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THE PATHOLOGY AND TREATMENT OF DIABETES MELLITUS, VIEWED BY THE LIGHT OF PRESENT-DAY KNOWLEDGE.

BY

F. W. PAVY, M.D., F.R.S.

The last of three lectures delivered before The Royal College of Physicians of London, 24th November, 1908, published under arrangement with the author.

[The first of Dr. Pavy's lectures deals with the normal disposal of carbohydrate in the body, with the arguments that may be brought against the so-called "glycogenic" theory, and with the mechanism associated with the passage of carbohydrate from its seat of absorption in the walls of the alimentary canal to that of utilization in the tissues. He points out that sugar does exist in the normal urine in proportion to the quantity in which it exists in the blood. The diabetic can handle carbohydrate up to the point of his tolerance and over this, the ingested carbohydrate is excreted as sugar, just as if so much sugar had been intravenously injected. Beyond the point of tolerance, carbohydrate must increase the sugar in the blood. The question of the function of the liver in safeguarding the circulation from sugar sufficient to cause glycosuria is discussed, and the negative view upheld. Incidentally there are some interesting figures upon the efficacy or otherwise of so-called "Diabetic foods."

The second lecture deals with the state in which food is conveyed in the circulatory system to the tissues, the author believing that the existing theories imply that the food material is carried in a form susceptible of excretion through the urine, and that such implication is untenable. The protein food molecule is broken down into fragments that can be at once re-synthesized into a reconstructed protein; this process probably occurs at the seat of absorption. The process is completed by lymphocyte autolysis, and the reconstructed protein reaches the blood through the thoracic duct. The digested material in blood plasma which has escaped

from the capillaries into the lymph spaces for tissue supply is also elaborated by the lymphocytes into available protein. The lymphocytes are ultimately autolysed into the proteins of the blood, this constituting the disappearance of the digestion lymphocytosis.]

LECTURE III.

I will now give attention to the sugar that may fail to be assimilated at the seat of absorption. There are grounds for considering that, in the absence of any large ingestion of carbohydrate food, it becomes mainly disposed of at the seat of absorption. What, however, escapes being here dealt with, passes to the liver, and becomes checked from further progress by being taken into the cells and converted into glycogen. Thus the liver constitutes a second line of defence against the flow of absorbed sugar into the systemic circulation, obviating the production of more or less glycosuria that would otherwise ensue if the sugar flowed on instead of being stopped.

There is nothing in the stoppage of sugar and its conversion into glycogen by the liver cells but what is comparable to the effect that is capable of being produced by the agency of the living cells of yeast. By intracellular enzyme agency, condensation or synthesis of the sugar molecules with the elimination of water is evoked in like manner as is known elsewhere to occur, and the product constitutes a store ready to be drawn upon as need may arise.

It does not fall within the scope of the matter in hand to enter into the question of the transformation of carbohydrate into fat, but it may be stated that doubtless the liver performs a steatogenic office. It now stands as an established point that carbohydrate may constitute a source of fat, and the *foie gras* derived from the goose may be taken as affording an allustration of the liver being capable of functioning in this direction. The point to claim consideration is to see how the storage of carbohydrate under the form of glycogen in the liver can be transported to the seat of utilisation in the tissues without passing as free sugar, and thereby being placed in a position to flow off with the urine. We learn from Bernard's puncture of the fourth ventricle, that if glycogen does actually escape from the liver in the form of sugar, the fact is revealed through the production of glycosuria, varying in intensity according to the amount present in the organ.

The glycogen of the liver constitutes simply a storage of carbohydrate derived from the food, and responds in amount to that of the sugar that may happen to be reaching the organ through the portal vein. There is nothing unintelligible connected with it. Its accumulation runs

strictly in a line with that occurring in unicellular organisms, for which yeast may be adduced as an illustration. It is open to common observation to find in living nature that redundant carbohydrate, wherever existing, is put for storage into a form like that of glycogen, starch, cellulose, etc., in which form it steadily remains till a demand for it arises, when enzyme action is brought into play, and it is broken down into suitably adapted molecules for appropriation to the purpose needed.

Glycogen is known to be a body of wide distribution in the various textures throughout the animal organism. Viewed in the manner represented, its origin is readily to be accounted for. Let it be supposed that carbohydrate is taken on by a biogenic molecular complex. If employed in the production of energy, it will be consumed and disappear. If not, and the supply of carbohydrate is kept up, it will be cleaved off and stored up under the form of glycogen.

The operation is analogous to what occurs in the case of fat. Fat similarly entering the molecular complex, if utilized will disappear, whilst if not utilized, may be thrown off and stored, accounting for the fat granules and globules discoverable in cells on microscopic examination. The term fatty degeneration is ordinarily applied to this condition, and it is viewed as pathological, but it is in truth representative of a widely occurring physiological operation. It is true, it may occur under circumstances where cell action has been interfered with by a damaged cell state. Here, certainly, it may be regarded as falling within the domain of pathology. Muscular growth in response to increased muscular work is truly a physiological phenomenon, but when the work which gives rise to the growth is of an abnormal nature, as, for instance, in the case of the heart under the influence of valvular disease or arterial sclerosis, the condition falls under the name of hypertrophy, and is regarded as pathological, although the line of action is the same. Thus, a line of action which may be claimed as pathological may be based upon a physiological operative procedure.

The gist of what I am endeavouring to urge is that it is within the protoplasmic molecular complex that the play of changes takes place which gives rise to the phenomena of life; that carbohydrate, fat, nitrogen-containing matter, and, in addition, oxygen enter this complex; that the inter-actions occurring are attended with energy production through the instrumentality of oxidation as a final result, and that when it happens that the oxidisable supply is taken on in excess of consumption by oxidation, it is cleaved off as storage material under the form of glycogen in the one case, and of fat in the other, and thus circumstanced, it is available for subsequent utilisation when demand for it may exist.

What is observed to occur in connexion with the leucocytes of the blood, and with muscular fibres, stands in illustration of the two kinds of cleavage spoken of.

Glycogen, then, is to be regarded as simply a reserve of carbohydrate material, ready, as in the case of fat reserve, to be drawn upon and utilized when it becomes wasted. Its special accumulation in the liver is to be accounted for by the position in which the organ stands in relation to food supply. The main purposes to which it becomes applied are bioplasmic growth and energy production. For the latter, the chief seat of utilization is in the muscles, and here the storage amount present is found to be in a great measure dependent on rate of usage. With limb muscles deprived of activity by nerve section or tendon division, observation has shown that a larger accumulation is met with than in the muscles of the other limb left intact. Conversely, observation has likewise shown that under exercise, as, for instance, when a muscle is tetanised, a decrease of glycogen takes place.

Külz showed by his experiments on previously well-fed dogs, that under very forced exercise, glycogen might be made almost completely to disappear from the muscles and liver in about 6 to 7 hours. As far as the muscles are concerned, the glycogen is lying close at hand and has simply to be taken by the bioplasmic material that uses it up. I consider it must be assumed that, as in the case of starch in the vegetable kingdom, the glycogen molecule requires to be broken down into sugar molecules before passing into the molecular complex in which consumption takes place, and it may be reasonably inferred that, in accord with what is commonly noticeable, there is concerted enzyme action set into play to bring about what is required.

