Among the test substances used, potassium iodide parallels the sodium chloride most closely, though in a review of 114 cases of renal and cardiac disease at the Presbyterian Hospital, in which we have followed various functional tests, a delayed potassium iodide excretion has occurred in non-oedematous cases of nephritis.


Effect of NaCl intake upon urine volume of a patient who at autopsy showed extreme atherosclerotic, contracted kidneys, who had continued a salt-free diet for himself for six weeks previous. Note during the period of 1 gram NaCl intakes, the marked oliguria transformed by the addition of 6 grams of NaCl daily to polyuria, by 4 grams daily to normal outputs. Note corresponding with this the fixation of specific gravity and of NaCl concentration.
Effect of salt-poor diet in subacute nephritis. Note the simultaneous increase in urine volume and both absolute and per cent. of NaCl excretion after absorption of oedema began, with return of greatly delayed potassium iodide excretion to normal. The curve on the upper portion of the chart gives the specific gravity, and on the lower the NaCl concentration in percentages.
with a normal total and percentage salt output. Schlayer believes that the iodide excretion suffers earlier than the sodium chloride.

With the restoration of kidney function and the absorption of oedema, we have observed the return to normal of greatly delayed potassium iodide excretion. A most striking example of this was a patient with so-called chronic parenchymatous nephritis, who had had some swelling for eighteen months and marked oedema for two months. Her general anasarca was uninfluenced by salt-poor diet for five weeks. The salt outputs were below two grams a day, often below one gram. Extra water was not excreted, nor was any of an added ten grams of sodium chloride. Potassium iodide required 144 hours before its disappearance from the urine. With persistence in the salt-poor diet and hot packs, rapid absorption of the oedema followed. Sometimes as much as fifteen grams of sodium chloride were swept out in twenty-four hours, and the weight dropped forty-six pounds in thirty-one days. With this, the time required for the excretion of potassium iodide was reduced to seventy-two hours. The other functional tests were almost normal, the sulphonephthalein excretion being forty-nine per cent at the worst. Now, one year after the patient's discharge, she remains absolutely free from any evidence of nephritis, either urinary or cardio-vascular; an added ten grams of salt is excreted promptly, and the potassium iodide elimination is complete in less than forty-eight hours. I consider the potassium iodide test as giving an interesting side-light upon kidney function and its restoration in these cases, rather than as a guide to treatment.

What constitutes normal elimination time depends largely upon the test employed. Schlayer, using the Sandow test, considers sixty hours normal. Von Monakow, who tests with starch paste and nitric acid, makes forty-four hours the upper limit. We have found the latter test much more satisfactory, and I believe that few normal individuals continue to excrete amounts of iodide recognizable by this test for more than thirty-six hours. Faint traces are sometimes detected for a surprising length of time by the Sandow test.

The one essential guide to treatment, as Widal's studies have shown, is the absolute salt balance. It is immaterial practically, though highly important theoretically, whether the cause of the salt retention be in the kidneys or in the general tissues. For the purposes of this discussion, therefore, I shall omit further mention
of the underlying problem of oedema or the reverse problem of salt retention without oedema. Salt and water are retained, and the oedema is to a large extent dependent upon this fact. The graphic record of daily salt intake and output, with the weight curve, permits of exact knowledge concerning the degree of salt retention. The management of the salt intake in such cases of renal oedema is altogether analogous to the management of the carbohydrate intake in mild diabetics. As long as oedema persists, the salt of the diet should be kept at a minimum. After the absorption of oedema, the ability to excrete added salt should be tested occasionally, and the intake increased correspondingly as the excretory function is restored. By the exact estimation of sodium chloride tolerance and the adjustment of intake at a point below the ability of the kidney to excrete salt, chronic cases may be kept free from oedema and its attendant discomforts over long periods of time, even where functional recovery is not complete.

At the same time, the management of the water balance demands equal attention. This is of special importance in acute nephritis, as von Noorden has shown. Intelligent care is possible only with the use of graphic records of water and of salt intakes and outputs. The best charts, I believe, are such as Schlayer uses, with columns in different colors. The relation between intake and output for both substances is far more important than the absolute amounts. Not the least contribution which the study of renal function has made to the treatment of nephritis is its method of visualizing the actual response of the kidney to our therapeutic measures from day to day.

ON THE STUDY OF RENAL FUNCTION: THE PROGNOSTIC VALUE OF STUDIES OF RENAL FUNCTION.

L. G. ROWNTREE, M.D.,
Baltimore, Md.

Despite the increased light shed upon medicine generally by science, the aphorism of Hippocrates holds true to-day, "Experience is fallacious and judgment difficult." Constant daily contact with nephritis in ward rounds, interspersed with occasional visits to the pathologist, serves to convert such an opinion into a conviction. Even the best clinical training and experience do not fully equip the physician to cope successfully and authoritatively with the problem of prognosis in certain cases of nephritis, nor do they reveal the exact status of his patient in many other pathological conditions of the kidney. To his assistance then are lately brought renal functional tests.

The ultimate object of any line of work is often furthered by a temporary abandonment of the consideration of details concerned in its various phases, and the replacement of this by reflection upon it in its entirety and in its relationship to its environment. A comprehensive review of any field of research, particularly in regard to its relationship to the fundamental sciences involved and in regard to the absolute advancement resulting from it, is seldom amiss, since it often results in the disclosure of the uselessness and limitation of certain procedures, suggests new and better methods of attack and establishes within us a truer conception of the purport and importance of the work.

The development and introduction of numerous renal functional tests are in accord with the general trend of medicine of to-day. The importance of knowing the ability of any organ to carry on its work rather than the appearance of the cells engaged in the work is being ever more emphasized.

Determination of renal function is of vital interest alike to the internist and surgeon from the standpoint of diagnosis, prognosis
and treatment. The widespread nature of the importance of such determinations is probably not so apparent to those confining their attention purely to its medical or surgical aspect, but to those interested in methods of determining renal functional capacity as such it becomes firmly impressed as investigations are made in relation to acute and chronic nephritis, orthostatic or other albuminurias, arteriosclerosis, uremia, myocardial insufficiency, polycystic kidneys, obstruction in the lower urinary tract, cystitis, pyelitis, uni- and bilateral hydronephrosis, pyonephrosis, pyelonphritis and ureteral renal calculi, hypernephromata, renal tuberculosis and the numerous allied conditions calling for differential diagnoses.

The clinical diagnosis made, in any individual case before offering a prognosis, certain problems must be investigated. (1) What pathological condition underlies the clinical picture? (2) Is the condition localized to the kidney or is any other system (cardiovascular) involved or likely to be involved? (3) What is the functional capacity of the kidney? Is this permanent or temporary, subject to change? (4) Is or is not the condition one amenable to treatment? Only by attention to all these factors can anything approaching correct prognoses be attained.

Renal functional capacity is usually ascertained in one of two ways: First, tests of excretory capacity through the quantitative determinations of the excretion of various substances in the urine, dyes—methylene blue, indigo carmine rosaniline, sulphonephthalain, other chemicals—potassium iodide, lactose, salicylates, sodium chloride, urea, sugar following phloridzin and the enzyme diastase. Second, tests of the retention through quantitative determination of the concentration of certain substances in the blood, ions through electrical conductivity, molecules through cryoscopy, urea, incoagulable nitrogen and cholesterol.

The recent work of Folin and Denis\(^1\) indicates that the concentration of urea 0.5 gm. and of total incoagulable nitrogen 0.6 gm. per litre heretofore considered normal, must no longer be so considered, since in sixteen strictly normal individuals the highest non-proteid nitrogen which they found was 26 mg. and urea nitrogen 13 mg. per 100 gms. blood. Slight nitrogen retention* may appar-

* One would expect the urea and total incoagulable nitrogen in the blood to be approximately inversely proportional to the excretory efficiency of the kidney since this is the only channel of elimination (practically speaking) for the nitrogenous waste products.
ently occur in many diseases, but in our experience with a large num-
ber of cases using the older methods and also Marshall's new urea
method, we feel that no great prognostic significance is to be attached
to concentrations of urea less than 0.55 gm. and incoagulable nitro-
gen 0.50 gm. per litre. Greater concentrations than this, together
with a serum freezing point lower than —.60 are of the greatest
prognostic importance. Evidences of retention reaching this degree
we refer to as cumulative phenomena.†

These tests all prove of value prognostically, but some much more
so than others. Those of most importance in Group I are the
dye substances, especially the phthalein, and of Group II cryoscopy,
total incoagulable nitrogen and urea. The phthalein test is of
prognostic value in all pathological conditions, whereas certain cases
of severe nephritis even in uremia show no marked increase in
incoagulable nitrogen or urea. So the presence of cumulative
phenomena is of the greatest prognostic significance, while their
absence is not.

Functional studies reveal only the excretory capacity of the
kidney. By themselves they do not make the diagnosis or settle
the prognosis. Just as routine blood examinations occasionally
reveal an unsuspected leukemia, the routine use of functional tests
brings latent kidney involvement to light. These tests should be
used routinely in conjunction with other procedures to aid in
diagnosis, prognosis and selection of lines of treatment. Their
importance in different cases varies. It is possible that a series
of ten or twelve different tests may add little or nothing to our
knowledge of the condition after a careful clinical study, whereas
after equally as careful a clinical study one test, verified, may
change all of our ideas concerning the diagnosis, prognosis and
treatment; as for instance, in one of our cases where a boy prior
to functional studies was considered the subject of a diabetes
insipidus with an excellent immediate prognosis, and after one
phthalein test, was recognized as a case of advanced chronic inter-
stitial nephritis verging on uremia, which was substantiated at
autopsy within two weeks. Because of our inability to determine
in advance in what cases the functional studies will be of value,
their routine employment becomes of permanent importance.

† The urea concentration in the blood may be very high in pneumonia as
shown by Herter. Throughout this article, in speaking of its prognostic
value, we refer only to uncomplicated cases of renal or cardio-renal disease.
Clinical or functional studies alone are inadequate from the standpoint of prognosis. The application at any one time of one or a series of functional tests reveals only a limited amount of information, e.g. the excretory power of the kidney at that particular time. This, apart from other considerations, may be of no great prognostic significance. In order to become so the data from such studies must be considered in conjunction with a careful clinical study of the patient, and the underlying pathological processes responsible for the clinical and functional pictures must be recognized, identified and understood.

Aside from or in the absence of clinical studies, repeated functional estimations with the employment of the appropriate tests over a varying period of time will reveal the nature (stationary, progressive, retrogressive) and degree of renal involvement and so prove of prognostic value. But even repeated functional studies prove of greatest value when associated with careful clinical studies, for it has been definitely established that functional pictures carry very different significance in various pathological (clinical and experimental) associations. Diseases may be functionally identical, clinically and prognostically different and vice versa. To illustrate, a very low condition of function as indicated by a very low phthalein output, together with marked delay in the excretion of chlorides, iodide and lactose, may be encountered in experimental chromium nephroses or in marked passive congestion (experimental or clinical). This may be followed within a week by a practically normal renal function, owing to regenerative processes in the first instance, and to the reestablishing of cardiac compensation and better circulation in the second, whereas findings identical with those originally encountered, occurring in a case of chronic interstitial nephritis, indicate impending uremia and a very grave prognosis. Again, identically low functional capacity in cases of urinary retention, associated with pyelonephritis and hydronephrosis on the one hand, and in chronic nephritis on the other, do not have the same prognostic significance since the surgical condition is amenable to treatment, whereas no efficient therapy is at hand in chronic nephritis. From this, the necessity of understanding the absolute significance to be attached to the findings of any functional test becomes apparent. Lepine has objected to the employment of any one substance for the purpose of estimating functional capacity of the kidney on the ground that the kidney does not excrete all substances with the same
facility and that data obtained from a study of the excretion of one substance, therefore, cannot be applied to others. He believes that each substance has its own coefficient of excretion. That there is not accurate and exact parallelism of excretion of all substances by the kidney, one is forced to admit, but that there does exist a certain degree of parallelism, the same general tendency of excretion for all of the substances so far used is unquestionably true. The difference is of one degree. Familiarity with the meaning of these variations in degree to which peculiar prognostic significance attaches is most desirable therefore.

The value of any of these excretory tests is purely empiric because of lack of sound physiological information dealing with the ultimate physics and chemistry of the excretion of any substance by any part of the kidney—tubules or glomeruli. Experience has taught us that the failure of phthalein to appear in the urine, or its excretion in mere traces in the course of chronic nephritis, indicates impending uremia and grave prognosis, even in the absence of any definite knowledge concerning the excretion of any other substance. In other words, failure to excrete phthalein empirically signifies incapacity on the part of the kidney to carry on its work—hence a bad prognosis. But this does not hold for all substances. Failure to detect diastase in urine by the customary technique employed means renal injury, possibly severe renal injury, but not necessarily so.

How can we utilize functional tests to the greatest advantage prognostically? (1) The prognostic value of functional studies must be considered from two points of view: (a) As to the immediate outcome (days, weeks or months are here concerned); (b) As to the ultimate fate of the patient and the future course of the pathological processes. At present their value from the first point of view is definitely established and is here discussed in its various phases. Prognostic significance other than immediate will be revealed only in the course of years. In association with Dr. Thayer and Dr. Baetjer, an attempt is being made to learn of the condition, through correspondence and re-examination where possible, of all of our patients previously studied. Data sufficient for conclusions are not yet at hand. Surgically, little prognostic value other than immediate can be considered, since surgical interference so radically changes the conditions. (2) We need a much greater familiarity with the significance and reliability of the findings of all
these tests in all renal lesions, experimental and clinical, medical and surgical. (3) We must learn the relative ease with which each and every approved test responds to increasing degrees of injury of any type, such information as has been presented in experimental nephroses by Schlayer and his co-workers, Pierce, Hill and Eisenbrey⁴, Austin and Eisenbrey⁵, or in chronic passive congestion in more recent studies. (4) Experimentation and clinical experience must teach us upon which tests reliance as to prognosis can be placed in each and every type of renal disease. (5) We need a much deeper insight into the nature of the processes at work in certain diseases, e.g. eclampsia, kidney of pregnancy, certain types of nephritis, etc. We must learn whether certain symptoms, conditions and phenomena are actually due to the accumulation of toxines, ferments, etc., whether this accumulation does result from the failure on the part of the kidney to excrete them, or whether the kidney is the usual channel of their excretion. May not, for instance, certain of these phenomena be the expression of deprivation of the body of certain substances through excessive excretion through hyperpermeability? More light is needed on the factors responsible for hypertension, oedema, uremia, etc. We must learn to recognize in what conditions the excretory power of the kidney is a real criterion to the patient’s actual condition. Prognostically, their value will thus be enhanced through a knowledge of the limitations of these tests. (6) Functional tests will become more generally used and hence of more value when we know which ones can be discarded without loss, and which combination of tests (the smaller, the better) will yield all the information necessary in any given type of disease.

Value in Medical Cases.

Until very recently, little or no prognostic value has been attached to functional studies in medical cases, although their worth in this connection is fully as great as in the surgical. The introduction of new tests, notably the phthalein test, and improvements in the technique relating to the old ones, are largely responsible for the change in the attitude of the profession. The limitations of the value of such tests must be clearly recognized. In all forms of renal disease, a prognosis only so far as renal efficiency or inefficiency can be made through their use. Death may occur from innumerable other factors concerning which they give no information.
In acute nephritis the prognosis is largely dependent upon the etiology. When associated with specific fevers it becomes impossible to ascertain whether the patient is suffering from a toxemia due to non-excretion, or one due to a specific toxin of the fever. The capacity of the kidney to excrete can be readily determined, but this means but little, prognostically, on account of the rapidity with which marked changes in this respect occur. Clinically, we have seen cases with but 10 per cent. phthalein output for two hours, excrete 28 per cent. four days later, and the normal amount within two weeks. Experimentally, chromium animals with a zero output for two hours have returned to a normal excretion within ten days, while twenty-four hours later, more chromium having been given, the phthalein was again not excreted. It is evident, therefore, that frequent repetitions of tests are very essential to prognosis in acute nephritis. But when a patient exhibits, as one of ours did, no phthalein, no lactose, together with a high blood urea concentration, the case must be considered a grave one, though not hopeless. The immediate danger from the renal-inadequacy factor is at least determined.

The functionally mild nature of a chronic nephritis is readily recognized. Associated with the albumin and casts, a slight increase in blood pressure, palpable vessels (arteriosclerosis?) and slight cardiac hypertrophy, there may be encountered a somewhat delayed lactose and phthalein excretion, a normal total salt output with a vascular hyposthenuria, but no evidence of cumulative phenomena. In such a condition the immediate outlook is favorable, but tests should be applied intermittently to determine whether the condition is stationary or progressive, and the rate of progression. In prognoses caution should be observed on account of the possibility of acute exacerbations becoming superimposed on the chronic process. Aside from this, the case may develop gradually into an advanced nephritis with marked renal insufficiency exhibiting uremia, into a nephritis with a cardiac insufficiency or with a vascular accident (apoplexy).

Advanced nephritis is indicated always by decreased excretory capacity and usually by cumulative phenomena. Although, clinically, it is difficult often to determine the severity of the condition, this is readily obtained through functional studies. Perhaps the majority of cases of chronic interstitial nephritis are clinically latent, unrecognized until the occurrence of serious or even fatal
complications. Uremia, clinically, may appear to come out of a clear sky, whereas its unsuspected proximity can be readily recognized, and its occurrence can be easily predicted through functional studies. In chronic nephritis, failure on the part of the kidney to excrete phthalein or lactose, together with marked cumulative phenomena, indicates renal insufficiency impending uremia and calls for a grave prognosis.

Other cases with marked clinical nephritis, even with mild uremia, but with less marked functional involvement, may be more difficult for prognosis. Many factors must be considered. Will the heart dilate? Will an apoplexy occur? Will an acute attack be superimposed? But so long as the renal function remains fair, say 30 per cent. phthalein for two hours, with cumulative phenomena absent, and none of the above complications arise, death from renal-insufficiency uremia is not at all likely and an immediate favorable prognosis can be given. Care must be used in predicting more than this. The tests should be repeated in order to follow the course of the disease.

That a good or normal phthalein output is occasionally encountered in the presence of definite nephritis has been pointed out in our earlier publication. At the same time, the absence of hyperpermeability to phthalein in all our studies was commented upon. Pepper and Austin have lately called attention to a case of nephritis with marked albuminuria, cylindruria and oedema in which the phthalein and total incoagulable nitrogen were normal, while the chloride output after additional salt was somewhat delayed. The phthalein output in this case, 67 per cent. for one hour, strongly suggests hyperpermeability. Baetjer,7 in our clinic, has encountered four cases during the winter which clinically and functionally resemble Pepper and Austin's case and in all of which hyperpermeability to phthalein and lactose was strongly suggested. This type of nephritis is not well understood. Since all of the patients studied are still living,* the nature and extent of the anatomical lesions are as yet undetermined and the value or significance of functional studies in relation to them is not clear.† Since the patients have

* Pepper and Austin's case was decapsulated but the condition has not improved (personal communication).
† It is possible that this increased permeability is not a passive condition but an active functional response to some unknown renal stimulant which differs essentially from an ordinary diuretic.
continued to live, the tests furnished correct information so far as immediate prognosis, at least, is concerned.