With regard to the glycogen in the liver, which, as seen, equally disappears, this is seated at a distance from where utilisation occurs, and the point now to be considered is how it becomes transported from one spot to the other and meanwhile escapes being placed in a position to show itself in the urine. We know when it happens, as after Bernard's puncture of the fourth ventricle, that the glycogen passes into the blood in the form of free sugar, the fact is revealed through the medium of the urine, but we have no disclosure recorded of any glycosuric effect having been produced by forced exercise, notwithstanding the short period within which the liver has been found to have become emptied of its glycogen.

The problem, then, now before us is how is the transport service carried on between the seat of glycogen accumulation in the liver and the seat of utilisation in the tissues, without leading to any show of its occurrence through the detectable appearance of sugar.

I have dealt with this matter in my "Carbohydrate Metabolism and Diabetes" (page 68), and have suggested that the transport is effected by the glycogen molecules becoming in the first instance broken down by enzyme action, just as occurs with starch molecules in the vegetable kingdom, into molecules of sugar, and then that these sugar molecules become linked on as side-chains to protein molecules, and thus conveyed in a locked-up, large molecular state to the tissues, where they become taken off accordingly as they are wanted.

This is nothing more than what happens in the ordinary course of chemical procedure. I have previously spoken about side-chains being taken on to a central ring or nucleus, and the capability of their being afterwards withdrawn without disruption of the nuclear body. The matter resolves itself into a question of the strength of affinity operating in one direction or the other. So it may be with sugar molecules linked on to a molecular blood complex. If they should be brought under the influence of a tissue complex in want of them, and thereby possessing a stronger affinity for them, it is only in the natural order of things that they should pass from the one to the other.

The train of phenomena would be that as the side-chains of the complex tissue molecules become worked off, they require to be replaced by fresh side-chains from the blood, and, in turn, the removal of these side-chains creates a demand which leads to the storage being drawn upon. Now, if the storage, as in the case of glycogen, is not of a nature to be adapted for shifting its position, it must of necessity be placed in a suitable condition for doing so. Here comes in the requirement for enzyme action, and it is suggested that as the storage is wanted, provision is made, through enzyme agency, for its supply in a form to meet what is needed.

Viewing matters in this way, the side-chain want in the blood leads to the storage glycogen being put into a suitable state to fill the void, and thus circumstanced, the carbohydrate becomes transported from the seat of accumulation in the liver to the seat of utilisation in the tissues without passing in a state to run off with the urine, as, in the free small molecular state of sugar, it would otherwise do in proportion to its extent of presence in the blood.

The idea here broached stands in conformity with the accepted view of what occurs in connexion with the transport of oxygen. Hæmoglobin is the agent concerned in the process. Taking on oxygen in the lungs, it travels as oxyhæmoglobin to the tisues, and gives up the oxygen that is needed to replace that which has been consumed in the bioplasmic molecules. Thus unloaded and made ready for recharging, the hæmo-

globin is conveyed back to the lungs, where a fresh intake of oxygen occurs. Thus the round is effected by the capacity possessed by hæmoglobin of taking oxygen into chemical union of a sufficiently feeble nature to permit of its being subsequently dissociated to meet the demand of the tissues. I urge that we have here a parallel of what occurs in the case of the transport of carbohydrate from the seat of accumulation in the liver to that of utilisation in the tissues.

In this transport of carbohydrate I have assumed that it passes in the form of a side-chain linked on to a large-moleculed constituent of the blood. As yet we have no distinct evidence before us to show what this constituent really is. Probably it is of a protein nature, and if so, we have material at hand to open out a consistent train of reasoning of much interest and importance standing at the root of what is being dealt with. Let me enter into particulars and expound what I refer to.

What is wanted for transport service is that the carbohydrate should be loosely linked on to the carrying molecule, so as to be susceptible of being disjoined without involving the disruption of the molecule itself. Evidence, as we shall see, is producible attesting the existence of such a state. At the same time, let me say that evidence is also producible having the effect of showing the existence of carbohydrate in another state in the molecule—in a state so closely locked-up as not to be susceptible of liberation apart from the disintegration of the molecule. Both points it will be found, have important practical bearings connected with them.

That the existence of carbohydrate in a loosely combined and in a firmly locked-up state in a molecule is no mere hypothesis is capable of being made manifest by what is seen when amygdalin is exposed to different kinds of enzyme action. A molecule of amygdalin has two molecules of carbohydrate within it. When subjected to the action of glucase, the ferment which transforms maltose into glucose, a molecule of glucose is split off without the production of any further effect, which means that the other molecule is left untouched. In contact with emulsin, however, both molecules are liberated, with benzoic aldehyde and hydrocyanic acid as associated products. The conclusion to be drawn from these results is that the two carbohydrate molecules within the amygdalin molecule are differently placed—that one is in a position to be easily detached without leading to other disturbance, whilst in the case of the other, its liberation involves molecular disruption as an attendant phenomenon.

A study of the effects of phloridzin affords immense help in unravelling the intricacies of the question that is being considered, and it

points in a very decisive manner to the existence of carbohydrate within the molecular complex, as a side-chain attachment on the one hand, and in a locked-up state in the nuclear centre on the other. It, moreover, goes further, and gives grounds for associating the side-chain attachment with transport service, leaving the locked-up portion as constituting a component incorporated during the construction of the molecule, whether in lymphocyte growth from food, or in bioplasmic growth elsewhere.

Phloridzin, as is well known is an active producer of glycosuria, and its action in this direction is exerted through the co-operation of the blood and the renal cells. The sugar does not, as in other forms of glycosuria, take origin elsewhere and travel to the kidney preparatory to elimination, but comes into view during the act of secretion of the urine, and in the absence of the kidneys phloridzin fails to produce any visible effect within the system. It is obvious, therefore, that some constituent of the blood other than sugar must be concerned in the production of the glycosuria. The output of sugar is sufficiently large and continues to show that there must be something to feed the blood to keep up the discharge occurring, and, coincidently with the outflow, it is noticed that a disappearance of storage glycogen occurs. Indeed, phloridzin supplies us with one of the most effective means of rapidly clearing away glycogen from the liver and the muscles.

That the blood is fed in the way suggested is supported by the evidence derivable from liver ablation experiments. It is possible for the life of an animal to be maintained for some hours after the removal of the liver and its associated viscera in the abdomen. In a paper published in the Journal of Physiology (Vol. XXIX, 1903), "On the Mechanism of Phloridzin Glycosuria" by Pavy, Brodie, and Siau, results are given which show that the sugar elimination declines after phloridzin injection at an infinitely greater rate in the liver ablation experiments than in control experiments where the viscera in question were left intact. It further appeared, when the sugar elimination had almost completely stopped, that a fresh start was given to it by transfusing into the vessels defibrinated blood derived from another animal.

Taking the fact that glycogen, as a result of phloridzin administration, disappears from its seats of accumulation, and that sugar contemporaneously shows itself in the urine, let us follow the matter on and see what the fact mentioned leads up to. The glycogen itself does not travel to the kidney and there constitute the source of the sugar that springs into view. As a first step in the operation occurring, it is not permissible to do otherwise than conceive that the glycogen molecules must be broken down into molecules of sugar. Now comes the import-

ant point bearing upon what next transpires. The condition is unassociated with hyperglycæmia, but hyperglycæmia should be present if the sugar molecules passed as such into the blood. It seems to me that we are driven to the conclusion that the sugar molecules must enter into combination with a constituent of the blood and then become set free again by the influence brought to bear when the kidney is reached. If a transport of sugar in one way or another occurs, as the evidence before us denotes it does, and it is not effected by passage in a free state, the only inference to be drawn is that the sugar is thrown out of sight by entering into a combined state.

Physiologists accept this explanation of the phenomenon of transport connected with phloridzin glycosuria. If admitted here, why should it not be equally admitted as applicable to what happens in connexion with the ordinary occurrences of life? Forced exercise leads to a rapid emptying of the liver of its glycogen, without producing any show of the passage of sugar through the circulation in a free state. If the sugar goes into combination in the one case, why should it not do so in the other? The circumstances stand in reality upon an analogous footing. The abstraction of carbohydrate from the blood to compensate for its consumption in the muscles during forced exercise, will create a demand for its replenishment, and thence lead to the store of glycogen in the liver being drawn upon. In the case of phloridzin glycosuria, the outflow of sugar that occurs in the kidney will, similarly to forced exercise, draw off carbohydrate and give rise to a demand for reinstatement from the glycogen store. The line of procedure is the same in the two cases, but the initial condition that leads to the demand for the replenishment of carbohydrate in the blood is different.

Support is given to the view that has been set forth by the modified conditions belonging to pancreatic glycosuria. Here hyperglycæmia precedes the glycosuria. The disappearance of glycogen occurs just as in phloridzin glycosuria, but the source of disappearance is conversion into sugar at the seat of storage. The kidney simply eliminates the sugar that is conveyed to it in the blood, and if the elimination is prevented by extirpation of the kidneys, the sugar goes on increasing, with the result of exceedingly high percentages having been noticed. The abnormality proceeds from a local transformation of glycogen into sugar, which recognisably passes into the blood in a free state, and subsequently flows off with the urine.

The instance that has been cited in reality shows what occurs when sugar from vanishing glycogen reaches the blood in a free state. In phloridzin glycosuria, there is equally a disappearance of glycogen, but

nothing is seen, as far as the blood is concerned, of the sugar derivable from it. Proof is given that the sugar has not undergone destruction by the fact of its coming into view when the kidney is reached. It is simply for the time being concealed by entering, as may be legitimately assumed it does, into combination with a constituent of the blood. If, in the presence of these circumstances, things can run on in this way, is it not permissible to assume that sugar may be transported in a locked-up state from the intestinal seat of food absorption, and from that of glycogen storage, to where it is required for service? By admitting this, all difficulties at once disappear.

I have previously referred to Professor MacLeod's article in Leonard Hill's "Recent Advances in Physiology and Bio-Chemistry" and criticised the grounds upon which he has sought to maintain the validity of the glycogenic doctrine. Although, in dealing with this point, he contends that there is a functional transit of sugar through the circulation in a free state, he falls in with the view of transit in a combined state, declaring in the first place (page 319) "there is reason to believe that a loose chemical compound—of a colloidal nature—exists between serum globulin and dextrose;" next remarking (page 363) that the mother substance of the sugar eliminated in phloridzin glycosuria is undoubtedly the serum proteid; and then saying (page 364) that the proteid which has been thus deprived of its sugar "becomes recombined with more of it during its circulation through the rest of the body." This, it will be seen, precisely represents what is claimed as constituting the physiological mode of transit.

There are further facts connected with phloridzin glycosuria that give support to the view that has been expressed. If repeated administrations of phloridzin are employed in a well-fed animal, continued elimination of sugar occurs without any material alteration of the associated nitrogen elimination. The carbohydrate of the food in the first part of its onward march after absorption, follows the normal course, but afterwards, through the agency of what occurs in the kidney, becomes diverted into a wrong direction and flows off with the urine as sugar. This is what happens whilst there is food supply or a glycogen reserve to be drawn upon, and the circumstances are compatible with the carbohydrate being linked on as a side-chain to a blood-contained molecular complex.

With the absence of food, and when the glycogen has been swept away from its seats of storage, the position of things with regard to the relative elimination of sugar and nitrogen becomes altered. The sugar falls until it arrives at a fixed relationship to the nitrogen, and when

this point is reached, it is assumable that both sugar and nitrogen are being derived from the breaking down of the molecular nuclear centre that was constructed at the time of the building up of the protein molecule Evidently, in the one case, the carbohydrate is liberated without the destruction of the molecule, and in the other, the liberation is an accompaniment of molecular disintegration.

I have just spoken of the elimination of sugar in phloridzin glycosuria being connected with food supply. The carbohydrate in the food runs off as sugar in the urine, and it does this without showing itself as sugar in the blood. The only deduction that can be drawn from this occurrence is that it passes in a state of combination, and, in view of the intensity of the glycosuria that is sometimes observed, it is evident that the capacity for transit in this state must be very great. In pancreatic diabetes, the eliminated sugar is similarly connected with food supply, but the carbohydrate of the food reaches the circulation, and passes through it to the kidney in the form of free sugar. Thus, in both these conditions, the food carbohydrate passes through the system and makes its appearance in the urine as sugar. In connection with the one, it passes through in a concealed (combined) state, as I contend happens in its conveyance in the healthy person to the tissues for utilisation. In connexion with the other, it passes through in a free or uncombined (unassimilated) state, just as it does in ordinary diabetes. Herein, then, it may be considered that we have the two modes of transit, that in health and that in diabetes, represented.

I must not allow the subjoined remarks by Professor Halliburton, in his advocacy of the glycogenic doctrine, contained in the article that has been already referred to on "Diabetes Mellitus from the Physiological Standpoint" inserted in the July number of the "Practitioner," 1907, to pass without comment. At the present stage a fitting place is offered for referring to them, and I will proceed to avail myself of it. The question of the sugar formation by the liver is being spoken of, and the following line of reasoning is set forth. "At the present day, the prevalent opinion among physiologists is of the nature of a compromise between the two extreme views. The liver is, no doubt, able to convert part of its glycogen into fat, but most of its glycogen is regarded as leaving the liver as sugar (dextrose). In coming to the latter conclusion, physiologists are influenced by what they learn from surviving organs generally. An excised organ is undoubtedly on the road to death, but while it still retains vitality, the phenomena it exhibits are similar in kind to, through they may be different in degree from, those which it exhibits during life. It is impossible to suppose that, at a

given moment, arbitrarily called death, an organ can turn round and do what it never did before. Even in the case of blood-coagulation, which appears to be a direct instance to the contrary, there is no doubt, from recent research, that the blood is always tending to clot even during life, and is prevented from doing so by the production of anti-substances (anti-thrombin produced in the liver), which neutralise the activity of the thrombin or fibrin ferment."