Cardio-Renal Cases.

All grades of nephritis and myocardial insufficiency may be associated, and only through the use of clinical and functional studies can the cases be properly interpreted. By the combined studies it is possible in any given case to determine the relative responsibility of the kidney and heart, from the clinical picture presented, and thereby to arrive at a better prognosis.

Experimentally, it has been shown that in moderate degrees of passive congestion the excretion of lactose, iodide and salt may be delayed, while the phthalein output remains normal. Where the congestion is more severe the phthalein is decreased, but returns to normal with the earliest signs of improvement of circulation. Strauss and Hohlweg found that incoagulable nitrogen and urea of the blood are increased in chronic passive congestion, but not so strikingly as in nephritis, findings which we are able to corroborate.* Low phthalein and the cumulative phenomena therefore bear great prognostic and diagnostic significance in this group of cases, since they are only encountered with rather advanced nephritis or with a very severe passive congestion calling for a grave prognosis.

Moderately advanced nephritis, associated with a moderately myocardial insufficiency, often exhibits a fair renal capacity, in which case the prognosis rests more on the response of the heart to treatment than on the nephritis. An increase in the phthalein output may be the first evidence of restoration of cardiac compensation and hence it indicates a favorable immediate prognosis. The absence of cumulative phenomena, together with a fair phthalein output in any clinically severe cardio-renal disease, points to the heart as the responsible factor.

A very low excretory capacity with marked increase in blood urea, or total rest nitrogen, or a very low serum freezing point, indicates either that the kidneys chiefly must be considered etiologically, or that the heart is in an extremely precarious condition, in either case the prognosis being grave. With or without cumulative phenomena, a very low excretory capacity, persisting after clinical evidence of

* In pure chronic passive congestion we have never seen the rest nitrogen higher than 0.630 gm. per litre.
cardiac improvement, indicates severe nephritis and an unfavorable prognosis.

**Myocardial Insufficiency.**

Marked renal insufficiency may result from pure chronic passive congestion. Very exceptionally, clinically and experimentally, the functional studies reveal a decrease in function equaling that seen in the most severe grades of nephritis. Since the congestion for this must be of a most extreme grade, death is imminent on account of the heart. As a rule in myocardial insufficiency, with a symptomatic and urinary picture identical with that seen in a moderately advanced nephritis alone, or in nephritis associated with a cardiac break, renal function as indicated by both excretory and retention tests is surprisingly good. When low renal function is followed by an increased phthalein output, the amount of increase gives a fair approximation of the extent of cardiac improvement.

**Polycystic Kidneys.**

All conditions of renal function may be here encountered, and a prognosis can be based upon functional findings in this condition, just as in chronic interstitial nephritis. A case has been reported exhibiting a normal function, death resulting from an intercurrent disease, while a zero phthalein was found by Pepper and Austin in a case dying in uremia. A case now under observation, the diagnosis being confirmed by collargol skiagram, has a fair function only, 20 per cent. phthalein for two hours.

**Surgical Cases.**

Uremia, after operation, has been responsible for a large proportion of the mortality in renal surgical cases, so that any method capable of furnishing information as to the probability of the occurrence of such a condition is of great importance to the surgeon.

Emphasis upon one point is needed, viz., a **fair or a normal renal function must not be interpreted as meaning that uremia or anuria will absolutely not develop after operation**, or as meaning that the post-operative function will be the same as that before surgical interference. Many accidents may occur. The subject of a perfectly normal function may, after operation, develop anuria and die, although other things being equal, he is much less apt to do so than
a patient who, prior to operation, has a low renal capacity. The great value of these studies, surgically, lies in their ability to reveal those cases which are suitable and those which are unsuitable for operation as far as the kidneys are concerned. They can indicate that uremia is certain to occur following operation in a given case, that certain cases are hopeless, others poor, good or excellent surgical risks, but they offer no absolute security that the subject of a good surgical risk will not develop renal insufficiency.

The previous knowledge of the renal function is also of prognostic importance in the event of development of post-operative uremia, for the occurrence of this condition, in one who has been previously shown to have a continuously low function, means a grave prognosis, whereas, in one who has had a good renal function, recovery is more probable.

The tests are of value in two classes of cases: (1) those with retention of urine, renal injury following, due to obstruction in lower urinary tract with back pressure upon the kidney resulting in functional changes, in hydronephrosis, or in pyelonephritis, etc.; and (2) those with unilateral or bilateral renal disease.

Obstruction in Lower Urinary Tract.

As a result of obstruction in the lower urinary tract, pathological changes may occur in the ureter and kidneys, dilatation of the ureters varying grades of hydronephrosis and, as a result of the long continued high pressure, atrophy of the parenchyma of the kidney. Not infrequently, infection occurs with the development of a pyelitis, a diffuse or localized pyelonephritis, or pyonephrosis. The occurrence of these complications is often difficult of recognition and is often overlooked, especially in the absence of symptoms of renal inadequacy. Cystitis and associated albuminuria and cylindruria are usually present, albumin and casts not contraindicating operation. The urinary output may be normal in many instances, also the urea output and total solids, and yet the patient be on the verge of renal failure. Disastrous results may be certain to follow any surgical intervention at this time, yet often nothing outside of functional studies can furnish this information.

A marked decrease in the excretory phenomena alone, or associated with cumulative phenomena, means severe derangement of renal function, which may be of either a temporary or permanent
character. No prognosis should be given and, except in emergency, or where the surgical procedure employed is the only method of improving or relieving the renal disturbance present, no surgical interference attempted without further study in conjunction with suitable preliminary treatment (Young's treatment—catheter drainage and abundance of water). Under this regimen repeated tests will quickly demonstrate the nature of the derangement, cases of nephritis and of true interstitial destruction showing no improvement, whereas purely functional changes or those secondary to pyelonephritis show markedly increased function.

This constitutes a very striking group of cases. A patient in uremia, with low excretory functional findings and with cumulative phenomena, may in the course of a few weeks return to an excellent clinical condition with a renal functional capacity approaching normal. Only one such experience is necessary in order to impress upon physician and surgeon the importance of determining (through time, preliminary treatment, and repetition of tests) the nature of the depressed function, temporary or permanent. The prognosis of the operation, so far as uremia and anuria are concerned, is infinitely better in those cases showing marked improvement in renal function following the adoption of the preliminary treatment above mentioned.

All tests are not of equal prognostic value in this group of cases. The phthalein has already established its place. Lactose is of no significance since its total suppression is frequently encountered when the phthalein, diastase, cryoscopy, blood nitrogen and urea, all show a fair or moderately good renal function, the truth of which is demonstrated in the subsequent history. In a series of 20 such cases lactose was recovered in the urine in only six instances. Glycosuria following phloridzin is also very slow in appearance or fails to appear at all. These two tests therefore exaggerate the degree of functional changes and bear no prognostic significance.

The phthalein test of permeability along with cryoscopy, urea and rest-nitrogen determinations of the blood give a sharp index of the functional capacity.

Unilateral and Bilateral Surgical Diseases.

The prognosis in unilateral and bilateral surgical diseases of the kidneys depends upon the surgeon's ability to recognize prior to nephrectomy which is the diseased kidney, or more diseased kidney, and what is the functional capacity of the kidney that is to be left to
carry on renal function, as well as upon his technical skill and the nature of the pathological condition present. Tuberculous and pyogenic infections, unilateral and bilateral calculi, hydronephrosis, hypernephromata and congenitally deficient or non-developed kidneys are the conditions in which the test has proven of most value.

The urea, indigo carmine, methylene blue and diastase, cryoscopy, phloridzin, Alberran's polyuria test along with clinical studies and urinalysis of the separated urines will all indicate which is the diseased or more diseased kidney. But in this class of cases, the shortcomings of most of these tests are very evident, since one kidney may be doing two or three times as much work as the opposite one and yet be incapable of assuming the additional work or of carrying on adequate work unaided. It may be doing the major part of the work, but only at the expense of its reserve power. But phthalein has prognostically one great advantage over other functional tests, in that it indicates the absolute as well as the relative value of each kidney, so that one knows not only which is the diseased or more diseased kidney, but the amount of work each is doing relative to the other, and what is yet of greater importance, the amount of work for each relative to the normal, since this allows a prognosis concerning the capacity of the remaining kidney to carry on renal function. In double renal tuberculosis, in which, for instance, the amount of pus from each side is practically the same,* the phthalein test may demonstrate that one kidney has a function far in excess of the other, in fact so good a function that a successful nephrectomy can be done.

It must be admitted that depressed function, the result of inhibition due to ureteral catheterization, is sometimes encountered, in fact more frequently than we formerly believed. But in every case demanding ureteral catheterization, a total renal determination should also be made through which any discrepancy can be readily detected and error be thereby avoided.

Of prognostic significance also is the development of increased functional capacity in the remaining kidney after a nephrectomy. In those cases in which determination of function has been made after an interval of a month following operation, the capacity has not only been greater than that of the same kidney, but equal to, or

*Not infrequently in bilateral renal tuberculosis the more recently involved kidney secretes more pus than the other and only through functional tests can the true condition be recognized.
greater than that of the combined function of the two kidneys prior to surgical interference. The amount of increase function that will develop can of course not be predicted from functional studies, but the increase after nephrectomy can be determined from day to day and so aid in prognosis.

A perfectly normal urine in every respect except quantity may be excreted by a congenitally deficient type of kidney. Such a kidney may be capable of doing only one-fifth to one-tenth of the total work required. The literature furnishes numbers of instances of death following a nephrectomy, owing to the presence of this unrecognized deficient kidney, which has been left to do all the work. In the last four years of our experience, four such cases have been encountered, and in the last case only, the presence of a low phthalein from this kidney revealed its true nature and prevented the removal, on the opposite side, of a tuberculous kidney which had many times a greater function than this supposedly healthy kidney. Had the nephrectomy been performed, the prognosis would have been extremely grave.

In certain cases, owing to malformation or stricture in the lower end of the ureters, and especially in bladder tuberculosis, it may be possible only to catheterize one ureter. When infection of the bladder exists, microscopical and chemical examination of the urine collected transvesically is obviously unreliable as indicating a healthy or diseased condition of the uncatheterized side. It is therefore necessary to use functional tests to determine the presence or absence of disease and the extent of the disease where it does exist. A prognosis may be safely made concerning the ability of any kidney to carry on the renal function alone, even when catheterization of the ureter is impossible, and where the urine has been collected through a diseased infected bladder, provided a catheter can be inserted into the other ureter. The use of these tests should not be limited to renal surgery, since their routine employment would undoubtedly influence the surgeon’s attitude in many instances.

**Uremia.** Uremia is a clinical condition, a syndrome, resulting from renal insufficiency from any cause. Its appearance is often sudden and unexpected, its course, acute and severe, rapidly ending in death, or chronic, lasting through months. Through functional studies it is possible to ascertain that it is impending, even when no indications whatever of its proximity are revealed by the clinical study. With a continued failure on the part of the kidney to excrete
phthalein and lactose, etc., association with the continuous marked and increasing accumulation of urea, or total incoagulable nitrogen, or low serum freezing point, one is perfectly safe in predicting the early appearance of uremia, regardless of the underlying pathological condition.

Uremia once present, the clinical severity is not a safe criterion for prognosis. Apparently desperate conditions sometimes reveal a fairly good renal function with an ultimate recovery, whereas very mild symptoms may be present until shortly before death. It always, however, indicates a serious condition, always calls for immediate therapeutic consideration and always suggests a grave prognosis, but it does not always indicate a hopeless one.

It has already been intimated that identical functional pictures carry very different prognostic significance in different clinical and pathological associations. Extremely low functional capacity in chronic nephritis means death, whereas in obstruction in the lower urinary tract with urinary retention and back pressure, the injury may be mostly functional, so that following appropriate treatment a fair or good capacity is again established. Nothing is more surprising than the rapidity and extent of the functional and clinical improvement. Whenever renal function markedly increases, surgical interference is much less liable to be followed by post-operative uremia, whereas in practically all cases with persistent low function it has followed operation used as a last resort, and death has ensued.

Markedly different clinical and functional conditions are encountered even in the medical uremia. Some cases of mild uremia, with nausea, vomiting and even stupor, show a phthalein output which is relatively high, 20-35 per cent. for two hours. This type is much more apt to be associated with cardiac or vascular changes, with oedema frequently a prominent feature. The uremia symptoms may here be an expression of a very different pathological condition than that encountered at other times, e. g., oedema of brain rather than a pure toxemia. These cases often improve and leave the hospital; if death supervenes, it is usually a cardiovascular affair and not a typical uremia.

Very occasionally with very low excretory function (traces of phthalein) and marked cumulative phenomena, the patient will continue to live in a chronic uremia for a surprisingly long time. In several instances such a patient has lived for some months, and in
one instance for as long as a year. This patient is in a desperate condition but still continues to live. Vicarious activity probably varies markedly in different individuals, and though incapable of carrying on life alone for any length of time, it probably is a material aid in the maintenance of life when the kidneys are just verging on inadequacy. The balance is not long maintained, however, and death is continually imminent.

Uremia cannot occur without valuable evidence appearing, as decreased excretory phenomena, but cumulative phenomena do not always arise. With Hohlweg we consider increased blood urea and rest-nitrogen indications of renal insufficiency and not of uremia.

The Prognostic Value of Each Test.

The employment of one test alone does not always yield all the information desirable. When only one is used, the phthalein test is undoubtedly the one of choice. Where it reveals decreased renal capacity, one of the blood tests, urea, total incoagulable nitrogen or cryoscopy, should be employed to determine the presence or absence of cumulative phenomena. These probably carry about the same significance.

Dye substances other than phthalein need not be employed prognostically, since they yield less quantitative and less reliable results and add nothing to prognosis.

The phthalein is the test for general use under all conditions. Its findings can be verified and its indications strengthened by the employment of selected tests in different conditions.

The iodide and salicylate tests are not of great prognostic value.

Lactose is unreliable, since its total suppression occurs in moderate lesions of a given type, but suppression in chronic nephritis indicates a severe lesion.

The urinary urea is of value only in relation to unilateral renal disease.

Phloridzin has a tendency to exaggerate the degree of functional injury and hence is not of great value.

Salt. A marked tubular hyposthenuria carries much prognostic significance, otherwise the chlorides are of only slight prognostic value.

Water. A very marked oliguria or anuria persisting is of significance.
Diastase may be tremendously depressed in moderate degrees of renal injury, while at other times it is not affected proportionate to the injury, hence it is not reliable for total capacity. In unilateral cases the diseased kidney is correctly indicated.

The value of total incoagulable nitrogen and of urea in the blood has been enhanced by the introduction of newer and more accurate methods by Folin and by Marshall. Increased concentration of these substances does not always occur in severe renal involvement, hence their normal concentration in the blood does not indicate normal kidneys. Their increase signifies renal injury, and the extent of the increase is of extreme value in determining the extent of the injury. They are not of value in determining the diseased kidney where only one is involved.

Cryoscopy occupies a similar position with about the same significance. A study of the combination of these three tests is needed in order to determine the extent of parallelism in their findings.

With cholesteremia we have no experience and with Ambard-Constant not sufficient to justify an opinion.

Bibliography.

7 Baetjer. To appear in an early number of Arch. Inter. Med.

For detailed consideration of various tests, see previous communications on functional studies by the author and his co-workers:

Arch. Inter. Med., 1912, IX, 284; 1913, XI, 121 and 258.

Discussion.

Dr. Hugh Cabot (Boston): I believe that the choice of this subject of the Study of Renal Function for a general discussion this afternoon will be found to be an exceedingly happy one. There is no department of medicine, however wide or however narrow, in which we are not concerned with this question; and it is only of
recent years—and not even to-day sufficiently—that we have been realizing our responsibility with regard to knowing as practically, or as nearly as we can, the advances in the study of the kidney function.

The papers read here this afternoon have been of unusual value. Dr. Christian has brought to us his wide knowledge of the work of others, and his special knowledge, regarding the diagnosis of renal disease. Dr. Rowntree has come to us with uncalled-for modesty with a study of, I believe, the most valuable test from the point of view of prognosis, and has sketched for us its relation to the other tests in the field. Finally, we have had the view of the clinician, thoroughly equipped to use these tests, presented to us by Dr. Janeway.

We may look at the study of kidney function from two angles. First, there is the view of the clinical pathologist, who attempts to correlate the finding in the urine with those in the kidney; and it cannot be said that to him the tests of renal function have been, as yet, of great value. The other point of view, with which I have been particularly concerned, is the value of the study of kidney function with regard to prognosis. I, being essentially a blood-minded person, am desirous of knowing whether or not I may, with more or less safety to the patient, operate in the presence of renal disease. It is, however, a fact that to-day too many surgeons neglect this matter of the study of kidney function, saying that the study of the urine will give them sufficient knowledge. It has already been pointed out that the ordinary routine examination of the urine will not give information on which the surgeon is at liberty to act; yet many go ahead, on the assumption that it will.

To come strictly to the point that I want to discuss, the value of these renal-function tests in enabling us to discover beforehand the probable mortality in any group of operations: The various tests have already been referred to, and I shall not go into them beyond saying that in my work I have come to rely on comparatively few of them. None of the color-tests, specifically so-called, seems as valuable as the phthalein test of Rowntree and Geraghty. We have used it in a very large number of cases and have come to regard it very highly. Another test that we rely on, which is of more confirmatory value than original value, is that of nitrogen retention. I am inclined to think of the work of Folin as bringing it much more nearly within the reach of the clinician. The surgeon may
depend on these two tests, if properly carried out, to give him a very good idea of the operative prognosis.

As a type instance of what I am considering, let us look at the cases, as they come to us, of obstruction of the lower urinary tract—a typical obstructing prostate. In a man in comparatively good condition, with only a moderate blood-pressure, with considerable residual, both without retention,—apparently a good risk,—we may find that the renal function, by phthalein and other tests, is reduced. We desire now to improve that function, institute methods of drainage, and it may appear that his condition is improving; but a careful study of renal function may show a steady fall in the amount of phthalein excreted and a very considerable nitrogen retention. This may be in advance of any clinical manifestations of trouble. Often the excretion of phthalein will fall from as great an output as 25 per cent. in the first hour after it appears, to unmeasurable traces; and not until it gets to the bottom of its fall will the patient show clinical symptoms. Then the excretion will begin to rise, and then the test, if all goes well, will begin to rise; but the patient will often improve more rapidly than does the test. If we operate on that patient, assuming that his condition is as good as it appears, in the face of a failing renal function, we shall kill him. If we operate during the rise, the prognosis is better; but we should wait until the rise has reached its crest, when the prognosis will be far better than when the patient first came under observation.