It is a matter of surprise to me to find that Professor Halliburton has written in this way in the face of what is contained in my work on "Carbohydrate Metabolism and Diabetes," a presentation copy of which was forwarded to him. At page 68, the text runs: "the suggestion presents itself that sugar is taken on as a side-chain by a proteid constituent of the blood and transported to the tissues, where it is taken off for subjection to utilisation. The suggested operation is identical with what occurs in connexion with the transport of oxygen. Oxygen is taken on by hæmoglobin, and, in a state of combination, transported to the tissues, where it is taken off and applied to utilisation. Glycogen is a storage material consisting of very large molecules and therefore not adapted for shifting its position. I should think that the first action that occurs is the breaking down of its molecule into molecules of glucose, which become instantly taken on by the alluded-to molecules of the blood. There may be concerted action between the breaking-down and taking-on processes, and that there is such in operation is rendered probable by the fact that there is no show of sugar in connexion with the occurrence. Enzyme action, it may be considered, of necessity constitutes a part of the process, and the enzyme concerned, and set in motion as needed, may, in the presence of altered conditions, be intelligibly conceived to be capable of producing the deviation from the natural living state with respect to sugar that so quickly takes place as a post-mortem occurrence in the liver."

On the following page, in speaking of the effect of phloridzin, the statement is to be found: "The first effect of the phloridzin is to sweep away the glycogen that is present in the different parts of the body. If this passed through the circulatory system as free sugar there ought to be hyperglycæmia in proportion to the glycosuria, which there certainly is not. This being the case, the only conclusion to be drawn is that the katabolised glycogen (sugar) enters into side-chain or loose combination with a constituent (proteid) of the blood, and is thus conveyed to the kidney where it is set free and eliminated."

It will be seen that the view that can be now put forth, emanating from the knowledge that has been acquired during the last few years, and

embodied in the work alluded to, has failed to receive Professor Halliburton's consideration. The effect of the proposition is to take away the ground from beneath his argument and destroy its reality. Previous to the recognition of carbohydrate as a constituent of protein, there could be no conception of what is permissibly entertainable now, and it must be admitted that a difficulty stood in the way of reconciling the facts observable in connexion with the changed state of things occurring in the liver at the moment of death. On the one side, evidence showed that if sugar passed into the circulation as had been suggested, the fact of its doing so could not escape being revealed by the urine, and the state of the urine negatived the possibility of the occurrence taking place. On the other side, there was the active production of sugar that was observed to occur in the liver as a post-mortem effect, and which, if occurring during life, would have established a different state of things from that actually found to exist. In these circumstances, it could only be said that the enzyme action allowed to come into play after death must be inhibited by the conditions existing during life.

With the knowledge that we now possess, it may be considered that no incompatibility exists. Concerning enzyme action, a considerable advance has been made, and it is consistent with what is now known to consider, in relation to the transformation of glycogen into sugar, that the agent concerned in effecting the process does not primarily exist in the liver in the state of enzyme, but in that of zymogen. Enzymes are dual bodies, and the mother substance of them, zymogen, possesses no activity. The co-operation of another body, the activator, is required to give it enzymic power. In other instances, the activator is brought into play as it is required, and here the conditions leading to a demand for carbohydrate from its storage may set the activator free and start the enzyme into motion in the manner needed. It may well be that the altered conditions occurring at death may lead to a removal of the restraining influence that held things in proper check during life. The same may be said with regard to blood coagulation. The zymogen, or proferment, of thrombin is present, but is devoid of activity, so long as the co-operative agent is held from exerting its activating effect.

Looking at the distinguished position that Professor Halliburton holds as a teacher of physiology and the weight that his writings carry in the mind of members of the medical profession, I cannot help regarding it as very regrettable that the evidence which nullifies his argument should have escaped being noticed. It is medicine that suffers in connexion with the matter, for without a right physiological basis, there can be no rational comprehension to guide the medical practitioner in

dealing with the wrong metabolism which stands at the root of diabetes.

Is it to reversed enzyme action that the conversion of glycogen into sugar is due? Everyone admits that the building up of glycogen from sugar constitutes an important function of the liver. We look to enzyme action as the agency effecting the process, and it is now recognised that, by altered surrounding conditions, the line of action that has been in operation may be changed into one of a reverse nature. I see nothing inconsistent with the building-up enzyme in the cells of the liver being influenced by its environment in such a manner as to lead to the occurrence of a reversal of action, and thus to give rise to a breaking down of the previously built-up glycogen into sugar.

It is interesting to note the analogous behaviour that is traceable between carbohydrate and fat in their connexion with bioplasm, and to this point I will now proceed to direct attention. We have seen that carbohydrate becomes incorporated in the bioplasmic complex, and that, if not consumed when there brought into relation with oxygen, another component of the complex, it may, under circumstances of redundancy, be cleaved off as storage material.

The effect of modern research is to give to fat a place in the bioplasmic molecule, and thus to put it into the same position as carbohydrate. I need not, I consider, here enter into the details of this matter. It will suffice to state that there is evidence to show that fat may exist in a locked-up state in a protein compound in like manner to what occurs with carbohydrate. In these circumstances, the fat is in an out-of-sight state, but is susceptible of being brought into view by the disruptive agency of peptic digestion. It is only recently that this subject has fallen under consideration, but already it has made its way into prominent notice.

With the point reached, the position of things stands as follows: the bioplasmic molecular complex, which may be regarded as the representative of a living unit and thereby as the seat of the metabolic changes which give rise to the phenomena of life, contains both carbohydrate and fat incorporated within it. Through intramolecular action, set in motion by agencies of an enzymic nature, the various occurrences noticed to ensue may be conceived to be brought about. In the molecule, oxygen also enters as a constituent, and thus circumstanced, it is brought into close relationship with the carbohydrate and fat components with which the interactions occur that give rise to the development of energy. The play that takes place is not considered to consist of straight off or unbroken oxidation, but of oxidation, step by step, of the components of the

chain of which the vanishing molecule is made up. The result, when the intramolecular procedure is normally carried out, is the production of carbon dioxide, water, and ammonia,—products devoid of latent energy. Should it happen, as may in the presence of abnormal conditions be the case, that arrest at an intermediate stage takes place, the effect is the throwing off of a product retaining unexhausted energy.

I have shown that, with a redundancy of carbohydrate, glycogen is dissociated for storage purposes. Condensation, or building up within the bioplasmic molecule, must be here in operation, seeing that it is in the form of sugar, and not glycogen, that the carbohydrate enters the molecule. Precisely the same sort of thing happens in the case of fat. Under the existence of a redundancy, fat becomes, by cleavage from the bioplasmic molecule, microscopically visible where none, whilst in a locked-up state, was previously to be seen. Here again constructive work must be performed, inasmuch as neutral fat is devoid of the needed dialysability to permit of its passage through cell membranes to reach the bioplasm within. The transport must occur in association with a dialysable state, and an enzyme—lipase—exists widely distributed through the body, which performs the office of breaking down fat into fatty acid and glycerine, when transmission through a cell membrane is wanted. This operation, followed by saponification, provides for the transmission, and then, should the conditions be such as to lead to neutral fat coming into view, a re-synthetic action is brought into play. What has been stated stands in accord with the teachings of the present day, and it is seen that the line of procedure in the case of fat fits in with that appertaining to carbohydrate.

These phenomena cannot for a moment be conceived to issue from the effect of mere chemical action working independently of the influence of living power. Everything tends to show that actual incorporation in living matter precedes metabolic activity. Living matter is made up of more or less highly complex molecules, and, thence, saying that a body enters into the constitution of living matter is tantamount to saying that it enters into the composition of the complex molecules of which it is made up. This renders it justifiable to speak of living action as resulting from incorporation of food-stuff in the bioplasmic molecules and its subjection to the influences that are there existing. Intramolecular activity in this way stands at the foundation of living action.

Now, taking carbohydrate and fat, it has to be said of them that they both, in a suitably hydrolysed state, become linked on to the bioplasmic molecules. What subsequently occurs depends upon the circumstances

at the time existing. If they are oxidised, they disappear in the form of carbon dioxide and water, giving rise to the liberation of a concordant amount of energy of one kind or another. If they are not consumed in this way, and the supply of nutrient material goes on, they become dissociated and laid by as storage stuff, the carbohydrate in the form of glycogen, and the fat in the form of glycerine or neutral fat.

I strongly demur to the terminology that is in common use among pathologists in connexion with this matter. It is a terminological inexactitude to speak of these operations as falling generically in the category of degenerations. They are virtually in themselves of a physiological nature, and, moreover, constitute representations of, it may be said, the largest and the widest spread class of action occurring in the living world. Look at the production of starch, cellulose, etc., and of fats in the vegetable kingdom, and of glycogen and fats in the animal kingdom, as the issue of indisputable physiological procedures. It is through bioplasmic agency that the phenomenon is brought about. Either carbohydrate or fat, entering the bioplasmic complex and not being oxidised or consumed, will not remain fixed there, but be dissociated or thrown off in one form or another, according to the potential conditions existing. Carbohydrate may enter and be thrown off as carbohydrate, and fat as fat; or, it may be, that carbohydrate may be taken on and fat cleaved off, or fat enter and carbohydrate be cleaved off.

Illustrations demonstrative of these actions are readily obtainable from the vegetable kingdom. With respect to the production of fat from carbohydrate, I may cite a passage from Sachs, quoted in my "Physiology of the Carbohydrates" (page 247). "Before maturity such (oily) seeds contain no fat, but only starch and sugar. Such unripe seeds (e.g. of *Pæonia*) may be detached from the mother plant, and allowed to lie in moist air with the result that the starch disappears and is replaced by fatty oil." With respect to the production of carbohydrate from fat, the growth of the oily seed suffices to afford a demonstration. From the oily seed placed in contact with water, a young plant springs, just as happens with its starchy congener, the fat obviously constituting the source of the cellulose that comes into existence. Concordantly, there cannot be any doubt about fat emanating from carbohydrate as a metabolic procedure in the animal kingdom, but concerning the production of carbohydrate from fat, I do not consider that any point of evidence is yet before us that can be definitely said to settle the question.

I submit that, in the dissociation process of which I have been speak-

ing, carbohydrate and fat stand upon identically the same ground. The matter is very simple and intelligible. Both form an integral part of bioplasm. If in excess, arising from supply, or from production within as in the case of fat from carbohydrate, of the consumption taking place, they become dissociated as storage material.

The dissociation seems to play a balancing rôle. What is not used is for the time thrown off. This is well seen in the case of yeast cell growth in association with a plentiful supply of sugar. The sugar is taken, and that which is in excess of application is thrown off as glycogen. The adipose tissue cells, although replete with fat, go on taking it if it is presented to them. Because it is not actually wanted does not stop the process of taking on. When the supply fails and it is wanted elsewhere, then a reverse action occurs, and it is taken back and transported to where it is needed for consumption, just in the same way as occurs with carbohydrate. What I submit is that, as a general principle of action, the taking on does not necessarily cease when what is taken on is not consumed.

Here lies the foundation of the so-called degenerations. They simply represent thrown off material which has been incorporated into bioplasm, or produced within it, in excess of consumption. The liver is full of activity in this way. Standing in the position it does in relation to food, it is brought into contact with supply material to a greater extent than happens elsewhere, and do we not accordingly find that in this organ, more than anywhere else, accumulation of fat and carbohydrate is observed to take place?

Thus I have been dealing with the supply as standing at the foundation of the condition that may happen to be met with. Taking the other side of the question, a check to consumption may be the determining cause of accumulation. Whilst consumption is balanced to supply, no opportunity exists for the occurrence of dissociation. Should consumption, however, fall short, surplus material will come into existence and show itself as a dissociated product. The two main sources of dissociation of this kind are deficient supply of oxygen and inactivity. From whatever cause arising, these conditions are known to give rise to accumulations of both fat and glycogen. Damage of cell bioplasm through toxic agency, as, for instance, from diphtheria, etc., will by the instrumentality of its check to activity, give rise to the condition that is being considered.

Under the view set forth, the whole matter is placed upon a rational basis and made clear and intelligible. Degradation of protein into fat,

after the manner that was formerly entertained, does not enter into the question. The operation, in fact, consists of a throwing off, precisely as is done upon a most extensive scale, as a normal metabolic procedure, in both kingdoms of living nature. The act of throwing off, as has been seen, is subordinated to the influence of the collateral conditions existing. When these conditions are normal, the process is a physiological one, and there is nothing of a degenerative nature about it. It is only when the throwing off is occasioned by a pathological state that the term "degeneration" can be justifiably applied to it. The distinction that applies to the terms "growths" and "hypertrophy" is strictly applicable in connexion with the point under consideration. To use the term "generation" in the manner that is too often done, is absolutely unscientific and misleading.

We learn, both experimentally and clinically, that the pancreas is mixed up with carbohydrate metabolism, and let me now pass to the consideration of this subject, and see the kind of reading that may permissibly be put upon the facts that have been disclosed in connexion with it.

Our predecessors of many years back recognised that disease of the pancreas was from time to time met with in the post-mortem examination of persons who had died of diabetes. The recognition in modern times that diabetes follows experimental extirpation of the pancreas, stands in conformity with this, and, as it is found experimentally that for the production of the effect the extirpation must be complete, so from modern clinical experience it is learnt that partial disease of the organ may exist without being attended with diabetes, whilst with extensive disease of it, diabetes may be expected to be found as a concomitant.