This type of condition in the kidney appears to me to be one not readily demonstrable, even by the pathologist. It depends on the acute congestion of the kidney and milder degrees of pyelonephritis, which do not produce a very permanent impression on the kidney, but reduces its functional capacity very rapidly and makes it a kidney from which we can ask little or nothing. Nevertheless, the power of the kidney to recover its function seems entirely good, and if we can give it a sufficient opportunity to do so, our prognosis will be of the best, and our mortality of the lowest.

Dr. Rowntree has already referred to the value of these tests of the severity of the disease in the two kidneys, so that one may be able to decide in advance of the operation whether the remaining kidney is of sufficient soundness to be compatible with life. That is a subject into which too little investigation is being made to-day in the general surgical world. I believe that it is possible at present
to determine with great accuracy whether the remaining kidney is sound enough to maintain life. That being determined, we have removed the largest factor in mortality.

Some attempt has been made to draw a line across kidney function, below which operation is dangerous, and above which it is safe. The more I see patients with impaired kidney function, the more am I impressed with the fact that no such line can be drawn. A kidney with low function may be incompatible with life in one patient, and quite compatible with it (but with very considerable added strain) in another. So far as I can make out at the present time, the most important thing is a stable kidney function. If the function is low, but is yet stable, and if the patient can be put to some strain without an important variation in the function's being produced, he is a far better risk than one with twice as good function, yet in whom the least strain produces bad results. Stability is more important than low level of kidney function. The latter does not necessarily contraindicate operation. Under these circumstances, if the level, although very low, is constant, we may advise operation and do it wisely under circumstances that make us willing to accept a very considerable risk; but we know what risk we are assuming, and do not give a comparatively favorable prognosis to a patient with a kidney whose function is such that the risk is rather grave or very grave, but is still one which we may properly take, if we realize what risk we are taking.

Dr. George Dock (St. Louis): Dr. Rowntree has given us an axiom from Hippocrates that is always worth while remembering in diagnostic matters. There is another axiom bearing on the matter of urinology, which is often used with more or less effect. Thomas Fuller, in his article on "The Good Physician," says: "The good physician trusteth not the single witness of the water if better testimony may be had. For reasons drawn from the urine alone are as brittle as the urinal. Sometimes the water runneth in such post haste through the sick man's body it can give no account of anything memorable in the passage, though the most judicious eye examine it," etc. This I have had written over the door in my urinologic laboratory for a long time; but, although the spirit of it is still applicable, I think we can say that the pessimistic sting of it has been materially taken away in the last few years.
I should like to reiterate Dr. Cabot’s congratulations to this body for having heard the very comprehensive and clear and complete description of modern kidney-functional tests that we have had the opportunity to hear this afternoon. I cannot add anything to what Dr. Cabot has said; but it is noteworthy that we have had the statements from many who are actually doing the work that is necessary—the experimental work in the production of known kidney lesions; and also the clinical material, and then the careful clinical studies, including treatment, by Dr. Janeway.

Now urine-examination is very old, and a good deal of it is very good; but until recently it suffered, I think, from an unmistakable tendency that applies to all medical diagnosis: that is, the tendency to rely on a single diagnostic method and miss the complete examination of the sick man. For example, for a long time we depended on albumin tests. Too many patients were neglected or were allowed to be perfectly reckless on the basis of a single examination for albumin. The same thing was done with casts. We all remember how terribly the urea examination in urine was abused for years; and uric-acid examinations would have been much more abused, except for the fact that there were no easily applied methods of making them. When cryoscopy was put forth, many people looked on it as a complete relief from the other methods of time-consuming examination; take the freezing point of the urine, and you had the whole thing there.

It is a very interesting thing that the old methods of examination of the kidney function have been included in the papers and especially emphasized this afternoon by the speakers. The authors missed none of these well-known methods of examining the patient’s condition. Physical examination, blood-pressure, and everything else were mentioned. Still more recently, however, there have been devised very exact methods of examining the blood, as elaborated by Folin and Marshall, and others. This advance can hardly be overestimated, and practically it means this: that in no clinic, no matter what kind of clinic it is, can these discoveries be neglected. I do not mean to say that they must be used blindly; but unless they are used as fully as their importance warrants in every individual case, then the patient will undoubtedly be a victim of malpractice.

Just how some of these examinations may be made, has often been stated. I shall not go into details; but in the last couple of years I had an opportunity of seeing at the hands of some of my
colleagues, and in my own clinic, some of the undoubted gains following the use of these methods. I shall mention only a single case that happened just before I left:

A man with the ordinary history came to the ophthalmological clinic on account of failing vision. He had albuminuric retinitis; and, although he seemed to have no indication of kidney disease, they sent him to the internal clinic to find out what was the matter with him. We found a typical condition, with slight enlargement of the left ventricle and high blood-pressure, but no history of serious interference with the kidney function. The urine was being passed in normal quantities. It had a specific gravity of 1012, and contained a trace of albumin and a few hyaline casts. It was, then, an ordinary case of contracted kidney; and the patient, in the ordinary course of events, would have had given him some advice about the diet and would have been told a few other things, and then sent home. I, however, applied, in the first place, the phthalein test, and found his excretion to be only 8 per cent. in three hours. We concluded that he was sicker than we had supposed. We put him to bed and treated him as well as most patients would have been treated under these conditions; although I should not like to claim that we did everything that was possible in the circumstances. Within twelve hours, he went suddenly into uremic convulsions, which it required a great deal of active work to modify. Even now, immense practical gains can be made from the application of these tests; but the most important thing consists in piling up evidence. Curiously, few cases that have been subjected to these newer methods have come to autopsy. The striking thing that comes out of Schlayer's communication (and a great many others have had the same experience) is that the patients on whom you make these tests do not ever seem to come to autopsy. I do not know whether or not they are treated better than they used to be, but there is a surprising lack of anatomical information. We need not only a much fuller knowledge of kidney function, because we are still ignorant of many details; but we need in the case of kidney disease an enormous amount of light on renal anatomy. The difference in the classifications and the many classifications of kidney diseases, as well as the hopeless difference of opinion regarding the classification of even the common kidney diseases, show how much we still have to learn. After we have applied the methods that we have and others that will, no doubt, be discovered, to the
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study of the functions of the kidney during life, then complete anatomical information will give us an amount of exact knowledge for diagnostic and prognostic purposes such as we have never had at all in kidney diseases, and in very few other diseases.

I should like to suggest now, in regard to some of the anatomical work that has to be done, that it must be as complete and just as careful in all parts as the clinical work, in order to bring good results. We have long known that the anatomical structure in all parts of the kidney is not uniform; and the most minute and accurate studies must be made in all parts of the kidney in order to finally clear up the exact conditions in kidney diseases.

DR. JOHN T. GERAUGHTY (Baltimore): The subject has been handled so thoroughly that I will make my remarks very brief, and limit myself entirely to the practicability of these tests and also the indications for their use.

The number of functional tests has become so great that it is impracticable to employ all of them in any individual case; and even, if not impracticable, nothing would be gained by employing all of these tests. The information furnished by many is of the same character, but more accurately furnished by one test than by others. For example, there is a parallelism between the excretion of the different dye substances; but, as phthalein furnishes more accurately all the information obtainable from this group of substances, no advantage attaches to the employment of all.

For chromocystoscopy alone, indigo-carmine is unquestionably the test of choice. Again, rest-nitrogen and blood-urea bear about the same significance.

Lately we have discarded the nonproteid nitrogen estimations, and are depending entirely upon the blood-urea (determined by Marshall's method), or upon cryoscopy, for evidence of cumulative phenomena.

From a practical standpoint, certain tests can be entirely discarded without loss; such as cryoscopy of the urine and electrical conductivity of the urine. Total urea estimations are of doubtful value, and diastase determination furnishes only information that is obtainable more accurately and quickly by other means. Certain other tests, such as potassium-iodide elimination, can be discarded as furnishing at times unreliable information. We have seen potassium-
iodide excretion delayed in cases with normal function (proven by subsequent history), and excreted within normal limits in cases of the most severe nephritis. The tests which we consider of the greatest value in the excretory group, based upon actual experience, are: phthalein, lactose, and chlorides; and of the tests of retention, blood-urea, rest-nitrogen and cryoscopy. The indication for the specific employment of the individual tests are as follows:

Chlorides, in all forms of nephritis and cardio-renal disease, especially if oedema is present; hyposthenuria being noted, together with its type.

Lactose is indicated for the detection of slight injury to the kidneys, and also in severe nephritis; since its suppression indicates a bad prognosis. It is not particularly helpful in surgical diseases.

Of the retention tests, either blood-urea, rest-nitrogen, or cryoscopy, is indicated wherever a severe lesion of the kidneys is suspected. We consider that one of these should be used as a routine, in conjunction with phthalein, wherever functional tests are desirable—particularly if the phthalein function is low.

Tests in conjunction with ureteral catheterization: In this connection, phthalein, urea and diastase are most serviceable. The diastase and urea give practically the same information, but only give relative functional values, while phenolsulphonephthalein gives both relative and absolute values. The total function should always be estimated by means of phthalein without ureteral catheterization, in order to detect the amount of catheter-inhibition, should this exist. Where severe bilateral lesions exist, one of the retention tests should be used.

Practicability of Tests. The simplest and easiest test is undoubtedly the phthalein test, as it requires the least amount of time and apparatus. The lactose test, if quantitative determination is required, necessitates the employment of an expensive polariscope. Furthermore, the preparation of the lactose for injection requires attention and consumes time. Its use also requires familiarity with the technique of intravenous injection.

Diastase requires the daily quantitative preparation of soluble starch, accurately graduated pipettes, a large series of test-tubes, a water-bath, and one-fiftieth normal iodine solution. For total estimation, it requires twenty-four hours specimens of urine with preservatives. The time necessary for a single determination is scarcely warranted by the information obtained.
THE PROGNOSTIC VALUE OF FUNCTIONAL TESTS.

Urea estimations of the urine can be accurately and rapidly done by the Marshall method; and, from the standpoint of practicability, it leaves little to be desired. It is useful only in conjunction with ureteral catheterization.

Chloride estimation, by the Lutke Martius method, requires standardized solutions, and carefully graduated apparatus. It consumes considerable time, and, besides, requires daily collection of the urine with a knowledge of daily chloride-intake.

All retention tests require, of course, the withdrawal of blood; and cryoscopy is, undoubtedly, the simplest, provided that proper apparatus is at hand. It requires careful attention to the details and consumes considerable time.

Blood-urea can be done by either the Folin or the Marshall method, and the total rest-nitrogen, preferably by Folin's method, but any of these methods is impracticable for the general practitioner.

Where only one test can be employed, the most value is unquestionably to be obtained from the use of phthalein; and this is particularly so from the standpoint of the surgeon. From practical experience with a number of the more promising tests, the information obtained is frequently unreliable. Phthalein alone has proved of value.

Estimation of function in renal surgery by means of phthalein has become so important that its position is firmly established. The surgeon to-day is not justified in performing a nephrectomy or other significant procedures tending to disturbed renal function, without having first learned the renal function.

Ureteral catheterization alone is not sufficient, with demonstration of apparently normal urine; as it not infrequently happens that the obviously diseased kidney is much the better kidney.

DR. WILLIAM S. THAYER (Baltimore): For the last two years, in association with Dr. Rowntree, Dr. Fitz and Dr. Baetjer, have studied the renal function of a considerable number of patients under my observation, in and outside the wards of the Johns Hopkins Hospital. These studies have taken into consideration the intake and the output of salt and water, the elimination of iodide of potassium and lactose after the manner of Schlayer, as well as the estimation of the incoagulable nitrogen in the blood and the excretion of phenolsulphonephthalein.
The delicacy of the lactose test, in the absence of chronic passive congestion, in revealing early disturbance of the vascular apparatus of the kidney, especially in association with the manifestation termed by Schlayer "vascular hyposthenuria" appears to be undoubted.

I can only emphasize, in my turn, the great importance, from all standpoints, of the systematic consideration of the intake and output of chlorides and water in renal disease.

The prognostic value of the estimation of the content of the blood in incoagulable nitrogen will probably be considerably enhanced through the recent introduction by Denis and Folin of simpler and more accurate methods of study.

All observations of the last three years have especially convinced us of the real diagnostic and prognostic value of the 'phthalein test of Rowntree and Geraghty. It is simple and easily carried out, and it appears to be a fairly reliable index of the renal function at the time of its application. The interesting parallelism between the 'phthalein excretion and the incoagulable nitrogen content in the blood, pointed out yesterday at the meeting of the American Society for Clinical Investigation, by Frothingham, will be remembered by those who were present. In Frothingham's experiments the increase in the incoagulable nitrogen appears a little later than the decrease in the 'phthalein output, but follows it very closely.

The elimination of 'phthalein is materially reduced in severe passive congestion of the kidney; it increases, however, immediately with periods of improvement, that which does not occur when sufficient damage has been done permanently to impair the renal function.

The detection of a low 'phthalein output, in some instances where there is no question of chronic passive congestion, may be of great importance from a diagnostic and prognostic standpoint. How important this may be, may be illustrated by referring again to a case mentioned by Dr. Rowntree: The patient was a boy, twelve years of age, who was admitted to the Johns Hopkins Hospital two and a half years ago, complaining of polydipsia and polyuria of several years' duration. For two years, the child had complained of pain in his legs, rather sharp in character and interfering with his walking. When he entered he was passing about 2,500 c.c. of urine in the twenty-four hours, of a specific gravity of about 1005, without albumen and without formed elements in the sediment.
The physical examination showed a pale boy with rather dry skin and with no demonstrable cardiac hypertrophy. His maximum blood pressure was ninety-five,—the radial arteries were, however, palpable, and thicker than one ordinarily sees in a small boy. The eye grounds showed no changes. The 'phthalein test, a week after entry, showed a total excretion in two hours of 7 per cent., and on the following day, the excretion was but 3.1 per cent. The test enabled us properly to interpret symptoms that we might well otherwise have regarded as those of diabetes insipidus. Within a day or two, the quantity of urine began to diminish, a trace of albumen appeared, and, inside of a week, the boy died in uraemic coma.

At the medical clinic of the Johns Hopkins University, we have already followed to autopsy probably fifty cases in which the 'phthalein test has been carefully made. In many instances, our ante-mortem opinion as to the extent of renal change, based upon the studies previously referred to, has been recorded. We are at present tabulating these cases, in the hope that conclusions of some value may be justified.

As Dr. Janeway has pointed out, we are concerned here in the main with chronic progressive disease, the aetiology of which is still, in many instances, uncertain, with conditions to combat which we have, at present, few weapons of decisive value. With what means we have now at our command, we have considerable power to detect renal disease. The most important immediate question which confronts us in many cases is as to the extent of the damage done and what is the outlook for the future. Let us not forget that these tests are tests of function and not tests of anatomical change. And, after all, that which is important for us to know is not so much what the kidney looks like, but how permanently are its functions impaired, and especially, what are the limits of its present powers, and how long may they be expected to last—when may we look for the onset of fatal decompensation? Here we must acknowledge still our serious limitations, for we can not invariably test the limits of functional capacity any more than we can test the exact limits of the compensatory power of the heart muscle. How far we can approach this has been brought out by Dr. Rowntree and by Dr. Christian. These are, however, questions of special importance in slow chronic nephritis.

When the excretion of lactose is suppressed, when the 'phthalein excretion is under 10 per cent. in two hours, where a previous per-
sistent vascular hyposthenuria has begun to disappear, where the urea content of the blood is high, the question is simple. But where the polyuria still persists, where the blood pressure is high, the lactose excretion delayed and the 'phthalein excretion moderately reduced, we are often asked: What is the outlook for life? How near are we to the danger line? These questions are not always easy to answer, for there are indications that occasionally decompensation may be sudden and unsuspected as it may be at times in disease of the heart muscle.

Nevertheless, such cases are exceptional, and I believe that to-day, thanks to the revival of the study of renal function, we are able to distinguish early disease of the kidney with greater accuracy, to estimate its extent more surely, and to prognosticate its future course more safely than we were a few years ago. More than this, as Dr. Janeway, especially, has pointed out, we have learned in some ways to treat our patients better, to improve materially their comfort, and to increase their chances of survival.

Of especial importance, it seems to me, from the therapeutic standpoint, are the observations of Mosenthal and Schlayer, which have been referred to by Dr. Janeway, emphasizing as they do and explaining the harm that may be done by undue persistence in the use of diuretics in renal disease. In every-day practice we have learned that the careless use of diuretics may be injurious, but the clear experimental demonstration of the reaction of the diseased or fatigued kidney to over-stimulation is a suggestive and helpful contribution.

**Dr. Mosenthal (New York):** It is somewhat difficult to describe what occurred in these experiments, alluded to by Dr. Thayer, without adequate charts, but I will attempt to do so. In cases of human nephritis it is found that after repeated administration of diuretics the kidney not only frequently fails to react with diuresis to the later doses of the drugs, but that there may be a diminution of the amount of urine secreted. Such a fatigued condition, as it may be termed, is brought about by the diuretics given as drugs, caffeine, etc., as well as by those taken in in the food as salt, water, etc. As an example of the latter the cases of oedema due to primary salt retention, now treated according to the precepts of Widal and Strauss, are familiar to all.
It was determined to find out if experiment could throw any light upon this subject. Two poisons which produce nephritis were used: potassium chromate and uranium acetate. It soon developed that the damaged kidney could be fatigued in different ways. The condition of the kidney as determined by the form of poison injected, the number of doses of the diuretics as well as their strength, were all important factors in developing kidney fatigue. Using salt and caffeine as diuretics two distinct types of fatigue were developed, the one brought about by salt and broken through by caffeine, the other in which the reverse held true. It was always possible to predict that the rabbits poisoned with uranium held true to the former type, those with chromium to the latter.

Exhibiting such an extreme variation in function it is rather surprising that the histological picture of these two forms of nephritis is very much the same. Transferring these observations to human nephritis it is obvious that except in the instances of the "Widal" or "Strauss" cases referred to above we do not know which diuretics will be of value in producing a flow of urine. If the drugs are employed in too high dosage or too frequently, more harm may be done than good, the urinary secretion may be diminished or even completely suppressed. It is therefore necessary for the intelligent treatment of these cases to use the various diuretics in small doses and by comparing the twenty-four hourly output of fluid with the intake to note the exact effect that is being achieved and accordingly increase, diminish or change the medication used. It is the nearest approach we have towards furnishing a rational drug therapy at the present time.