Something, then, derived from the pancreas is apparently concerned in contributing to the normal metabolism of carbohydrate, inasmuch as in the absence of this something, carbohydrate shows itself as sugar in the system in a manner that does not occur when the proper passage to utilisation is carried out. Now, in the proper passage of food molecules to utilisation, a preliminary linking on to the various bioplasmic molecules of the body is, at the present time, pretty generally admitted to take place. It is not conceived as at one time was done that the food molecule is consumed in the form of an isolated entity. Toxins, when in a position to be incapable of being taken on by the constituent molecules of bioplasm, fail to exert any toxic effect. It is only when they become actually linked on to the bioplasmic molecules that the inter-

actions that are needed to evoke the results which are capable of being produced by the particular toxin concerned, can occur. So with food molecules, they must be embodied into the bioplasmic molecules as a preliminary step to utilisation. Thus placed in these molecules, they are brought into relation with the other constituents, notably oxygen, which presumably is present in a loosely combined state as in oxyhæmoglobin, and put into a position to permit of the interactions attended with oxidation, and the liberation of energy that are observed to take place.

Analogy may be appealed to for assistance in the comprehension of the procedure involved in the linking on of the food molecule to the bioplasmic complex. We learn from what occurs in connexion with toxins and of lysins (hæmolysins and bacteriolysins), that there is an intermediary body, the amboceptor, through which the junction with the bioplasmic molecule is effected. In the absence of the play of this intermediary body, no junction and no effect follow the presence of the toxin and the lysin in the blood. A large amount of closely reasoned experimental work, with much of it of a test-tube nature, stands at the foundation of the conception that has been put forward, and gives to it a well-grounded qualification for acceptance.

Proceeding on with the matter, it may further be said that, whilst the body that is linked on (in immune phraseology called the complement) is thermo-labile or susceptible of destruction under exposure to a moderately elevated temperature, the agent that links on (amboceptor) may be exposed to a boiling temperature without losing its linking-on power, and is, therefore, in contradistinction spoken of as thermo-stable. This is an important point in connexion with the train of reasoning that I am about to set forth.

It is contended that the first step towards the utilisation of carbohydrate is linking on to the bioplasmic complex. Without susceptibility of being linked on, it simply filters through the body and runs out with the urine without being in any way touched. This is the case, for instance, with the disaccharides,—saccharose, lactose, and maltose, when under any circumstances reaching the circulatory system as such. With the mono-saccharides,—dextrose, levulose, and galactose, on the other hand, we find that these, when present in the circulation, do not wholly escape in a similar manner. A portion fails to pass out with the urine, and this portion, it may be assumed, becomes put into the combined state, and subsequently made use of in the ordinary manner. If no capacity existed for linking on these monosaccharides, it is not conceivable that

they would be any more susceptible of utilisation than the group which is not utilisable.

The effect following the introduction of the different sugars into the circulation by intravenous injection has been already alluded to. It has been seen that a certain amount of power exists of putting the monosaccharides into a position to be made susceptible of retention in the system. A great contrast, however, is to be perceived in the extent of power that exists at the seat of absorption in the alimentary canal to deal with the sugar derived from the food, as compared with that existing in the blood. Notwithstanding the large amount of carbohydrate that may be ingested with the food, we find, with its reception into the organism in a normal way, that it effectually become assimilated, or put into an altered state, and thus prevented the general circulation as sugar. Introduced, on the other hand, in a direct manner into the circulation, the evidence afforded, alike by the urine and by analytical examination of the blood, shows that it is only comparatively slowly and in limited quantity susceptible of being thrown out of view, by the power that is here encountered.

Protein and carbohydrate are similarly circumstanced in connexion with this point. The digestion products of both are rapidly put out of sight after absorption from the alimentary canal, and are not to be traced on into the general circulation. Introduced into the circulation, both are, to a certain extent, susceptible of being dealt with and removed from view, that which is not so dealt with, flowing off, in each case with the urine. Professor Starling, in a paper published in Vol. XIV of the *Journal of Physiology*, says with reference to the results obtained from the injection of peptone and sugar into the blood: "It will be seen from them that the behaviour of peptone after injection is almost exactly analogous to that of sugar."

What is it that occurs in connexion with the disappearance of carbohydrate to account for the phenomena? A portion may be taken by the tissue bioplasmic molecules, if there is a want of it to replace side-chains that have been worked off. Evidence, however, is forthcoming to show that there is to be found within the blood itself a means by which sugar may be carried out of view.

Besides carbohydrate in the form of sugar, carbohydrate in the amylose form is obtainable from blood. After the removal of the sugar by treatment with alcohol, the precipitated matter is capable of yielding a certain amount of carbohydrate in the amylose form, after having been subjected to the breaking down influence of boiling with potash. This,

under ordinary circumstances, is found to amount to about 1 per 1,000 of blood. I have for a long time known that the amylose carbohydrate that is thus capable of being obtained from blood, shows itself in greater amount after the introduction of sugar into the circulation. I gave illustrations of this in my "Physiology of the Carbohydrates," published in 1894, and regarded the fact as constituting a noteworthy point.

Later, I recognised that if I introduced sugar into the circulation in conjunction with a boiled aqueous extract of pancreas, the amylose carbohydrate was to a decided extent further increased. The experiments on this point are set forth in my "Carbohydrate Metabolism and Diabetes" (page 71 *et seq.*). It seems to me that without doubt, the conclusion may be drawn from them that the pancreatic extract supplies something which contributes to the conversion, by the bioplasm existing in the blood, of sugar into amylose carbohydrate. The following supplies an epitome of the results obtained.

I need not here enter into the question of the mode of estimation of the amylose carbohydrate. This matter has been fully referred to in my previous writings, extending over many years past. Suffice it to say, that, upon the strength of some hundreds of estimations, I consider that confidence may be placed in the trustworthiness of the results yielded by the procedure adopted.

In the first place, 11 determinations are given derived from normal rabbit's blood. The figures for the mean of these stand at 1.41 grammes of amylose carbohydrate per 1,000 grammes of blood, the maximum figures being 1.55, and the minimum 1.25. The figures, therefore, throughout the list stand very closely together.

In 5 determinations made from blood collected at varying periods up to 30 minutes after the intravenous injection of 1 gramme per kilo. bodyweight of dextrose dissolved in saline solution, the mean figures were 1.61 per cent., the maximum being 1.80, and the minimum 1.52. Two determinations were made after the lapse of an hour from the time of the injection. The figures came out at 1.43 and 1.34, showing that any effect that might have been previously produced had passed off.

In the case of levulose similarly dealt with, the figures in 2 experiments from blood collected at 15 and 30 minutes after the injection were 2.60 per cent. and 2.67 per cent. as against 1.81 in one experiment from blood collected at the end of an hour. Looking at these figures, no doubt can exist of the amylose carbohydrate having been raised by the levulose injection.

Two experiments were made to see the effect of injecting saline solu-

tion alone. The figures from blood collected at the end of 15 minutes came out in each case at 1.35 per cent.