Dr. Henry A. Christian (Boston): I should like to emphasize further the damage that can be done to patients with nephritis by using diuretic drugs. All forms of diuretic drugs are capable of injuring patients with nephritis. That is a matter that we observed in our patients in the wards. It is a matter that we can demonstrate experimentally on animals.

Caffeine, diuretin, theocin, potassium acetate, etc., administered to animals which have severe nephritis, will materially shorten the lives of the animals. In other words, the injudicious use of any diuretic, far from being a benefit, may be distinctly injurious to the patient. Naturally, that is more definitely the case in patients with acute nephritis or chronic nephritis with acute exacerbations,
than in patients with chronic nephritis. It seems very probable that the functional study of the kidney is to give us a considerable insight into this question of the use of diuretics. Until we get more information on the subject, I am very certain that we shall do as we have done in the past: sometimes injure, and not benefit the patients, by using diuretics. I refer to the simple diuretics, and I refer to them as used in ordinary therapeutic doses, and not in very large doses. While we have shown in our experimental animals an actual increase in the anatomical lesion in the kidney, due to the use of these drugs, an anatomical lesion is not a very good measure of the disturbance in kidney function; but, when we have it, we can be certain that we have produced extensive functional disturbance. I should like to emphasize the point that we can do great damage by using diuretics injudiciously.

Dr. Theodore C. Janeway (New York): I welcome the opportunity to say, in closing, a word that I was unable to say in my part of the discussion. It is this: I should like to have it clearly understood that these functional kidney tests are divided strictly into two groups, and that they proceed to the solution of two wholly different problems. The test brought out by Dr. Rowntree is a test which aims at the solution of the old, pressing clinical problem, the prognosis, especially as a guide to surgical procedure. It is admirable and answers that need better than anything else that we possess to-day. From the medical standpoint the test is a rough quantitative measure of total kidney function—whatever that may be; I do not think we are in a position at the present time to say what is the total kidney function. It answers to the diagnostic need presented by patients with cerebral symptoms—whether due to focal vascular brain lesions, or to the toxic states which we call uræmia. I recall two interesting examples. One was a patient with high albuminuria, extreme headache, and the general picture of nephritis, who excreted phthalein. The headache persisted until the spinal fluid was drawn and it was found to be yellow tinged. She had had an old cerebral hemorrhage. The patient fell into a state of acute coma and died twelve hours later. At autopsy, a clot was found on the floor of one lateral ventricle, and the other ventricle was full of blood. The condition here is a widespread vascular disease, and sometimes the kidneys are spared remarkably. The phthalein test helps to clear up these
types. In addition I have seen liver disease with terminal coma discriminated by the phthalein finding of 70 to 80 per cent., and verified shortly by the autopsy. It has shown that chronic passive congestion is a real disease of the kidneys and not merely a functional sequel, the result of lesions elsewhere. The phthalein test shows us what the symptoms have always shown us, that it is a state dependent on anatomical lesions, well defined, and of practical importance.

The work of Schlayer, on the other hand, has proceeded from an entirely different standpoint, a fundamental one to medical men, but not of particular interest to the surgeon; that is the standpoint of the qualitative analysis of the disturbance in function within the kidney, which we must remember is both a compound and a complex organ. The individual kidney unit, the glomerulo-tubular structure, is highly complex. Up to the present time, normal physiology has not solved the problem of the correlation of function with anatomical differentiation of structure in the kidney unit. Until it does, we are in no position to demand of tests, in complicated pathological states, that they shall solve the same problem. What I think is going to come of this study of the physiology of the kidney is what resulted from the study of the physiology of the central nervous system. The careful study of the results in the focal lesions of the central nervous system and tract degenerations has made possible the greatest contribution to our knowledge of human physiology—cerebral localization. If we of the medical clinic coöperate with our colleagues, the pathologists in the autopsy room, and carry out over long periods of years the most exact functional tests of all kinds, at all times, not aiming at immediately practical results but at as clear an analysis of the functional disturbance as is possible; and in the end we are able in different institutions to bring together large groups of cases that have been studied for years, with the eventual histological findings in the kidney, we may do what the brain pathologists have done—add vastly to the understanding of the normal secretory activity of the kidney and its localization in essentially differentiated anatomical structures.
THE PRESIDENT'S ADDRESS.

WILLIAM C. GORGAS, M.D., LL.D.,
Ancon, Canal Zone.

SANITATION AT PANAMA AS IT RELATES TO SANITATION IN THE TROPICS GENERALLY.

I appreciate highly this opportunity of addressing this body on a subject that seems to me of so much importance as the effect that the sanitary work done by the United States at Panama is going to have upon the sanitation of the tropics generally.

My argument will be that Panama in 1904, when the United States began the construction of the Panama Canal, was universally looked upon as being one of the most unhealthy spots in all the tropical world; that this reputation was not undeserved but was warranted by the facts in the case; that the sanitary measures put into effect by the United States have enabled the constructors of the Canal to proceed for the past nine years with no greater loss from death and disease than would have occurred if the same work were being carried forward in most parts of the temperate zone; that this work has been accomplished at no very great expense; that, therefore, similar results can be obtained either by communities or individuals in any other part of the tropics.

That part of the Isthmus where the Canal is being constructed has been the point on the Isthmus where has lain the main route of crossing from the Atlantic to the Pacific since about 1520. At that date the city of Panama (old) was founded on the south coast and that of Nombre-de-Dois on the North. A highway was constructed from Panama City north to Cruces, on the Chagres river, twenty-two miles; from there boat was taken to the mouth of the Chagres river and then east to Nombre, some one hundred and twenty miles all told. This route was continuously used up to the construction of the railroad in 1855,—over three hundred years. For the past sixty years this route has been entirely abandoned and has consequently been covered with jungle. Still the pavement
of the roadway remains intact for long distances. About three years ago, with machete men to cut a passage through the jungle, Col. Sibert and myself crossed on this old road from Panama to Cruces. By following the old pavement we found little difficulty in keeping to the old road. During all the Spanish colonial period, from 1520 to 1820, a steady stream of unacclimated Spanish officials, soldiers and merchants, were going and coming over this route from the great Inca Empire in Western South America, Western Mexico and the Philippines. Afterwards the construction of the railroad and the rush to the gold fields of California caused another great influx of unacclimated persons from 1850 to 1870. But the greatest number of unacclimated persons ever on the Isthmus at one time was during the active period of the French Canal Work, from 1880 to 1890. During this whole period of nearly four hundred years the infection of yellow fever was present in Panama and the constant presence of large numbers of unacclimated gave it abundant food for spread.

No accurate statistics are attainable as to mortality during these earlier periods but all accounts agree that the Isthmus was a most unhealthy place from its first settlement. It soon became infected with yellow fever and malaria and this constant stream of unacclimated persons kept up the infection. During most of the Colonial period a great fair was held once a year at Porto Bello. There the merchants from all the Spanish colonies supplied by Panama, collected during the month of August. There was also collected all the bullion accumulated during the year by the Colonial Viceroys as tribute to the crown from the various Spanish Colonies. The fleet from Spain came in and during a month Spanish goods were exchanged with Colonial merchants for the products of the colonies, the bullion was loaded aboard, and the fleet sailed for Spain. During this month old writers say that ten or twelve thousand people were crowded into the town. After the fair was over the town was abandoned to the military garrison and a few hundred care-takers for the buildings. The reason assigned for the limit of the fair to a month was that, in general, by this time the crews were so depleted from disease that they had barely sufficient force left to navigate the ships. If they remained longer they would not have force enough to get away. This at the time was one of the great fairs of the world, very similar to the great fair at Novgorod, Russia.
Up to the time the United States took charge no statistics had been kept but many instances are recorded which amply demonstrate the unhealthy condition which invariably resulted when unacclimated people were brought to the Isthmus. Mr. Tomes, a newspaper correspondent, came down as the guest of the Railroad at its formal opening in 1855. He states that during construction the railroad brought over 800 Chinese. He gives the details, and a rather vivid description of their suffering from the health conditions they met on the Isthmus. He describes how, on this account numbers of them committed suicide, and states that at the end of a few weeks hardly two hundred were left, and that these were so debilitated by disease that they were useless to the company and had to be sent away. He goes on to say: "I never met with a wholesome-looking person among all those engaged upon the railroad. There was not one whose constitution had not been sapped by disease, and all, without exception, are in the almost daily habit of taking medicine to drive away the ever-recurrent fever and ague."

In 1852 the Fourth Infantry was transferred from New York to San Francisco via Panama. Capt. U. S. Grant (later the distinguished general) was quartermaster of the regiment. Dr. C. S. Tripler, afterwards very well and favorably known in the medical corps of the Army, was the surgeon. His official report describes very vividly the hardships of the trip across the Isthmus due to disease and climatic conditions. Out of a total force of 800 they lost from death, 80; 10 per cent. from the time of leaving Aspinwall till arrival at San Francisco.

The Superintendent of the Panama Railroad had his three sisters visit him at Colon in 1903. They contracted yellow fever and within a month all died.

The first French Chief Engineer, Mr. Dangler, brought to the Isthmus his wife and three children. Within six months all had died of yellow fever.

The Mother Superior of the French Sisters nursing at Ancon Hospital told me that she had come out with twenty-four sisters. Within a few years twenty-one had died of disease, mostly yellow fever.

One of the French Engineers who was still on the Isthmus when we first came told me that he came to the Isthmus with a party of seventeen young engineers. Within a month they had all died of yellow fever except himself.
SANITATION AT PANAMA.

The historian Froude states after a visit to the Isthmus in 1888: "In all the world there is not perhaps, now concentrated in any single spot, so much swindling and villainy, so much foul disease, such a hideous dung-heap of moral and physical abomination, as in the scene of this far-famed undertaking of nineteenth-century engineering,—the scene of operations is a damp tropical jungle, intensely hot, swarming with mosquitoes, snakes, alligators, scorpions and centipeds, the home, even as nature made it, of yellow fever, typhus, and dysentery, and now made immeasurably more deadly by multitudes of people who crowd thither."

The West Indian Pilot, an official publication for the guidance of mariners, in its edition for 1903 states: "The Panama Canal District is one of the hottest, wettest and most feverish regions in existence. Intermittent and malignant fevers are prevalent and there is an epidemic of yellow fever at times. The death rate under normal conditions is large."

Albert Edwards writes, speaking of the engineering difficulties under the French: "But these complications, serious as they were, were mere flyspecks in comparison to the death roll from yellow and malarial fever."

Mr. Bunau-Varilla, the French Chief Engineer, writes: "In September the diseases and death continued their work. The director of works, gravely ill himself, had to return to France, and so I was forced to assume the functions of general administration, with a working force decimated by disease and desertions.

Two talented engineers, M. M. Petit and Sordoillet were sent to me from Paris to take the post of division chiefs. Their coming had made me hope for seriously needed reinforcement, but unhappily, having arrived together, they were together taken to the cemetery fifteen days later, having fallen victims to the fatal malady which had so terribly torn open the ranks of our forces."

The only thing like general statistics that we have of this period are the records of the British Legation. The British minister during this period administered all estates of British subjects dying on the Isthmus. The large majority of our employees are British subjects from the West Indies. The same was the condition under the French. From this date I find that the French lost 22,000 employees during the active period of the Old Company, from 1881 to 1889. This would give a rate of about 240 per thousand per annum.
In thus summing up the health conditions on the Isthmus anterior to the year 1904, I do not wish to be vainglorious and take too much credit for ourselves. To accomplish what we have accomplished it was necessary that great discoveries of Ronald Ross and his co-workers and Reed and his Board should have been made. If we had done the work when the French did we could have done no better. All the world in 1800, at the time the French commenced work on the Isthmus, was ignorant of the method of the transmission of yellow fever and malaria. The gallantry of the French in facing the conditions they did on the Isthmus during the period of construction under the Old Company cannot be too greatly praised. Every young Frenchman in coming to the Isthmus knew that the chances were three to one that he would not survive six months. Yet there was no hesitation; they bravely faced the conditions; did as good and faithful work as it was possible for any body of men to do; and our records on the Isthmus show that about three out of four have left their bones near the work which they so faithfully and ably executed.

This was the state of affairs when we took over the work in May, 1904. The Isthmus was a place where an unacclimatized person could not live. In the process of becoming acclimatized, three out of four Europeans would die. Yellow fever, dysentery and malaria were rife. As the construction force was brought in, these diseases spread among them and deaths became numerous. It looked as if we were going to have the same experience as did all our predecessors, that three out of four of us were going to die of the diseases of the country. At first each man thought he was going to be the one who was going to survive, but as yellow fever spread and hardships increased, a feeling of depression began to pervade the whole force and each man began to feel pretty sure that he was going to be one of the three who was going to die in the process of getting acclimated. Demoralization reached its maximum when we had been on the Isthmus about a year. Several of the highest officials had recently died of yellow fever, others had left the work and gone home. In June, 1905 it looked to me as if the work would have to stop, for a time at any rate. Every possible space on ships going home was crowded to its utmost capacity with men who had become discouraged and given up. Among these were some of the highest officials. In 1906 the death rate among our negro employees had risen to 72 per thousand. A
writer in the Independent, describing the condition of affairs about this time, says: "The combined effect of all these difficulties, discomforts and dangers was the spring panic. Some perfectly well men came to the hospital in great fright and demanded admittance because they knew they had yellow fever. Fortunately the imagination is not powerful enough to create a single one of the minute organisms which are the cause of disease, and, so with the best intentions, they were not able to develop a case of yellow fever.

Men crowded the returning ships, paid high premiums for return tickets, or took deck passage for Jamaica and worked their way home.

Fear is contagious. Three or four men from the same room or table would be seized with the desire to go home, and would leave on the first train for Colon. Some assumed an attitude of indifference and bravado and disregarded all sanitary rules. 'Well, who's dead this morning,' became a salutation and the toast of the officers in India at the time of the plague was heard: 'Here's to the dead already, and here's to the next to die.' But there were those who 'stuck it out.' Neither cowards nor braggarts, they swallowed quinine until they were deaf to the hum of the loaded mosquito and went quietly about their work, two men's work or more. The orders they got were mostly signed by 'Acting' official. There were numerous changings of plans, shiftings of departments. Good men were suddenly dropped. Incompetent men promoted without cause. The new men being sent down from Washington were less promising than before. But sometimes they did not land. They would hear when they reached Colon how things were or be scared by smoking-room stories on the voyage down, and they would stay on the ship, paying their own passage back and forfeiting their wages. There was a feeling of discouragement in the air. There were those who argued that the Canal would never be finished; that the Washington people were keeping up a show of doing something for the graft they got out of it and men in charge at the Isthmus were railroad men sent down on purpose to impede the work."

I am proud to be able to state that during all this trying period there was not a single instance of desertion or of showing the white feather among all our doctors and nurses or elsewhere in the Sanitary Department. The Sanitary Department never lost hope. We knew absolutely from our experience in Havana that
if we could only get the opportunity to put the measures we had taken there into effect the result would be the same. But at this time I began to fear that we would not get this opportunity. While the Sanitary Department was in pretty good working order by this time, it seemed impossible for the various coördinate departments, and particularly the supply departments in Washington, to get into any sort of shape at all. I, having known for a year before the work was turned over by the French that I was to have charge of the Sanitation, came to the Isthmus while the French were still in charge, as one of the Board consisting of Dr. Ross, U. S. N., Dr. La Garde, U. S. A., and Major Gillette, U. S. A. The board spent a month looking over the ground and drew up a plan for sanitation.

The Commission gave me authority to purchase some fifty thousand dollars worth of supplies and to employ some fifty men. These we took with us to the Isthmus in the beginning. With this start and with what we could purchase on the Isthmus, we managed to get pretty well organized by the end of the year. But in the other departments the heads were appointed late and came to the Isthmus with no idea of local conditions. When they got here they found that they were unable to get either personnel or equipment, and so were entirely unable to perform their functions as far as the sanitary department was concerned. To add to our difficulties, about this time, June, 1905, the Executive Committee of the Commission recommended to the Secretary of War, that as the Sanitary Department was working on impracticable theories, Dr. Carter and myself and the men who thought with us,—believed in the mosquito theory of yellow fever—should be relieved and men with more practical ideas put in our places.

The profession, thru the American Medical Association, supported the Department most vigorously. The matter was carried to the President and he decided that the mosquito theory was the proper plan to be pursued, that the men then in charge of Sanitation must remain in charge and get the vigorous support of the Executive Committee. Mr. Roosevelt, who was then in the Presidential chair, was thoroughly familiar with the work in Cuba, and believed that the mosquito theory had been demonstrated beyond peradventure. Fortunately for us, about this time our work began to show its results. Yellow fever began steadily to decline. In November, 1905, we had our last case of yellow fever in the city of Panama.
and in May of 1906 our last case in Colon. During 1906 the Sanitary Department was raised to its maximum efficiency and by May, 1907, the sanitary work had been accomplished. The death rate from disease among our employees has been:

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These figures demonstrate that by 1908 we had a force of thirty-eight thousand employees on the Isthmus who were working in the sun, rain and weather at the hardest kind of labor, with a death rate from disease of 8.68, not any greater than the same men doing the same work would have had in the United States.

It is interesting to speculate upon what would have taken place if the President and Secretary of War had acted in accordance with the recommendations of the Executive Committee and decapitated the men then in charge.

At this time the mosquito theory was not generally accepted. In the Southern States there was a considerable number of physicians who had seen a great deal of yellow fever, and considered themselves, and were looked upon by their communities, as having special knowledge in this disease. These men, in general, had not in 1905 accepted the mosquito theory of the transmission of yellow fever. One of these gentlemen had been settled upon by the Chairman of the Commission as my successor. While this gentleman was a most competent and distinguished health officer he did not believe in the mosquito theory at that time, and would no doubt have put into effect the methods to which he was accustomed and in which he believed. These methods were based upon the belief that yellow fever was preeminently a disease due to filth. We know from our severe lesson at Havana that these methods can have no effect where we have a large amount of non-immune material present. By December, 1906, we had nine thousand non-immune connected with the Commission, of whom six thousand were Americans. It is highly probable that half of these would
have died of yellow fever had sanitation remained as it was in 1905. This would certainly have involved a suspension of the work till conditions could have been corrected, thereby causing a delay in the completion of the Canal of at least two years, and very probably public opinion would not have supported a project that involved such loss of life and the work would have been delayed indefinitely.

The actual expense of the measures that have accomplished these results has not been large, about three hundred and sixty-five thousand dollars per year or about one cent per day per capita. The expense of sanitation on the Isthmus is frequently spoken of as being large. This comes about from the fact that official reports give the expense of the Sanitary Department as having averaged about $1,600,000.00 a year. And very naturally, in reading this report one assumes that the expense of Sanitation and the expense of the Sanitary Department are synonymous, but not more than about one-fifth of the expense of the Sanitary Department is involved directly in the measures that have resulted in the eradication of yellow fever and the controlling of malaria. More than half the expense of the Department is involved in the care of the eighteen hundred sick that we have constantly on hand.

It is quite evident that if people can be protected against tropical conditions at Panama the same thing can be accomplished in any other part of the tropics. The results at Panama are so in the limelight that they are attracting attention from all parts of the tropics. As population begins to understand that it can protect itself against disease in the tropics at no greater effort or expense than is required against cold in the northern countries of the world, it will seek tropical countries for permanent abode. The returns for a given amount of labor applied to agriculture in the tropics are much larger than in the temperate zones of the earth. Health conditions being about equal, the general recognition of this fact will inevitably attract population to the tropics, and in the course of time I expect to see great empires again develop in the tropics as was the case in the earlier history of man.
THE LIFE OF TISSUES OUTSIDE THE ORGANISM FROM THE EMBRYOLOGICAL STANDPOINT.

BY ROSS G. HARRISON, PH.D., M.D.

Yale University, New Haven, Connecticut.

The subject which we are assembled to discuss has come into prominence within the past few years, though the ideas underlying it are old and familiar. It would not be profitable on the present occasion to trace its history in detail, but it may be pointed out that the subject rests immediately upon one of the fundamental concepts of modern physiology, which ascribes some specific function to each organ and tissue of the body, an idea carried out more minutely in the cell theory, which sees in the higher organism an aggregation of structural units or cells, each with some part to play in the economy of the whole. It further rests upon the fact of the survival of parts after the death of the organism as a whole, a fact so strikingly brought to view in Galvani's famous observation on the frog's legs, so familiar to every boy in the notion that the snake's tail won't die till the sun goes down, and now a commonplace discussed in every textbook of physiology. Almost the whole of our knowledge of muscle-nerve physiology, and much of that of the action of the heart, is based upon experiments with surviving organs, and in surgery, where we have to do with changes involved in the repair of injured parts, including processes of growth and differentiation, the power of survival of tissues and organs and their transplantability to strange regions, even to other individuals, has long formed the basis of practical procedures. With this in mind it seems rather surprising that recent work upon the survival of small pieces of tissue, and their growth and differentiation outside of the parent body, should have attracted so much attention, but we can account for it by the way the individuality of the organism as a whole overshadows in our minds the less obvious fact that each one of us may be resolved into myriads

of cellular units with some definite structure and with autonomous powers.

One of the most striking and interesting things described by Max Schultze\(^2\) in his study of protoplasm was the fact that certain cells of the body, the leucocytes, exhibit activities of movement quite similar to those of some of the most primitive animals.\(^3\) You will all probably recall the absorbing interest which this comparison of the amœba and one of your own white blood cells aroused in your course in general biology. But unfortunately we possess even now, fifty years after this work of Schultze's, but scant direct knowledge of cellular activity. The microscope has revealed to us much of the structure of cells and organs, and physiological experiments have taught us the intricacies of the mechanisms of movement, secretion and sensation, but as compared with our knowledge of these fields, that of cell behavior is extraordinarily meager. It is in making up this lack in our knowledge that the methods which we are discussing to-day will find their principal application.

No less important than in the ordinary physiological activities for the maintenance of the individual is the rôle played by the cell in reproduction and development. Embryologists have traced the origin of the egg- and sperm-cells in the body of the parent, and have followed the stages in the transformation of the fertilized ovum into the adult, but here, too, our knowledge of the activities of the individual cell, and their mode of interaction in producing the mature organism, is but in its beginning, for the experimental analysis of these processes is a peculiarly difficult problem.

Aside from the investigations of Schultze, Ranvier and others, which dealt with the activities of surviving cells, principally leucocytes, and not with processes of growth and differentiation, the first studies upon the activities of cells when removed from the rest of the organism, were those of the experimental embryologists. This method of investigation was used by Roux\(^4\) about twenty-five years ago when he killed by puncturing with a hot needle one of the first two cells of the segmenting frog's egg, and studied the development of the surviving one. Various methods of isolation


\(^3\) The movement of leucocytes was first observed by Lieberkühn—Müller's Archiv, 1854, p. 13.

\(^4\) Virchow's Archiv, Bd. 114, 1888, p. 113.
of parts were practiced by many other embryologists, amongst whom Driesch, Wilson, Morgan, Zoja, Fischel and others early became prominent—the school known for a time as the "egg shakers." They shook or cut apart the cells of the developing embryo to determine what became of the isolated or remaining cells under the new conditions. The same idea underlies the work of Born, who first discovered that pieces of frog embryos could be transplanted or healed together in almost any combination imaginable, and who employed the method principally to study the effect of surrounding organs and tissues upon the development of parts. It was this same method that proved most effective in my first experimental studies of the development of the nervous system, though ultimately the exigencies of the problem demanded a further step, i.e., the complete isolation of the undifferentiated nerve cell from the rest of the organism, and its culture for a considerable period in an extraneous medium. The exact need for this experiment will be explained in a moment when the first slide is shown.

Logically, then, this method of isolation of cells or pieces of tissue is but the application of the method of the physiologist when an organ is isolated in order to find out its function, or that of the experimental embryologist when he isolates the blastomere of the segmenting egg to determine its developmental potencies. Technically, the method is an adaptation of one that has been for years familiar to the bacteriologist—the hanging drop culture. Any originality, therefore, that may be claimed for this work is due to a combination of ideas rather than to the introduction of any particularly new device.

You are familiar with the chief phases of the discussion which has taken place regarding the constitution of the nervous system and with the arguments for and against the neurone concept. The embryological phase of the problem may best be stated by reference to the first slide (Fig. 1) which is a copy of one of Held's figures. The figure represents semi-diagrammatically part of a cross section through an amphibian embryo, showing on the left two long nerve fibers arising from cells in the medullary cord. The upper one, a sensory nerve, extends outward between the muscle

plate and the epidermis; the other, a motor fiber, runs to the inner surface of the muscle plate. On the right two similar cells are represented, but the fibers are in an earlier stage of development, being much shorter. At this stage there are many cells which have no processes at all. According to the view of His, Ramon y Cajal, and, in general, those who hold to the neurone concept of the nervous system, the nerve fibers are formed by growing out from the ganglion cells by means of a sort of protoplasmic movement. You will notice, however, that in the figure, in between the organs of the body, there is a network of protoplasmic threads which, according to the view of Hensen, has its origin in protoplasmic bridges left between the cells as they divide. According to this view, the nerve-fiber is not an outgrowth of the cells, but is merely a differentiation in situ from the protoplasmic bridges. There is no protoplasmic movement, but merely a progressive differentiation.

The reason why it was necessary to separate the embryonic nerve-cells from the rest of the organism in order to determine their importance in the formation of the fiber was because these bridges completely pervade the embryonic body, so that within the body the neural tube cannot be entirely isolated from them, and without isolation it is not possible to determine what the nerve-cells, or neuroblasts, can do when they have no protoplasmic bridges to act upon. To accomplish this it was necessary to find a culture medium in which the isolated cells would live for some days and to devise some form of preparation that would permit of continuous study under high powers of magnification. The method used is as follows: Parts of the neural tube of frog embryos are cut out under the binocular microscope, and the pieces, which must be very small, are transplanted to a cover-slip, with a drop of lymph from an adult frog. The cover is then inverted over the hollow slide, and the lymph clots holding the tissue in place. When the procedure is carried out under aseptic precautions, the tissues remain alive in the lymph for many days and undergo marked transformations. Some hours after a preparation of this kind is made the activities of the cells become noticeable. They begin to move out from the mass of tissue and in the course of forty-eight hours they have usually formed a wide fringe of cells, sometimes

in sheets and sometimes forming a looser network. Figure 2 shows the most usual change which takes place in the cultures. The bit of tissue when implanted was a compact mass of cells about half a millimeter in diameter, but now after forty-eight hours the piece has spread out and flattened. Holes have been formed in the tissue due to local liquefaction of the clot and the tension of the fibrin threads from the periphery, as Burrows has shown. Moreover, certain differentiations are found to have taken place. This is important, for though the main object is to find out what takes place in the nerve cells, it is also necessary to observe what other tissues do under similar conditions in order to determine whether their behavior in culture media is comparable to their behavior in the embryonic body. This was found to be the case. Portions of the muscle plates were observed after several days to have differentiated into full-fledged muscle fibers with cross striations; epidermis cells differentiated functioning cilia and the peculiar cuticular border which is found on their outer surface, though entirely isolated from the rest of the body. Pigment cells differentiated in many preparations, remaining alive and undergoing slow changes of form for a number of weeks. It could be seen that the tissues were differentiating normally under the imposed conditions. Therefore, it seemed to be a safe method for studying these processes. Let us then consider nervous tissue and see how it behaves.

The development of the nerve fibers in culture is shown in the accompanying views (Fig. 3, 4, 5, 6 and 7) which represent successive stages of the same specimen. In the first stage (twenty-four hours after making the preparation) a stout protoplasmic filament was seen to extend out from a mass of cells (Fig. 3). Soon it became very active (Fig. 4), and ten hours later (Fig. 5) the outgrowths had increased greatly in length and four separate fibers could be counted. After twelve hours more (Fig. 6), and again after twelve hours (Fig. 7) or thirty-four hours after the first observation, further growth was noted. The figures also show a few loose cells, and fibrin threads, none of which, however, are connected with the fibers. The specimen was kept still longer under observation—until some of the fibers had attained a length of over a millimeter. The end of each fiber, as is particularly striking in Fig. 5, is enlarged into a mass of protoplasm with fine filaments, or pseudopodia, which undergo movements. This amoeboïd protoplasm is the mechanism by which the protoplasm
of the nerve cell is drawn out into the fiber. In some cases nerve elements, i.e. cells with attached nerve fibers, were observed completely separated from the main mass of tissue, and the lengthening of such fibers was also noted. In other cases very intricate plexuses of nerve fibers were seen, with frequent anastomosis between filaments. These anastomoses were formed and again broken off from time to time.

The next slide (Fig. 8) shows more clearly the character of the protoplasmic movement carried on by the active protoplasm at the end of the fibers. The sketches, taken at about eight minute intervals with a camera lucida, represents the end of a single nerve fiber from a culture of nerve tissue from a frog embryo. The oval outline is a red blood corpuscle which was caught firmly in the clot and served as a fixed landmark from which to measure the progression of the end of the fiber. The scale shows that the rate of movement was slightly less than one micron a minute.

To convince you that these are really nerve fibers the next slide will show (Fig. 9) such a structure taken from a section of a normal embryo. The similarity to the fibers found in the culture preparation removes any doubt that we are dealing with the same thing, especially when it is considered that, as pointed out above, other tissues of the embryo differentiate normally under these conditions, and that embryological nervous tissue is the only thing that gives rise to such fibers in the cultures. The next slide (Fig. 10), showing a figure by Burrows, gives the final proof. This is a group of nerves taken from a culture of the medullary tube of a chick embryo. The preparation was stained in Held's molybdenum hæmatoxylin and under a higher power shows most beautifully the specific structure of nerve fiber, the neuro-fibrillæ.

These studies on the histogenesis of nerves have been confirmed and extended by others, especially by Burrows, M. R. and W. H. Lewis, and Braus. Braus was able to cut fiber growing in the plasma clot and to show that the peripheral part thereafter undergoes rapid degeneration. Ingebrigtsen has studied this more

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10 Anatomical Record, Vol. 6, 1912, p. 7.
fully and has given some beautiful figures of degenerating nerve plexuses. He has also shown that after cutting off the fibers from their cells of origin new ones may grow out into the medium.

In summing up this work on the cultivation of tissues as far as it concerns the development of the nervous system, it may be said without reserve that it has completely proved the correctness of the conception of His and Ramon y Cajal.

The development of the nerve fiber is brought about by a mode of protoplasmic movement. A small mass of active protoplasm is sent out from the cell, and by its progression it draws out the cell substance into a long thread, the nerve fiber. The same general type of movement, which is seen in the locomotion of the amœba or of the white blood corpuscle, and which plays such an important part in the healing of epithelial wounds, is therefore one of the essential factors in the embryonic development and regeneration of nerve fibers.

While the methods which I had used in the work just described were sufficient to solve the problem in mind, they had imperfections which prevented their wider application. The work would have stood still at that point had it not been for the improvements introduced by Dr. M. T. Burrows while working in the Sheffield Biological Laboratory at Yale during the spring and summer of 1910. Burrows has made many improvements in technique, but the essential step in advance was the perfection of a method of obtaining fresh unclotted blood plasma and using that as a culture medium in place of lymph. The plasma could be obtained from any species of vertebrate, while except from the frog, lymph was obtainable only with great difficulty. Besides, plasma could be obtained in almost any quantity, so that sufficient medium could be had to carry on extensive series of experiments with exactly the same medium, or with a medium modified in a known way. This was impossible with lymph. Burrows's first work was done with tissues from the chick embryo, a warm-blooded animal, and very interesting results were obtained, not only extending the work on the development of nerves but also including important observations on the occurrence of cell division, and on the movements of the isolated heart.14

After this pioneer work had been accomplished it became a simple matter to apply the method to the study of mammalian tissues. Carrel and Burrows\textsuperscript{15} carried on an extensive series of investigations, using adult as well as embryonic tissue, and showed that practically any tissue of any species, as well as tumor cells, might be cultivated in the same manner. The field was thus cleared for the study of a great variety of problems by this method. The methods which Dr. L. Loeb\textsuperscript{16} had devised some years prior to all of this work, and had employed to study factors influencing the growth of epithelial and tumor cells, were quite different from those just described and did not permit of the direct and continued observation of the growing tissues, though of course logically there is a similar underlying idea in the study of the behavior of cells and tissues when removed from the disturbing influences of the rest of the organism.

The most common criticism made of the results of these studies has been that the activities which take place in the tissue cultures are not normal because the conditions are so different from those found in the body of the organism. It has been stated that the changes observed are those of degeneration and necrosis, or at best mere survival phenomena. That the latter is not true is, however, not difficult to show. Loeb, for instance, in his first studies of epithelial growth in agar and blood clots showed that normal cell division by mitosis took place. Burrows described and figured plainly mitotic figures in his early cultures of tissues from the chick embryo (Fig. 11), and has since, as he will no doubt describe to you to-day, been able to observe the whole act of cell division in the live culture, and to make important observations on the physico-chemical factors involved. Oppel\textsuperscript{17} has also made a special point of this in his studies on the "explantation" of mammalian tissues (Fig. 12).

Cultures of tissues show, therefore, not only the normal processes of differentiation as they occur in the embryonic body, but also normal multiplication of the tissue elements. In fact, the increase in the number of cells may be very great when the nutrient medium is exactly suited, especially when waste products are eliminated by


\textsuperscript{16}Archiv f. Entwicklungsmechanik, Bd. 13, 1902.

\textsuperscript{17}Archiv f. Entwicklungsmechanik, Bd. 34, 1912.
repeated transplantation. The matter of longevity has not, however, been worked out fully. The oldest preparations in my original experiments remained alive over five weeks without any treatment, though after the first ten days but little activity was shown. Since then it has been found possible to keep cultures alive a much longer time, as Carrel's work has shown. We are, however, not justified in referring to the cells as potentially immortal or even in speaking of the prolongation of life by artificial means, at least not until we are able to keep the cellular elements alive in cultures for a period exceeding the duration of life of the organism from which they are taken. There is at present no reason to suppose this cannot be done, but it simply has not been done as yet.

While work with these methods has been successful in respect to the study of cell differentiation, cell movement and cell division, it has failed to be of use in the study of the gross form of organs. Embryonic cells from the medullary cord give rise to fibers in plasma, but they do not arrange themselves into the typical structures of the nervous system—such as the cerebrum, the cerebellum or spinal cord—nor do they show even the beginnings of the embryonic brain vesicles. We should not, however, be too much discouraged by this. In sponges and coelenterates H. V. Wilson has shown that new complete individuals may develop from isolated cells taken from adult specimens. Wilson cut up sponges and hydroid polyps and squeezed the pieces through very fine bolting cloth, thereby breaking them up into very small fragments or even into single cells. He found that such cells in cultures kept in sea water would segregate into small masses which then gradually developed into complete organisms of normal form as shown in this slide (Fig. 13). We do not know how high in the scale of animals this process may be carried out. Much will depend upon the improvements which can be made in the methods.

The next slide (Fig. 14), which is shown in order to point out one line along which our methods may be improved, represents a piece of apparatus which has been devised by Burrows for the purpose of affording the tissue culture a continuous supply of fresh nutrient medium. Instead of a plain hanging drop in an hermeti-
cally sealed cell, there is a much larger culture chamber, on the top of which there runs a wick which carries the culture fluid from a supplying chamber and discharges it into a receiving chamber. The tissue to be studied is planted amongst the fibers of the wick, which are teased apart where it runs across the top of the culture chamber. By appropriate devices the whole system may be kept sterile. The apparatus is so arranged that the culture may be kept under observation even with high powers of the microscope. It is obvious that the nutrient fluid may be modified at will and the effects of known substances upon the proliferation, movement, differentiation, and even upon the metabolism, of cells may be studied.

The relation of the chemical constituents of the medium to the behavior of the tissues of the chick embryo has been carefully investigated by M. R. and W. H. Lewis, who made the remarkable discovery that cell movement and differentiation may take place for a considerable time in purely inorganic media. The tissues will maintain themselves and undergo differentiation, as for instance the formation of nerve fibers, even in solutions of pure sodium chloride, and that of quite a wide range of concentration, though they do better in solutions which contain small quantities of calcium, potassium chloride and sodium bicarbonate. Still more activity is displayed in solutions to which certain organic substances, such as the sugars or protein decomposition products, are added. This is of course what would be expected. In the purely inorganic media the tissues are living upon themselves, and though the cells may even divide, spread out and differentiate, it is hardly justifiable to speak of their activities under such conditions as growth, though in proper organic nutrient media, such as plasma, actual growth or increase of volume undoubtedly does take place. Fig. 15, after Lewis, shows a beautiful preparation of sympathetic nerves which have differentiated on the surface of the cover slip from a piece of the intestine of a chick embryo in a saline medium.