Passing to the experiments with the pancreatic extract, two experiments were conducted in which the extract alone was injected. In one, the blood was collected at the end of 15 minutes, and the figures given were 1.77 per cent. In the other, the blood was collected at the end of 30 minutes, and the figures given were 1.52 per cent.

In 13 experiments, the pancreatic extract was employed with 1 per kilo. bodyweight of dextrose. The mean of the figures yielded came out at 2.03 per cent., the maximum being 2.47 and the minimum 1.57.

In 4 experiments of a similar nature with levulose, the mean figures stood at 2.07 per cent. with the maximum at 2.56 and the minimum at 1.74.

One experiment was conducted with the injection of the raw extract of pancreas in association with dextrose. The injection proved immediately fatal, and the figures met with were 1.04 per cent. These low figures are not surprising, seeing that the physical effect of the injection of the sugar solution would be to lead to a dilution of the blood, firstly from the fluid injected, and next from the hypertonicity given to the blood leading to fluid being drawn into it from the tissues.

Five experiments are recorded with the subcutaneous instead of intravenous, injection of pancreatic extract and dextrose. The mean figures stood at 1.77 per cent., the maximum being 2.09, and the minimum 1.52.

In one experiment of a like nature with the employment of levulose, the figures stood at 2.30 per cent.

With reference to the precise signification of these experiments, all that is at the present moment needed to be done is to urge that they suffice to show that the pancreatic extract really exerts an action in relation to the passage of sugar into amylose carbohydrate. I will now enter upon the question of *modus operandi*.

The amboceptor in immunity phraseology seems to stand as the representative of the co-ferment concerned in enzyme action. It is now known that enzymes are dual bodies, and that the two parts are capable of being separated from each other. When separated, neither possesses any enzymic power. One is destructible by heat and seems to be the active agent, corresponding with the complement in immunity language. The other does not lose its virtue by subjection to boiling, and thus stands in the position of that which gives power to thyroid and suprarenal extracts. Taking the expressed juice of yeast, which contains

zymase,—the enzyme which converts sugar into alcohol and carbonic acid, a given quantity of the fresh juice has been found experimentally to have its enzymic power doubled by the addition of an equal quantity of boiled juice. This means that an extra quantity of the co-ferment, which possesses no inherent active power, gives increased power to the essentially active principle of a "complement" nature that is present in the juice.

The effect of the co-ferment is seen to be comparable to that of the pancreatic extract, and both, on account of having been exposed to a boiling temperature, must be devoid of energy-exerting power. It is obvious that the co-ferment must, in some way or other, contribute the assistance to the potential part of the enzyme which enables it to bring about the increased effect that has been spoken of. The possession of a linking-on power of an amboceptor nature would suffice to supply what is wanted, and in functioning in this way, an explanation is afforded of its mode of action which satisfactorily fits in with the explanation given in connexion with operations of another, but probably allied, nature.

In the case of hæmolysins and bacteriolysins, it seems to have been experimentally reduced to demonstration that a something becomes developed within the blood which plays the passive part of connecting a lytic body (complement), present as an ordinary constituent of the blood, with that which undergoes dissolution. Without the aid of this connecting body (amboceptor), the red corpuscle and the bacterium fail to be attacked, notwithstanding they are surrounded by "complement." The amboceptor is reasonably assumed to possess a linkage capacity which leads to its joining up the complement with the red corpuscle or the bacterium, and thus placing it in a position to exert its lytic influence upon them, which, in the absence of the junction, it is powerless to do.

Through the instrumentality of the amboceptor, then, the complement is linked on to the bioplasm, and until this occurs no action takes place. The food molecule also requires, as I have before said, to be linked on to bioplasm before it can be turned to account. I think it is now pretty generally admitted that it is within, or as an integral part of bioplasm, that it is made use of, and that whilst outside bioplasm, it can no more be metabolised than a toxin molecule that has had its linking-on capacity abolished can produce a toxic effect.

Molecular configuration has been spoken of in connexion with the chemical union of bodies and it has been asserted that there must be a mutually adapted configuration to permit of junction taking place.

Now, why may it not happen that amboceptor aid is required for linking the sugar molecule on to bioplasm? The facts before us bearing on the position held by the pancreas in relation to the matter under consideration, suggest that it is. Acceding to the proposition that an amboceptor is needed for the linking on of the sugar molecule to bioplasm, and that the pancreas is concerned in its supply, everything fits in and becomes placed on a clear and intelligible footing. If the aptitude does not exist for the monosaccharide molecule to be linked on to bioplasm, it becomes placed in the same position as a disaccharide molecule, which, whilst remaining as such, plays no part in connexxion with living matter, and, if reaching the system, becomes thrown off with the urine in the same way as any other extraneous or unutilisable material.

The point reached is that the facts before us suggest that the pancreas supplies amboceptors which, by effecting the attachment of the sugar molecule to the bioplasmic molecule, place it in a position to be disposed of according to the existing environment. It may undergo oxidation and disappear with the liberation of energy. It may become transmuted into glycogen (amylose carbohydrate). For this, it must be conceived, to pass in the first place, into bioplasm, in the same manner as the hydrolyte is conceived to pass into union with the enzyme preparatory to being converted into another form. Or it may be transformed into fat by a process analogous to that of transmutation into glycogen—that is to say, as a result of a molecular rearrangement taking place within the bioplasmic complex. The liver cells, in a marked manner, afford illustrations of the capacity existing in bioplasm of producing glycogen and fat from sugar. The action is comparable to that of a ferment, in so far that a body enters in one form and is thrown off in another.

In the case of the intravenously injected sugar without the pancreatic extract, it has been seen that a small increase in the amount of amylose carbohydrate obtained upon that normally obtainable, occurred. This may be taken to be attributable, under the view adopted, to amboceptor derivation from the pancreas normally existing in the blood. The linking-on agency would be increased by the association of the pancreatic extract with the sugar solution, and here the amylose carbohydrate was found in a very distinct manner to be further augmented. The facts exist with which the reading given fits in as a rational deduction.

I look upon the leucocytes of the blood as one of the agencies concerned in the primary metabolism of carbohydrate matter. They admittedly feed upon material that may chance to be present in the blood, and in this way extrinsic nutrient matter that may happen incidentally

to reach the blood may be appropriated and built up into bioplasm, which, like that of the lymphocytes, may pass by autolysis into the blood proteins. We have here an agency that may be instrumental in putting available matter of any kind that may in any way get into the blood, into a condition of elaborated blood pabulum.

As yet I have only applied the line of argument adduced to action occurring in the blood. But the blood is not the medium designed for the food carbohydrate to be dealt with. The work of construction into bioplasm is performed before the blood is reached by the agency of the lymphocytes. Upon this subject I have already fully spoken. Leucocytes are little masses of growing bioplasm. Lymphocytes are, in this sense, the same, and the same train of occurrence in connexion with growth may be reasonably assumed to ensue. By analogy the line of working with respect to the point before us may be carried from the one to the other. If the amboceptor is in operation, as a means of linkage of the sugar molecule to the bioplasmic molecule in the leucocyte, it may be equally taken to be similarly in operation in the lymphocyte.