The culture methods offer a promising means for the study of another group of phenomena, the response of cells to directive stimuli. Such factors as light, heat, the galvanic current, chemical substances and contact with solid objects are known to influence the direction and velocity of movements of various organisms and, as is quite familiar, some of these factors have been invoked to explain the behavior of leucocytes within the body, both in normal

21 Anatomical Record, Vol. 5, 1911.
processes and in various phases of inflammation. It is natural to suppose that they play a part in embryonic development though the basis for this opinion is largely inferential. The most direct evidence we have bearing upon these questions is the reaction of cells to solid objects in culture media. In my earliest experiments there was indication that, in order for movement and differentiation to take place, the tissues must have some solid support, for it was only in those specimens in which the lymph had clotted well that good results were obtained. This suggested a more exact study of the problem, which resulted in the proof that the factor of contact is really of essential importance.22

Experiments were made in sets of four. The fluid medium was the same in all. Only the solid support was varied. The tissue to be tested in each set was exactly the same. In the case described here the tissue was a small piece of the small intestine of a nine-day chick embryo. The first (Fig. 16) is a preparation cultivated in clotted blood plasma, and shows the characteristic ring formation with cells radiating in various directions. The second (Fig. 17) is a preparation in defibrinated serum in which the piece of tissue was kept in such a small drop that it remained in contact with the under surface of the cover slip. Here we find that the epithelial cells have spread out in a very thin membrane on the glass, a type of formation which Lewis has described in detail. In the third preparation (Fig. 18) defibrinated serum was also used but the drop was supported on a spider web. Here the cells are found upon the web fibers. In the fourth or control preparation (Fig. 19), also in defibrinated serum, a very large hanging drop was used so as to avoid contact with the cover slip. No growth has taken place. When the medium is varied, as for instance when saline solutions are substituted for blood serum, similar reactions to contact are observed. Examination of the spider web preparations under higher magnification (Fig. 20) shows that the cells are closely adapted to the course of the web fibers. They are often spindle-shaped and then they resemble very closely the sheath cells of Schwann upon embryonic nerve fibers. Where two web fibers cross, the shape of the cells is often tri- or quadri-polar.

The exact nature of this kind of response is uncertain. Burrows23 has subjected it to a further analysis and pointed out that the

23 Not yet published in full. See p. 83-84 of this volume.
phenomena may be largely explained by the action of the products of metabolism in the medium, particularly the production of acid substances, which may alter locally the surface tension of the cells and thus produce movement. This cannot be discussed in detail here, but whatever may be the explanation, the fact of reaction to solid substances stands out very clearly, and no doubt the same kind of reaction plays a rôle in development inside the body. This topic brings us again to the nerve problem discussed above. Experiments show that outgrowing nerve fibers, like cells of other embryonic tissues, require solid support for their movements. Pieces of the central nervous system of chick embryos planted in clotted plasma show usually a luxuriant growth of nerve fibers after twenty-four or forty-eight hours, while exactly similar pieces of tissue planted in large hanging drops of defibrinated serum show no growth at all. Growth takes place in fluid media only when contact with the glass coverslip or the bottom of a culture dish is maintained. These facts lead to a different interpretation of the meaning of the protoplasmic bridges within the embryo from that which Hensen,24 Held25 and others of their school have given. In sections of vertebrate embryos (Fig. 1) nerve fibers appear as if creeping along under the surface of the epithelium or wandering amongst the protoplasmic bridges as vines cling to a wall or entwine themselves in a trellis. In other words the function of the intercellular protoplasmic network is not to give substance to the developing nerve fiber but merely to afford it mechanical support. The results which have been described to-day, while forming but a beginning, will nevertheless suffice to show that in this new method we have an efficient means of studying problems of development. We can go much further by such experimental methods than we can by the mere observation of the so-called normal embryo. The old fear of getting hold of something that is abnormal must be cast aside, as obstructive to progress. If chemistry had stopped when it became necessary to go beyond the study of the "normal" substances found on the earth's surface, it would have been little but descriptive mineralogy. It is the same with the study of organisms and the processes of development. The individual, as

we find it in nature, is but an accident; it is a certain aggregate of living material which is able to adjust itself to the environment that it finds, just as the chemical substances found in nature are those that are stable or, in other words, adjusted to their environment. There are an infinite number of other chemical compounds that man can make under different conditions, and it is the study of their transformations that has made the science of chemistry. It is not too much to hope that a science of development may likewise be created, provided we go ahead and study its phenomena by every means of analysis at our command without regard to whether it is normal, i. e. whether it occurs as such in nature, or not.

To you, who are participants in the triumphs of modern medicine, which has not hesitated to avail itself of effective experimental methods, it may seem superfluous that this plea is made. Unfortunately, however, experimentation does not enjoy the confidence of all embryologists and anatomists.

To sum up in a word the substance of the foregoing, it may be said that the new methods of the study of cells and tissues by their isolation from the organism are throwing new light upon the phenomena of differentiation and cell division, growth and cell movement, all of which are fundamental factors of development. Those who are to follow, in discussing the subject from the physiological and pathological standpoints, will I trust make plain that the same fundamental properties of protoplasm are manifested in the functional activity of tissues, and in their pathological conditions, and that problems in these fields may be successfully attacked by the same methods of study.

EXPLANATION OF FIGURES

Fig. 1. Cross section through the spinal cord and adjacent portions of an axolotl embryo (after Held).

Fig. 2. Piece of tissue from frog embryo (medullary cord with small portions of muscle plates attached) cultivated in lymph; two days after preparation.

Figs. 3-7. Five views of the same preparation showing the development of nerve fibers from the frog embryo in a lymph culture.

Fig 3. Twenty-four hours.

Fig. 4. Twenty-five and a half hours.
Fig. 5. Thirty-four hours.
Fig. 6. Forty-six hours.
Fig. 7. Fifty-eight hours. Magnified less than the preceding figures.
Fig. 8. Seven successive views of the end of growing nerve fiber showing its change of shape and progression. Red blood corpuscle shown in outline marks a fixed point.
Fig. 9. End of nerve fiber as seen in a sagittal section of a young frog embryo.
Fig. 10. Group of nerve fibers which have grown from an isolated piece of neural tube of a chick embryo (after Burrows).
Fig. 11. Mitotic figure in a culture of mesenchyma of a chick embryo (after Burrows).
Fig. 12. Mitotic figures in plasma cultures of the spleen tissue of the cat (after Oppel).
Fig. 13. Polyps of Eudendrium which have grown from dissociated cells (after H. V. Wilson).
Fig. 14. Culture apparatus for the irrigation of tissues (after Burrows).
Fig. 15. Portion of sympathetic nerve plexus in a forty-two hour old culture of a piece of intestine of a six-day chick embryo (after Lewis).
Figs. 16-19. Four cultures of the duodenum of a nine-day chick embryo.
Fig. 16. In clotted plasma.
Fig. 17. In a small drop of defibrinated serum in contact with the cover slip.
Fig. 18. In defibrinated serum supported by a spider web.
Fig. 19. Control culture in defibrinated serum in a large hanging drop without contact with any solid object.
Fig. 20. Portion of Fig. 18 under higher magnification showing cells closely applied to the spider web fibers.
Fig. 8.
THE TISSUE CULTURE AS A PHYSIOLOGICAL METHOD.

MONTROSE T. BURROWS, M.D.

Anatomical Laboratory, Cornell University Medical College, New York City.

The original necessity that led to the invention of the tissue culture method by Harrison developed out of researches aiming towards the proof of the origin of the nerve fiber. For the final proof of this problem it was necessary to completely isolate the growing nerve from other tissue cells and at the same time be able to observe its movements.

The working hypothesis was derived from observations made on growing nerve in many of his operated embryos. Harrison thought that if naked nerve fibers could traverse a blood clot interposed in their path within the body they could likewise grow in a similar clot outside the body. Previous work upon the survival of cells in vitro had conclusively shown that many body cells could live apart from the animal organism. The necessity lay in finding a technique suitable for using this fact as a means to promote the knowledge of growth. Ranvier, by a method identical to that of Harrison, observed the movements of leucocytes in vitro, and later Joly, repeating Ranvier's experiment, using the blood of Triton, noted division in many of these blood cells. These authors failed apparently to recognize a broader application of their method and it was forgotten.

Other methods, as the one devised by Leo Loeb in 1898, were not applicable to the study of the living tissues while in the culture and were therefore of little advantage over the study of prepared tissues from the animal body. The tissue was placed in a test tube and observation was impossible except through later study of sectioned and stained material. The primary object in growing tissue outside the animal body is in order that it may be microscopically observed in the living condition; this object was not possible by Loeb's method.

The ease of observation, the tissue isolation and the narrow and easily regulated environment of the culture which Harrison described and had shown to be fully applicable for the study of
growth and differentiation of highly specialized tissues presented the more promising hopes. If it was possible to observe the growth and differentiation of the nerve fiber it was likely possible that many other cells could be studied and their conditions of function, growth and metabolism analyzed.

In the spring of 1910, through the kindness of Professor Harrison, I was allowed to take up a study of these cultures in his laboratory with the idea of more fully developing this method so as to make it applicable for a more careful physiological study of growth. The difficulties of such applications lay, as Harrison pointed out, in the lack of a suitable medium and tissue. It was primarily necessary to find a medium which would allow the use of a large number of tissues of other animals. The tissues must be dependent for nourishment upon the medium used.

Lymph, which Harrison had used, could be obtained from frogs but only in small quantities and its consistency varied widely at least in fibrin content, even in the different lymph sacs of the same individual. The medium which approached lymph most nearly in general consistency was blood plasma. This could be obtained from any animal and in quantities sufficient for the preparation of a large number of comparable cultures.

I found by the application of the well-known laws of blood coagulation that plasma could be readily prepared. Blood was collected directly from the heart, a vein or an artery through an oiled canula into a tube lined with a layer of paraffin and kept cold by surrounding it with ice. The chilled liquid blood was centrifugalized by placing the tubes in large centrifuge receptacles which were filled with salt, ice and water mixture. The supernatant plasma when free from cells was pipetted to a clean tube and preserved in the ice box. The plasma of frogs and chickens could be kept by such a method for days or months. Recently I have discarded the use of oil and paraffin. Clean glassware answers as well for the preparation of plasma from the blood of any animal and greater cleanliness is assured.

I continued this work with tissues of chick embryos. The embryos could be readily obtained and represented a warm-blooded animal. The tissue cells were nourished in nature by a vascular system. They thus differed from the tissues of frog embryos in not having a cellular yolk supply. Any extensive growth
TISSUE CULTURE AS A PHYSIOLOGICAL METHOD.

of such tissues when isolated in a culture must be dependant for nourishment upon food obtained from the media. The cells of the young embryo frogs studied by Harrison might, on the other hand, receive ample nourishment from the yolk contained within them.

The growth from pieces of the tissues of chick embryos was more extensive but essentially the same as Harrison had observed from pieces of frogs. It consisted in a survival and an extensive out-wandering of cells into the medium about the tissue. I was able to confirm by a study of pieces of the neural tube all previous observations made by Harrison as well as to observe other forms of cell activity most necessary for increasing the possibilities of study and for making more conclusive the proof of life in vitro. Mitotic division, not observed in cultures of frog tissues, was most common in cells which wandered into the medium from the tissues of chick embryos. The cultivated pieces of the hearts of embryos functioned. Rhythmical beating continued for many days, apparently to the exhaustion of the media.

Carrel and I, during the winter of 1910 and 1911, tested the applicability of this method to the study of adult tissues. We showed that plasma could be readily prepared from all animals and that tissue of both adult and embryonic mammals survived and showed activity in hanging drop cultures where either plasma of isoplastic or homoplastic origin was used. Malignant tumors were tested and their activity fully established. The animals used were chickens, rats, mice, guinea-pigs, dogs, cats and man. Many other laboratory animals have been carefully tested by other observers. The growths included both the epithelial and connective tissue cells. These observations have been fully confirmed by the work of Lambert and Hanes, Loeb and Addison, Braus, Weil, Hada, Oppel and others.

The tissues of all animals grow luxuriantly, excepting human tissues. The reaction of normal human tissues, whether embryonic, adult, carcinomatous or sarcomatous, is practically the same. There is rapid and complete liquefaction of the plasma clot. The entire clot may go into solution within two or three hours. Small growths may be observed but they consist only of a few cells wandering out over the cover glass. I tried in recent experiments to obtain growths by repeatedly transplanting the tissue to fresh media.
This gave no result. At each transfer the medium was liquefied until death of the tissue was in evidence. The dead tissue did not liquefy the medium. The clots remained firm about it for several weeks.

Simplification and further possibilities for a more careful analysis of growth were introduced by the work of Schorer, M. R. and W. H. Lewis. Schorer showed that nerve cells of chick embryos could be grown in agar. M. R. and W. H. Lewis confirmed this work and demonstrated growths of the tissues of embryo chickens in many liquid media, such as sodium chloride, Ringer's solution, Locke's solution and serum. It was interesting to note that the tissue grew even in widely different concentrations of pure sodium chloride, varying from two and one-fourth to seventeen parts per thousand. No growth took place without sodium chloride. The growth was prolonged and increased by addition of calcium and potassium. Additions of maltose or dextrose, or protein decomposition products, increase proliferation; bouillon agar increased it still more, while the most luxuriant growths were obtained in plasma.

The growths in Locke's solution or more complex synthetic media were often quite extensive. Some few mitotic figures were observed in the stained preparations.

The growth that took place about tissues in a plasmatic clot was practically the same as that growth seen from various tissues into a wound of the animal body. It is upon this similarity that the normality of tissue growth in vitro has been based. Connective tissue is active and grows generally as isolated cells into the surrounding media. The cell is most often spindle-shaped although irregularly shaped cells are not uncommon. All tissue cells grow quite characteristically to their kind. Epithelium from skin remains together in sheets or membranes. Few cells, however, often become separated and wander away as isolated elements. During their wandering they show some ameboid-like movements. The group form of the cells generally remains characteristic of the various sources from which they are taken. Thyroid epithelium tends generally to form tubes rather than membranes. These tubes are readily and easily distinguished from the tubular growths of kidney or other organs. Nerve cells invariably give rise to axis cylinder processes, as Harrison and I have shown for embryos and Marinesco and Minea for the spinal ganglia of mammals. Blood cells and their
close relatives from the spleen, bone marrow and lymph nodes wander out as isolated and very actively amœboid elements.

Reproduction has been observed in connective tissue cells, blood cells and epithelium of glands and skin. The most active reproduction is seen in cultures of malignant tumors and embryonic tissues.

The survival of all cells in these cultures depends upon their ability to react to the media. To reach a suitable environment for life and activity they must wander from the tissue into the areas of richer nutrient media. Adult striated muscle fails to show any extensive ability to move, while embryonic muscle shows both active amœboid movement and corresponding changes in the fibrin.

In a more recent article I have shown that the isolated heart muscle cells of the chick embryo not only migrate but they can divide as well as differentiate and beat rhythmically. A careful study of these cells has shown further that each of these various states of activity is associated with some definite change taking place or established in the fibrin clot of the culture. That such was the case was not only shown by direct observation but by the fact that the cell could be changed from one state into the other. By changing the environment of a functioning cell, it was observed to divide. If the daughter cell were again brought into suitable surroundings they differentiated and beat rhythmically. It was interesting to note that these cells could not only be kept living in these active states in a culture at body temperature but it was likewise possible to keep cells in an inactive state of life for as long as six months. Remove such inactive cells to a new and fresh medium; they wander and divide.

These observations and additions to the technique of tissue cultures opened a broader field of physiological study and pointed out the possibilities most suitable for study by the tissue culture method. It was possible to reproduce many of those kinds of cellular activity that are seen in the animal body. A full analysis of the conditions which are associated with movement, division and differentiation in a tissue culture would have direct application towards a solution of many problems of growth in the body as well as a fuller understanding of the coördination and regulation of these activities so as to produce a proper organ and body form.

Ruth in 1911 showed that wound healing could be imitated in culture. He found that if holes were cut in pieces of frog skin the wound, if not too large, would heal. This healing took place.
largely through movement of the epithelial cells. The fibrous edges remained inactive for a time, later they moved together passively. He reproduced the picture of primary healing without scar.

Harrison showed that the necessity of solid bodies for the movement of cells could be fully demonstrated by means of the tissue culture. He observed that cells placed in liquid media remained spherical and would not move. When these cells were brought in contact with a solid body they changed their shape and moved out along the side of the solid. Such cell movement took place in lymph and plasma cultures by the contact of the cell with the fibrin strands. In liquid media they could move over the free surface of the liquid, the surface of the cover glass or along strands of spider web placed in contact with them. Carrel and I noted that movements of cells in liquid media took place only along solid support, such as cotton and silk threads which were placed in contact with the cells. These experiments confirmed more fully earlier observations upon the necessity of solid support for movements of cells in a wound (Leo Loeb).

Loeb and Harrison chose to call these movements evidence of stereotropism.

Carrel and I in 1910 and 1911 observed an increase in the movement of cells after adding distilled water and tissue extract to the plasma which was used as a medium. Ruth noted an increase in the movement of the epithelial cells of frog skin in plasma diluted with distilled water.

Carrel in a more recent article has emphasized this fact, giving it as evidence of making wounds in the body heal in a few days or hours.

Before one could draw such conclusions it was necessary to study more completely the laws governing the movement of cells in a culture and to establish some definite means of control. Further, are conditions in a tissue culture comparable to those in the animal body? Before drawing conclusions as to the specificity of a given substance it was necessary to study for control the effect of other simple diluting substances occurring normally in a coagulum.

Repetitions of these experiments made it seem certain that this increase in the migration of cells with each proportional increase of the diluting agent added to the plasma was not in any great part dependant upon a direct action of the dilutant on the cell but was
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dependant upon the mechanical changes its addition produced in the clot. To make this more clear some of the conditions influencing the movement of cells in the simple plasma cultures will be discussed.

The rate and the extent of cell movement in a culture, one can assume, vary with the qualitative and the quantitative changes of the stimulus or stimuli which initiate and guide them. They vary, likewise, with changes in the metabolism of the cell.

Harrison had considered that the stimulus for movement of cells in a tissue culture was contact with solid bodies. He termed this stereotropism. As Jacques Loeb states, "Stereotropism is no real tropism, inasmuch as in this case no lines of force exist." When a cell is spread over a solid surface, such as a cover glass, it would not change its position as the result of this contact alone. Opposite points of contact of the cell would be equally irritated. Changes in the shape of cells and migration are manifestations of one and the same property of protoplasm, namely, movement. It is well known that cells such as an ameba respond by movement to many external forces or stimuli. The cells in a tissue culture respond in a similar manner. When a cell spreads from spherical to a spindle form or from a spindle to a spherical form without changing its position, one must assume that the stimulus is acting equally on opposite points of the cell. Movements from place to place are dependant upon a greater spreading in one direction than in the other or a retraction at one pole and a flowing out of the protoplasm at the other. To cause a change in position opposite sides of the cell must be affected differently.

I had come to assume, therefore, that the solid body, although necessary for the maintenance of the proper shape and the migration of the cell, was not the active initiating stimulus for the migration of cells in a tissue culture.

Evidence in favor of such a view is shown by the following observations: When a piece of connective tissue is placed in a medium giving uniform support on all sides, the cells move out only in paths leading them directly away from the tissue fragment. They radiate out on all sides like light waves from a central illuminating body. Cells moving from a piece of tissue placed in a liquid medium and surrounded by a tangle of cotton threads, follow only those threads which lead them out and away from the tissue mass or other cells. Cross-threads are never occupied except when they lead the cell away from a mass of other cells.
It is well known that cells placed in fresh plasma or plasma liquefied by a few days of the growth of a tissue tend to send out processes, spread, and flatten over the surface of the supporting substance. As the medium about these cells later becomes exhausted and charged with acid waste products, the cells draw in their processes and become spherical.

When a piece of tissue is placed in the center of a drop of medium, an active metabolism of its cells causes rapid changes in that part of the medium which lies close in and about it. Acid can be demonstrated in the center of such a fragment even after a few hours of incubation.

Following such a local change in the medium, diffusion currents result. The waste substances within the tissue mass diffuse out into the surrounding areas of fresh medium. The fresh medium without streams into the tissue mass. The border cells of the tissue fragment are thus bathed on one side by a stream of acid waste products and on the other side by a stream of fresh medium.

The proximal pole of the cell is, therefore, continuously stimulated to draw in its processes, or at least its spreading is hindered, while the distal pole, on the other hand, is continuously stimulated to move outwards. The cell thus moves out and away from the tissue mass.

According to such a theory one must assume that the migration of a cell in a tissue culture is dependant upon changes brought about locally in the medium of a culture through the activity of the cell itself and neighboring cells. When a single cell is placed in a drop of medium, products of its metabolism are formed equally on all sides of the cell. Such a cell changes its shape but not its position. Place two cells together, they move slowly apart.

No better illustration of the dependance of one cell on another for the stimulus for migration can be given than through a study of the variations in the extent of migration of cells from pieces of tissue of different sizes. As illustrated in figure 1, the migration is greater away from the large than the small piece of tissue. The migration can likewise be shown to be greater away from a cellular than a fibrous piece of a given tissue. The greatest migration of cells has been found to be away from a cellular piece of a given tissue of 1 mm. in diameter or the largest piece of tissue in which all the cells remain active.

For the cells to react to these stimuli and produce them they must be well supplied with oxygen. Oxygen from the air diffuses into
solid clots to a depth of 0.5 to 0.7 mm. in quantities sufficient to preserve the oxy-haemoglobin color in red cells. A sharp line of demarcation between the oxy-haemoglobin and reduced haemoglobin remains at this depth even after many days exposure.

As the red cells suffer reduction of their haemoglobin, other types of cells suffer, in layers of plasma thicker than 0.5 to 0.7 mm., hindrances in their movement and their metabolism.

It has been found that the greatest movement of spleen cells is in the thin layers of plasma, 0.2 to 0.3 mm. in thickness, and away from a piece of spleen 1 to 1.5 mm. in diameter. The surface area covered by cells about similar pieces of spleen decreases with each increase in the thickness of the layer of plasma up to certain limits. Above these limits of thickness (a layer 1 to 1.6 mm. in thickness) the growth reaches a constant minimum, Fig. 2.

The cells of pieces of heart muscle or skin of this size do not grow so actively in the very thin layer of medium. The greatest movement of the connective tissue and the epithelial cells occurs in layers of plasma of 0.5 to 0.7 mm. in thickness. The cells grow differently than do the cell from the spleen and suffer in the thinner drops apparently from a lack of food supply. Curves 1 and 2.

The cause of the increase in the migration of cells in the thin layers of the plasma I have assumed to be, first, the better oxygen supply to the tissue fragment and the migrating cells. The increase in the supply of oxygen to the tissue fragment is associated with an increase of the metabolism of its cells and a greater production of the repelling substances. Second, the repelling substances diffuse in greater concentration into the thin restricted areas of the medium; and, further, the cells migrating into the thin layers move in a single plane so that each cell is followed by a continuous line of actively metabolising cells.

The utilization of these facts and a careful technic has made it possible to obtain a constant type of growth from a given tissue into a plasma clot.

After repeating and controlling those experiments upon movement of cells in plasma diluted with tissue extracts or water, I found that a similar increase in the movement was noted after diluting the plasma with isotonic NaCl solution, Ringer's solution, Locke's solution, or serum.

This increase in the movement of cells after using serum as a dilutant suggested strongly that the decrease in the fibrin was the
important factor. Plasma clots can be assumed to be composed of two constituents, fibrin and serum.

It is well known that fibrin clots, especially when they contain tissue cells, contract upon standing. The solid clot becomes smaller and the serum is squeezed out. The size of the contracted mass of fibrin is proportional to the quantity of fibrin present.

The same retraction of the clot occurs in a culture. The fibrin retracts against the cover glass. The serum drains off from the under free surface of the hanging drop. When pieces of tissue of similar size are planted in equally thick drops of plasma and plasma diluted with some liquid substance, the thickness of the solid medium varies in the different cultures after a few hours incubation.

As shown in figure 3, there is with each increase in the quantity of dilutant added to the plasma an increase in the area covered by cells about pieces of spleen of equal size. Comparison of figure 2 with figure 3 shows further that the area covered by wandering cells about the fragments of spleen placed in diluted plasma is similar to the area covered by cells about fragments of spleen placed in equally thick layers of contracted pure plasma.

This same relation between the thickness of the layer of medium and the migration of cells is seen in the study of movement of cells from fragments of heart muscle and skin placed in plasma diluted with various substances.

When the fibrin clots fail to contract, this definite type of increase of the movement of the cells is not noted in the diluted plasma. Spleen cells may show a slight increase in their movements in these less dense clots but the connective tissue cells suffer little more than an alteration in their arrangement.

The increase in the movement of cells in plasma after the addition of water, isotonic NaCl, Ringer's solution, Locke's solution, tissue extracts, or serum is in large part the result of mechanical changes occurring in the clot following a decrease in its fibrin content. Individual variations from the use of one or the other of these substances are small. Tissues planted in plasma diluted with water suffer early death, apparently, from hypotonicity. Isotonic NaCl activates movement somewhat more than Ringer's or Locke's solution. The cells survive longer in plasma diluted with tissue extract or serum than salt solutions. They die apparently in the plasma diluted with salt solutions from an early exhaustion of food materials.
TISSUE CULTURE AS A PHYSIOLOGICAL METHOD.

It is questionable from the data at hand whether any great effect would be produced by the use of these substances in the body where the source of the oxygen and the mechanical conditions surrounding the coagulum are different.

It was little hoped that the tissue culture would have an important application for the study of the factors concerned in cell division. Its important use for the study of this problem seemed limited to the study of a few cells, such as the abnormal mitoses in tumors. Lambert has been able to observe abnormal mitoses in tumor cells growing in a culture.

It has been of interest to me during the last year to notice that many cells dividing in this particular environment show amœboid-like movements. These movements were not different in appearance from the amœboid movements of locomotion. There was, however, a difference in the source of the stimuli which initiated them. The amœboid movements of locomotion were apparently always associated with external factors while those of cell division were associated with changes taking place within the cell.

Many authors have figured amœboid processes in dividing cells, but no one has apparently called attention to the relation of the processes to a surface tension theory of division, nor studied their relations to nuclear changes in the cell.

Quincke held that amœboid movements were the result of surface tension changes along the wall of the cell. He assumed that the cell was surrounded by a fatty membrane and behaves like an oil droplet. When a drop of rancid oil suspended in water was touched at a point on its surface with a piece of sodium hydrate, which caused a decrease in its surface tension, this part of the drop bulged and gave rise to a pseudopode-like process. Bütschli extended and confirmed Quincke's results. He also assumed that cell division was a surface tension phenomenon. The cleavage furrow represented an area of greater surface tension than the remaining part of the cell. McClendon has added much evidence in favor of such a view. McClendon's oil droplet model of cell division represents very completely the conditions as I have observed them. He suspended a drop of rancid oil and chloroform between water and salt solution. By means of two pipettes equal quantities of sodium hydrate were
allowed to flow simultaneously against two opposite points in the drop. The surface tension was lowered and the drop bulged at these points. To compensate for the bulging, constriction with following cleavage took place along the circumference of the drop midway between these points.

The changes in form taking place in the cell of a culture during mitosis are of two kinds. Primary with the onset of nuclear division the cell changes from a spindle shape to an oval or spherical mass of protoplasm, whose center is occupied by the nucleus. Later, after separation of the two groups of chromosomes, the cell elongates and cleaves at its equator. Following carefully the change in the shape of a cell from a flattened spindle to a sphere or an oval, it was found that this change often occurred as an active outward movement of that part of the cell wall nearest the nucleus.

The more distant end processes were apparently drawn inwards in compensation. Movements ceased in the small cells as soon as the walls were equally distant on every side of the nuclear spindle. Later in division, as the nuclear halves separated more and more from each other, they again came close to the wall at the poles of the cell. Following this approach, amœboid movements were seen at these parts of the cell. The cell slowly elongated with each movement, finally constricting at the equator.

That this movement was associated with the nuclear halves was more clearly shown by the study of cells whose early movements were hindered so that the dividing nucleus was excentrically placed. In these cases one line of chromosomes during its movements often came directly in contact with the edge of the cell. Following this contact an explosive outward movement at this part of the wall of the cell generally occurred.

One of the long disputed questions in physiology is that concerning the cause of the heart beat. Haller in 1757 taught that the heart was an organ independent of the nervous system. Remak in 1848, through the discovery of nerves in the frog's heart, naturally took the view that rhythm was initiated by the nervous system. Later the discovery of ganglion cells within the heart muscle strengthened this idea. In the latter part of the cen-
Tissue culture as a physiological method.

The opposing view, that the heart was an automatic organ, was again raised. The difficulty for a proof of automaticity lay in a failure to completely rule out the possibility of existing ganglion cells. The neurogenic school offset all arguments as advanced by the adherents to the myogenic theory, by constantly holding up the fact that there was a possibility of undemonstrated ganglion cells in the young chick hearts and in the isolated and beating pieces of heart muscle studied by Gaskell and Engelman.

By the use of this method of tissue isolation I have found it possible to attack this problem and to prove more conclusively the automaticity of the heart muscle cell. Heart muscle cells completely isolated from all other tissue cells or possible nerve connections have been observed to beat rhythmically. The cells were taken from the hearts of fourteen and eighteen-day chick embryos—hearts which in the body are richly supplied with nerves. The isolated cells beat with a perfectly normal rhythm and with a rate and force similar to the heart in the embryo or pieces of heart muscle isolated in a culture.

The tissue culture is of use in studying problems of cell metabolism. I have found that the accumulation of fat in the cytoplasm of the cells of a tissue culture varies with changes in environment similar to cells in the body. These accumulations have been considered for most part infiltrations and not fatty degenerations. As Leathes expresses it, it is an inability on the part of the cell to burn the normal quantity of fat brought to it. It synthesizes and stores it up. In the cells of a tissue culture, fat accumulations vary with the quantity of fat in the medium and with the general state of metabolism of the cell. Cells in an environment perfect for active growth do not contain fat or lose the fat they have synthesized. Any disturbance of the metabolism of any cell in this same environment is associated with an increase in fat in the cytoplasm of the cell.

By these brief illustrations I have tried to show you not only some facts that have been brought out by the tissue culture method but to illustrate how this method is applicable for the study of physiological problems of growth.
EXPLANATION OF FIGURES.

Fig. 1. A camera lucida drawing showing the variation in the migration of cells away from a large and a small piece of spleen.

Fig. 2. Curve 1 shows the variations in the migration of cells away from similar pieces of heart muscle into layers of pure plasma of different thicknesses. Curve 2 shows the variations in the migration of cells away from similar pieces of skin into layers of pure plasma of different thicknesses.

Fig. 3. Camera lucida drawings showing the variations in the migration of cells away from similar fragments of spleen (a, b, c, d, e, f) into layers of pure plasma of different thicknesses.

Fig. 4. Camera lucida drawings showing the variations in the migration of cells away from similar pieces of spleen (a, b, c, d, e, f) into equally thick layers of pure plasma and plasma to which various quantities of serum had been added.
Fig. 1. A camera lucida drawing showing the variation in the migration of cells away from a large and a small piece of spleen.
Curve 1 shows the variations in the migration of cells away from similar pieces of heart muscle into layers of pure plasma of different thicknesses.

Curve 2 shows the variations in the migration of cells away from similar pieces of skin into layers of pure plasma of different thicknesses.

Fig. 2.
Fig. 3.
Fig. 4.

a. Pure Plasma
Thickess after 48 hours 1.3 mm

b. 8 vol. of Pure Plasma + 2 vol. of Serum
Thickness after 48 hours 1.15 mm

c. 6 vol. of Pure Plasma + 4 vol. of Serum
Thickness after 48 hours 1.3 mm

d. 4 vol. Pure Plasma + 6 vol. of Serum
Thickness after 48 hours 1.00 mm

e. 2 vol. Pure Plasma + 3 vol. of Serum
Thickness after 48 hours 0.60 mm

f. 1 vol. Pure Plasma + 9 vol. of Serum
Thickness after 48 hours 0.35 mm
THE LIFE OF TISSUES OUTSIDE THE ORGANISM
FROM THE PATHOLOGICAL STANDPOINT.

ROBERT A. LAMBERT, M.D.,
Pathological Laboratory, Columbia University, New York City.

Those of us who are engaged in investigating the nature and cause of disease are interested in the new method of growing cells apart from the organism mainly on account of the possible application of the method to the study of various morbid processes affecting the human body. The technique appeals to us, first of all, because it represents the analytical method possibly in its highest state of development,—the study of the isolated cell itself.

Whether a fine analytical method of this kind presents any advantages over grosser means of investigation is a pertinent question, however. In our opinion, the new method does offer several very definite advantages which may be summed up in few words:

In the first place, it allows one to observe directly under the microscope changes taking place in living functioning isolated cells; thus making it possible to pursue with ease and satisfaction many questions in the field of pathological histology, the solution of which has seemed to wait on the discovery of a technique of this kind.

In the second place, it permits us to eliminate from consideration many factors, which in experiments upon the animal body are a source of much confusion (nervous control, for example).

In the third place, the isolation of some single factor for the purpose of special study is made possible.

In the fourth place, we are able to introduce more easily into an experiment known and measurable factors such as changes in the physical and chemical composition of the medium, introduction of specific toxins and poisons, variations in temperature, etc.

With these advantages in mind, let us consider the kinds of problems to which the new technique is applicable. It is obvious from what you have heard already that not every problem having to do with the activities of cells is open to attack by means of tissue
cultures for the simple reason that not every tissue can be made to grow in vitro (or at least, has not up to this time). This is especially true of some of the highly differentiated tissues of mammals. However, the number of tissues already successfully cultivated is not inconsiderable, including connective tissue cells, bone, cartilage, endothelium, skin and corneal epithelium, intestinal epithelium, malignant tumors (sarcoma and carcinoma) and possibly also thyroid and kidney epithelium. Certain cells, such as ganglion cells, appear to survive, though they do not proliferate. So that the application of the method, though not universal, is not narrowly limited.

The problems which seem to present the most fruitful fields of application may be grouped, somewhat arbitrarily, under three headings: First, morphological questions (that is, questions in pathological histology); secondly, questions in immunity, including cancer immunity, cellular and bacterial immunity; and thirdly, problems relating to the cultivation and study of the viruses of certain infectious diseases, especially those in which specific intracellular bodies have been described.

We shall take up, as examples of these three classes of problems, certain problems to the study of which we have personally applied the method. Other investigators have also been interested in applying the technique to pathological questions and I shall try to give due reference to their work in the proper places.

I think it will be advantageous to have the pictures, illustrating the chief points to be discussed, shown you as the different subjects are taken up. Let me familiarize you first of all with the appearance of a tissue culture. This is a low power picture of a growth of rat sarcoma, a tissue used in the majority of our investigations (fig. 1). Note the small original fragment in the center, and the halo of single wandering cells in the coagulum surrounding the fragment. Contrast the discrete wandering of the sarcoma cells with the sheet-like or grouped type of growth seen in the next picture, which is that of a culture of mouse carcinoma (fig. 2). I take this opportunity to emphasize this difference in type of growth, not only because it represents a general difference in the growth of epithelial and connective tissues, but also because it shows you that the growth of cells in vitro and in vivo are not essentially different.

The next picture, showing individual sarcoma cells, illustrates the phenomenon of amœboid movement (fig. 3). We have called atten-
tion elsewhere to the significance of this phenomenon as exhibited by
tumor cells.* I should like to suggest that in the spread of
tumor cells through the body the amœboid activity of the individ-
ual cell must play an important rôle. It is not necessary to think
that cancer cells at some distance from the primary growth have
either been passively transported by the blood or lymph stream or
are the result of a continuous centrifugal growth, when a cell is
perfectly capable of fairly rapid and progressive independent move-
ment. In a sarcoma culture we have seen a cell travel a distance
of 5 mm. in 48 hours, a rate that would easily enable a cell in the
center of the breast to reach the axilla in six to eight weeks.

But we are digressing from the main purpose of this paper, which
is to show you some concrete results of the use of the new method.
I wish to refer briefly in the beginning to several morphological
problems.

The first of these is the question of fatty accumulations in cells
growing in plasma and its relation to the pathological accumulation
of fat in the cells of the body. The statement has been made
recently, by several workers, that this fat is the result of a degen-
eration of the cell cytoplasm, or, indeed, that cells in cultures die
through a process of fatty degeneration. I think I can convince
you, in a few words, of the fallacy of this view. In the first place,
cells containing fat move about actively and undergo perfectly nor-
mal mitotic division. In the second place, it has been observed by
Carrel, Burrows, and ourselves that the fat may completely disap-
ppear when the cells are transferred to fresh culture medium; and,
thirdly, we have shown, by diluting the plasma with Ringer's solu-
tion, that the amount of fat accumulated by the cells is roughly
proportional to the amount in the plasma medium—an experiment
quite analagous to Rosenfeld's animal studies in which the accumu-
lation of fat in the liver of dogs starved and poisoned with
phosphorus was shown to be much less than in the livers of well
nourished dogs poisoned in the same way.

We have concluded, therefore, that the appearance of fat in the
cells is referable to some (unexplained) disturbance in metabolism
whereby the cells are not able to utilize readily the relatively large

* In this connection an observation made many years ago by Dr. Carmalt,
President of this Congress, should be mentioned. Dr. Carmalt observed and
recorded definite amœboid movements in the cells of a human breast
carcinoma teased in salt solution.
quantity of fatty substances at their disposal. The whole question of normal and pathological fat accumulation, it seems to us, is opened up for study by this technique.

Dr. Hanes, my co-worker, was very much interested in the question of the relationship of the cell granules to fat metabolism. It is a relatively simple matter to study this relationship in the living cell, using vital stains to make visible the cell granules. Dr. Hanes thought that he could see a transformation of the cell granules into fat, and Dr. Foot, who has also been interested in the question, has, I understand, made a similar observation.

Another problem of a morphological nature that has interested us is the development of foreign body giant cells. By adding lycopodium spores to cultures of chick spleen we have been able to produce in vitro, giant cells of the familiar foreign body type, enclosing the spores. The first two pictures represent low and high power photomicrographs of the living cells surrounding the lycopodium granules (fig. 4 and 5). The next picture shows the appearance of the giant cell in stained preparations (fig. 6). They are comparable in every way to those formed in a body. We were able to determine with certainty that they were formed by a fusion of cells and to decide in a general way as to the nature of the cells that go to form them. The cells are of the type of large mononuclear wandering cell, some possibly endothelial in origin. That connective tissue cells do not take part, the next picture demonstrates. Here we see lycopodium spores surrounded on all sides by connective tissue cells, which exhibit no tendency whatever to enclose the foreign objects (fig. 7).

A third morphological question in which we have been interested has been a comparison of normal cells and cancer cells in their growth in vitro, particularly as regards cell division. I might say, parenthetically, that the field of cancer research is one in which any new method ought to receive a hearty welcome, especially one that permits an intimate study of the cancer cell itself. These comparative morphological studies have not as yet led to any startling findings; they are in some measure simply confirmatory of observations made on tumor cells growing in the body. We have observed, as regards the process of division, that normal connective tissue cells divide in a very regular, orderly manner: only normal mitoses are observed and the time required for division, easily determined in the living cells, is quite constant; whereas, in sarcoma cells atypical
division figures of all kinds are seen, and the time required for division varies within very wide limits. You see in this picture a connective tissue cell undergoing karyokinetic division (fig. 8); the different phases follow each other in the usual orderly fashion. The next slide shows some of the atypical mitoses observed in tumor cells (fig. 9).

We have in this method an excellent opportunity for fine cytological study; we have never before been able to observe the phenomena of cell division in the living mammalian cell. I show you these pictures rather to emphasize this point, than to call attention to any results that we have obtained.

Another interesting and somewhat puzzling difference in the behavior of normal cells and cancer cells in vitro, lies in the greater ease with which normal tissues may be propagated in subcultures for any length of time. Not only do normal connective tissue cells appear to be much more hardy than sarcoma cells but they show oftentimes a markedly accelerated growth after the first or second transfer; sarcoma cells show on the other hand a diminished activity. One sometimes sees more than a hundred dividing cells in a single subculture of rat blood vessel. You observe four mitoses in a small field here, taken from a sixteen-day growth,—second transfer (fig. 10). We are unable to offer any satisfactory explanation for this difference.

We have planned to make a series of studies upon cancer cells and normal cells, comparing them in their resistance to various injurious agents, physical and chemical, using the method of tissue cultivation as a test of survival of the cells. One of these studies we have completed—the comparative resistance of sarcoma and actively growing connective tissue cells to heat. We have found that, although the difference is not great, connective tissue cells are definitely more resistant to high temperatures (42-47°) figs. 11 and 12. We have had for a long time, a means for determining the effects of injuries on cancer cells, that is, animal inoculation, but we have not possessed heretofore a satisfactory technique for testing the effects of such agents on normal cells.

Let us leave morphological problems for a time and turn our attention to some questions in immunity, in the study of which the new technique promises to be of service.
I think we may consider together with advantage two kinds of immunity, which, as far as our experiments are concerned, stand in rather striking contrast to one another,—cancer immunity and cellular or cytotoxic immunity. By cancer immunity we mean the resistance manifested by individual or certain strains of rats and mice to the inoculation of their transplantable tumors. The nature of this immunity has been, and still is, one of the great problems in cancer research.

By cellular or cytotoxic immunity we mean the reaction that is brought about by injecting an animal of one species with the cells of another species.

We were interested, in the beginning, in seeing whether the cells of rat sarcoma would grow in the plasma of a rat in which the sarcoma would not grow when inoculated, that is, an immune rat. We found that the tumor cells would grow just as well in the plasma of such animals as in that of susceptible or tumor-bearing animals. The question naturally arose then as to whether this experiment proved that in cancer immunity cytotoxins were not present in the circulating fluids of the immune animal. It seemed easy to settle this question by using a plasma for cultures in which antibodies of a cytotoxic nature were known to be present. In this way it could be determined whether a cytotoxic action could be demonstrated by means of tissue cultures.

To this end, guinea-pigs were immunized, by suitable injections against rat tissues, and their plasma used for cultures of rat cells. It should be explained that normal guinea-pig plasma affords a good culture medium for rat cells, a fact that is in itself interesting and significant. In the culture preparations made with this cytotoxic plasma there was complete inhibition of growth with partial or complete disintegration of the rat sarcoma fragments. We therefore concluded from these two series of experiments that cytotoxins are easily demonstrable in tissue cultures, and that cancer immunity is not a type of cytotoxic immunity.

These studies led us to take up the problem of the specificity of cytotoxins as regards tumor and organ cells,—a question that has been difficult to settle by means of experiments upon the animal body, on account of the difficulty of eliminating from the experiments many confusing factors. For example, those who have opposed the idea of specificity have attributed the lesions produced in the liver, kidney or thyroid, by injections of a hepatotoxic, nephrotoxic
or thyreotoxic immune serum to other causes, such as capillary thrombi or agglutinations in small vessels. As we pointed out in the beginning, such difficulties in the interpretation of results are obviously avoided in in vitro experiments.

Our experiments upon the question of cytotoxin specificity may be briefly summarized: two series of guinea pigs were immunized, respectively, with rat sarcoma and rat embryo skin. Later, plasma from each series of animals was used for cultures containing both kinds of tissue. These experiments showed that sarcoma may immunize completely against skin, and vice versa. There was no evidence of even a relative specificity. We found also that red blood cells would immunize against other tissues, an observation recently confirmed by Hadda and Rosenthal.

It has not only been possible to demonstrate the action of cytotoxins in vitro, but it has also been shown by Carrel and Ingebrigsten that such antibodies may be produced in vitro. They found that the cells of the guinea-pig bone marrow growing in plasma cultures, to which goat corpuscles were added, developed specific hemolysins for goat erythrocytes. This demonstration has been repeated by Lühe, who used rabbit spleen and hen corpuscles.

That tissues living in vitro may react with the formation of antibodies, or with the development of foreign body giant cells, leads us to suggest that it may be possible to produce outside the body, even such specific tissue reactions as the tubercle, and thus to study in a new way their development.

I wish to call attention, in conclusion, to another field of pathologi-cal investigation in which this new method may be applied;—that is, in the study of the viruses and specific lesions of certain infectious diseases in which the living agent has not yet been identified: rabies, vaccinia, variola, measles. The recent work of Bass upon the cultivation of malarial parasite serves to emphasize the suggestion that a cell host may be necessary for the cultivation of certain organisms outside of body. Bass found, as you probably know, that the plasmodium malariae multiplies in cultures only when the parasite can pass directly from one erythrocyte to another. Parasites free in the serum soon die.

In association with Dr. Steinhardt and Dr. Poor of the New York Board of Health, efforts have been made at studying two of the viruses mentioned above—rabies and vaccinia. We
tried first of all to see if the Negri bodies, the nature of which is still in dispute, would show any development or multiplication in vitro when fragments of brain from rabid animals were incubated in blood plasma. (It should be mentioned that ganglion cells of adult rabbits and guinea-pigs remain alive under such conditions for several weeks.) We attempted further, to see if the bodies could be produced in vitro by combining normal brain and virus. Our results were as follows:—No development or multiplication of Negri bodies in rabid brain cells took place in vitro, as far as we could determine. But structures indistinguishable from certain forms of Negri bodies were found in the normal brain cells incubated with rabies virus. We found, however, that in the control preparations in which normal brain alone was incubated, the same structures also appeared. In the latter case, the bodies certainly represented some degenerative changes in the brain cells. We therefore regarded our results as favoring the idea that the Negri body is not a parasite, but a specific cell degeneration. In this picture are shown for comparison a "degeneration" in a ganglion cell (normal guinea pig brain) incubated seven days in vitro in blood plasma, and a typical unstructured Negri body from a smear of a rabid guinea-pig brain. The two structures appear to us indistinguishable.

Developing the idea suggested above, we have attempted to cultivate the virus of vaccinia by combining in plasma cultures corneal epithelium (which exhibits a fairly active growth under these conditions) and a dilute emulsion of calf virus. Animal inoculations of the incubated preparations indicate that we have in this way obtained an active growth of the virus. The detailed results of these studies will be published later.

EXPLANATION OF FIGURES.

Fig. 1. Three-day culture of rat sarcoma showing independent outwandering of cells. The dark staining mass represents the small original fragment.

Fig. 2. Three-day culture of mouse carcinoma showing outwandering of cells in sheets and groups.

Fig. 3. Three cells from a culture of mouse sarcoma, showing pseudopods and fat granules (stained black).

Fig. 4. Culture of chick embryo spleen (low power) showing in the zone about the original fragment lycopodium spores surrounded by masses of wandering cells.
Fig. 5.

Fig. 6.
Fig. 5. High power photomicrograph of a small area from fig. 4 (unstained).

Fig. 6. Two foreign body giant cells formed in vitro in cultures of chick embryo spleen, containing lycopodium spores. (Drawing from stained paraffin sections; (a) giant cell enclosing two spores, formed in the zone outside the original fragment; (b) giant cell formed in original fragment. Spore is shown cut tangentially.

Fig. 7. Culture of chick embryo heart with lycopodium spores, showing outgrowth of connective tissue cells and no tendency to giant cell formation.

Fig. 8. Series of drawings made at ten-minute intervals of a dividing connective tissue cell in culture of rat blood vessel, seventy-two days after removal of the tissue from the animal body.

Fig. 9. A field in a culture of rat blood vessel (second transfer, seventeen days) showing three mitoses and two cells immediately after division.

Fig. 10. Mitotic figures from cultures of rat sarcoma; a, b, and c, normal; d, hyperchromatic cell; e and g show marked lagging of chromosomes; f, contains large vacuole; h, tripolar mitosis; i, cell containing three nuclei, formed by tripolar mitosis.

Fig. 11. Culture of rat sarcoma showing cells killed by exposure to 44½° C. for fifty minutes (dry heat).

Fig. 12. Culture of rat blood vessel, showing survival of connective tissue cells after exposure to a temperature of 44½° for fifty minutes.

Discussion.

Dr. Leo Loeb (St. Louis): The very interesting papers of Dr. Harrison, Burrows and Lambert, to which we have listened this afternoon, demonstrate the fertility of the conception of removing mammalian differentiated tissues out of their natural surroundings, to bring them in culture media into a new chemical and physical environment, to cultivate them in a manner similar to bacteria, and thus to study their reactions to stimuli, which we cannot analyze under ordinary conditions in the body; because here we face a complex of factors acting upon the tissues, and we are unable to separate such factors. By making tissues grow in culture media, we can build up a physiology of tissues. To express it more definitely: Physiologists have studied various epithelial cells only in so far as they perform certain specific functions as part of an
organ. They have never analyzed experimentally the factors under-
lying growth and movements, and similar phenomena of the com-
ponent parts of organs, of various epithelial cells, or of the con-
nective, and so on.

As to the methods used, in our laboratory we employ a method
which rests on the same principles which guided us in our first
attempts in this direction sixteen years ago. As in our earlier
experiments, we insert somewhat larger pieces in culture media in
the test tube; this method is more tedious, and has also certain
advantages over the cover-glass method. By this method, we can
study the influence of various gases on the life and growth of the
tissues; for instance, the action of hydrogen. We could study the
reactions between certain micro-organisms as, for instance, yeasts
and the tissues under more satisfactory conditions; and can elim-
inate the leucocytes, which play such an important rôle in the living
body. Furthermore, using the cover-glass method, we ordinarily
study merely the behavior of the outgrowing cells; while very
important changes that may take place in the transplanted tissues
may remain unnoticed, unless we also make use of embedding and
sectioning the whole tissue. The transplanted cells, living in culture
media, may, as I have repeatedly found, be very actively growing
without any outgrowth of cells being noticeable. The outgrowth
of cells depends mainly, as I pointed out in 1897, on secondary
conditions; especially on a stereotropic sensitiveness of connective
tissue, as well as epithelial cells, both of which grow only in con-
tact with solid or semi-solid bodies, and receive thus the direction
of growth. For the analysis of the chemical factors of these
movements my previous studies on the blood-cells of Limulus are
of importance.

With regard to the remark of Dr. Burrows as to what causes
the tissues to grow out of the culture media, and not back, I
would say that this is a question that I thought of for a long time.
I am not sure that the explanation of Dr. Burrows is correct;
because I placed two pieces of tissue next each other in culture
media, and found that tissue-cells may grow toward each other in
cases in which necrosis takes place. We found recently that dif-
ferent tissues vary in their action on culture media, especially on
coagulated blood-plasma or blood. The kidney of the guinea-pig,
and probably also of other animals, seems to have a tendency to
dissolve the coagulum to some extent,—much more than other
organs. Under these conditions, no outgrowth into culture media takes place on the part of connective tissue or kidney cells of the guinea-pig; but when we examine on sections the implanted pieces of kidney tissue, we may find it very actively growing by mitotic division. I may here state that these mitoses are not old ones, already present before transplantation, but are newly formed, as a comparison with the tissues used for transplantation amply demonstrates.

Furthermore, epithelial tissues grow out into the coagulum very much less actively than connective tissues. Carcinomatous cells are relatively mobile, and so may be, as I found in my earlier work, epithelial cells; but many kinds of epithelial tissues do not, in our experience, grow into the coagulum. Kidney epithelium may grow to some extent over furrows of the coagulum; but, according to my observation, it can hardly penetrate into the coagulum proper, as has been maintained by some recent investigators. Testicle, thyroid, and ovarian tissue do not seem to grow into the coagulum at all under the conditions of our experiments.

There is, in conclusion, one point to which I would like to draw attention, where I believe that possibly a misunderstanding exists as to the significance of the method of growing tissues in culture media in vitro. It has apparently been believed that a potential immortality of tissues could be rendered probable for the first time through this work. I believe this to be erroneous. This proof, as far as it can be given at all, can just as well be supplied by serial transplantation of tissues in the living body; but we can, I believe, go further, and state that as far as such potential immortality of tissues can be proved, the proof has already been given through the long-continued, apparently endless serial transplantation of tumors. Now tumor cells are merely ordinary somatic cells living under special conditions; and we may, therefore, conclude that, in the same sense as protozoa and germ cells, also, certain ordinary mammalian somatic cells possess a potential immortality.

Dr. Warren H. Lewis (Baltimore): Mrs. Lewis and I have been interested in the cultivation of tissues from chick embryos in media of known chemical constitution. Such tissues grow readily in Locke's solution, which contains sodium chloride, potassium chloride, calcium chloride, and sodium bicarbonate. Various modifications of Locke's solution were used by varying the per-
centages of the different salts, by the addition of dextrose or cane sugar and by the omission of some of the salts entirely from the solutions. The tissues will grow in many such modifications equally well; in fact one can get a certain amount of growth in a very simple mixture of sodium chloride, as, for example, of sympathetic nerve fibers. Sodium chloride is the one essential salt, for without it no growth appears.

The percentages of sodium chloride may be varied considerably, from one-half of one per cent. to one and one-half per cent., and still permit growth. The duration of growth varies from two to ten days and is often as extensive, as seen in lymph or plasma. Cell division is very common and frequently half a dozen mitotic figures may be seen in one field. There is a great similarity in the outgrowth in many of the different solutions used and it is apparently very difficult to alter the characteristic manner in which the different tissues behave by varying the percentages of the various salts. An increased percentage of sodium chloride does, however, delay the initial outgrowth of cells from the mother piece. We have studied the growth of connective tissue, smooth muscle, heart muscle, endoderm, sympathetic and central nervous system nerve fibers, plasma cells, and other types of wandering cells.

The hanging drop method was employed, for the most part, in a manner similar to the use of lymph by Dr. Harrison and plasma by Dr. Burrows and others. The use, however, of a fluid drop presents certain advantages in that the outgrowing cells cling to the underside of the cover glass and even tend to flatten out so that it is easy to study the living cells, even with an oil immersion, since most of the culture lies in one plane of the field. Cells, and even nerve fibers will, however, creep along on the lower surface of the hanging drop, the surface acting as a solid support. There is apparently no outgrowth into the center of the fluid. The stereotrophic properties of the cells, to which attention has been called by Harrison and Loeb, can thus easily be demonstrated in such cultures.

Of especial interest has been the study of the outgrowth of sympathetic nerve fibers from sympathetic nerve cells in the walls of the intestine, in that we have been able to observe a rich anastomosis of nerve fibers and nerve endings, not only in the living cultures but in specially prepared and stained cultures where the neuro-fibrillæ can be followed from one fiber to another.
Dr. Burrows has called attention to the use of pseudopodia in helping to pull apart the daughter cells in cell division through an axial pull. The pseudopodia as seen in many of our preparations of mitotic figures are not limited to an axial direction, but run in all directions from the dividing cell, and there seems to be no reason for concluding that they pull more strongly in an axial direction than any other.

Dr. Lambert has pointed out that the formation or accumulation of fat in the cells of tissue cultures is somewhat in proportion to the amount of fat in the media. We, however, often find considerable fat in cells that are growing in a fat-free media and in which the piece of tissue was washed before making the culture in one thousand or more times its bulk of simple salt solution for as long as half an hour. It would seem that in such cultures the accumulation of fat were more the result of distorted metabolism than normal storage. The amount of fat is sometimes so great that the protoplasm is very much reduced.

The rejuvenation of cultures by re-transplantation, or by the addition of fresh plasma or serum, can also be duplicated, to a certain extent, with the use of artificial media in which a certain amount of dextrose or cane sugar has been added. We have not attempted to carry this very far but have been able to more than double the life of the cultures.

The use of an artificial media as a basis would seem to be advantageous for the study of the influence of various substances and drugs on the life and activities of cells. We have found, for example, that cultures thrive in solutions containing as much as two and one-half, or even three per cent., of alcohol. The tissues live as long and are apparently as healthy as ordinary cultures, except for a more than ordinarily rich accumulation of fat droplets in the cells of many of the cultures.

Recently we have been interested in the mitochondria, small rod-shaped bodies which occur in various cells of the body. They are very abundant in the connective tissue cells from the chick embryos, and are easily observed both in the living cultures and in the fixed preparations. They are usually in the form of rods, threads or granules. Our method of cultivating tissues in salt solutions would seem to offer very favorable opportunities for their study.
The President: Is there any further discussion? Has Dr. Welch something to say? If not, these papers close the general sessions of the Congress, and adjournment is in order.

Dr. William H. Welch (Baltimore): You called on me a moment ago. As a past President of the Congress, I wish to express the appreciation which we all have of the officers of the Congress, and especially the President, and to give them credit for the success which has attended this Congress. It is amazing how vastly it has grown in interest and in scientific importance. The very fact that you, Colonel Gorgas, have been the presiding officer has added luster to the gathering. I am going to ask those present to express their thanks, by rising, for the efforts of the officers in making the Congress such a success.

Adjourned at 5 P. M., sine die.