This brings the ambocepter factor into connexion with the broad question of the passage of carbohydrate into the assimilated state. That it does become an incorporated constituent of protein is regarded as an accepted fact. With this before us, let it be supposed that through faulty action the carbohydrate molecule should fail to become linked on to the bioplasmic molecule, what, it may be asked, would be the state of things produced? The sugar molecule would be left untouched, and would thence pass on into the circulation in a free state, which is tant-amount to saying that there would be glycosuria proportionate in extent to the carbohydrate ingested and failing to become assimilated.

If the amboceptor is concerned in performing the office suggested in connexion with the appropriation of carbohydrate by incorporation into bioplsm, it may not unreasonably be considered to be similarly concerned in the transmutation of sugar into glycogen in the liver. The passage of sugar into glycogen constitutes a building-up operation. There are grounds for believing that the sugar in the first instance becomes taken into bioplasm. Afterwards, from the redundancy existing, a shedding off in the form of glycogen would follow, in conformity with what is conceived in circumstances of the kind to ordinarily occur. Viewed in this way, the amboceptor, if needed for the bioplasmic assimilative operation, may be reckoned to be also needed for the transmutation of sugar into glycogen in the liver.

Experience in connexion with diabetes points strongly to a fault of

the nature here depicted, standing at the foundation of the show of sugar that occurs. In the passage of ingested carbohydrate to its natural destination, a certain chain of events is passed through. A faulty link in the chain, through such a defect as has been spoken of, would suffice to lead to a breakage of action continuity. A faulty cog in the metabolic mechanism is amply sufficient to account for the arrested progress of onward movement that renders itself perceptible through the sugar that comes into, and ought not to come into, view.

The theory of glycolysis, as enunciated by Lépine, appropriately falls in here for consideration. As long as Lépine held to the canons of the glycogenic doctrine, which imply destruction, and thereby disappearance, of sugar in the transit of the blood through the systemic capillaries, there was a show of reason in seeking for an explanation of the disappearance. But how does the matter stand when he retires from his former position and denies the occurrence of the disappearance? This, in reality, is the issue of his recent experimental work, evidence being adduced by him showing the existence of more sugar (instead of less) in the blood returning by the veins than in that contained in the arteries. He, at the same time, speaks of a *virtuel* sugar (which I take to be the same as my combined or locked-up carbohydrate) as a source of the sugar that thus comes into view.

Lépine now endorses what I have all along contended for—namely, that there is not the evidence of sugar being destroyed in its transit through the systemic capillaries that was formerly taken to exist. If such be the case, glysolysis stands upon nugatory ground, and it has always been a mystery to me how a proposition, resting upon so inconsistent and illogical a basis, should have received the attention that has been given to it.

Even supposing there should be an element of truth contained in the results derived by Lépine from his pancreatic extract and blood incubation experiments, I think a different interpretation can be assigned to them from that which he has given. On the question of validity, the general opinion is that they are open to mistrust, but supposing any loss of sugar to have taken place, may it not have been through incorporation into bioplasm instead of through destruction? He affirms that the leucocytes are mixed up with the action, and likewise that chyle, with its lymphocytes and absence of red corpuscles, possesses greater glycolytic power than blood.

The trend of all modern work is to point to the chemical actions connected with living matter being of an intramolecular nature, and it is

difficult to conceive that action occurring outside the living molecule, as Lépine contends for, can constitute the mode of operation. No one thinks of structural formative power being otherwise than associated with the operations of actual living matter. Ought not the chemical phenomena to be viewed in the same way?

Under the assumption of the occurrence of glycolysis in the blood, Otto Cohnheim and others, particularly on the American side of the Atlantic, speak of diabetes being due to sugar failing to be *burnt* in the system. Nothing could be more gratuitous, unfounded, and misleading. There is not a particle of evidence to show that defective oxidising power exists in connexion with diabetes. The real fault is a condition antecedent to the oxidising operation. The food carbohydrate, when permitted to reach the general circulation in the form of free sugar, through failing to be assimilated, cannot do otherwise than run off with the urine, and thence escape being placed in a position to undergo oxidation. In the case of the dissociation of sugar from built-up bioplasm in the "composite" type of diabetes, there is no ground for thinking that defective oxygenating power has anything to do with the matter. Whilst the sugar molecule is being thrown off by the operation of a wrong lytic action, oxidation is proceeding in an ordinary way to permit of life being maintained.

(To be concluded.)

DEMONSTRATION OF THE SPIROCHÆTA PALLIDA FROM A MUCOUS PATCH OF THE CONJUNCTIVA.

BY

HANFORD MCKEE, B.A., M.D.

Upon April 21st last I was asked to see a patient at the Montreal Maternity Hospital because of the swelling of her right lower lid. The patient, H. R., 25 years old, was very poorly nourished, had a bad cough and was the subject of syphilis. She had a scar on the vulva, a rash had been present but had now almost disappeared. Her mouth was a mass of mucous patches; glandular involvement was marked.

Dr. Covernton had noticed some swelling of the right lower eyelid the day previously and to him I am indebted for calling my attention to a rare condition. She did not complain of any pain or unpleasantness about the eyes. The right lower lid was somewhat swollen, especially along the edge of the outer quarter; the eye was watery and the conjunctiva markedly congested. Upon pulling down the right lower lid there was seen on the palpebral conjunctiva, upon the outer quarter of its surface, an area which had a decidedly different colour than the rest of the conjunctiva. The peculiar pale blue hue contrasted so plainly with

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the reddened conjunctiva that the whole border of the patch was very definitely shown. Somewhat oblong in shape, it extended laterally from the middle fourth of the lid to almost the outer canthus and from before backward from the edge of the lid to the fornix. The diagnosis, from the clinical condition of the patient, and the appearance of the lid was, a mucous patch of the conjunctiva. Slides were prepared from the mucous patch by Dr. R. P. Campbell who was good enough to see the case with me and stained by Giemsa and modified methods. In all the spirochæta pallida was found in quantity. In some fields as many as six or seven typical spirochætæ were seen. Slides prepared from the mucous patches of the throat showed spirochæta pallida and refringens.

Burnett in Norris and Oliver says there would seem to be no reason why mucous patches should not occur during the regular course of the disease on the conjunctiva as well as on other mucous surfaces and several such cases have been reported. One case at least has been reported in which a true gumma had its seat on the conjunctiva. The only reference which Fuchs makes to syphilis of the conjunctiva is on syphilitic ulcers which he says are among the greatest of rarities; still rarer is the soft chancre of the conjunctiva. The position of the spirochæta pallida in eye conditions is as follows:—(1) the finding of spirochæta pallida in apparently healthy eyes of infants who have died from congenital syphilis, (2) its discovery in lesions set up experimentally in the eyes of monkeys and rabbits by the inoculation of syphilitic material, (3) its discovery in actual syphilitic lesions of the human eye. Stephenson found the spirochæta pallida in the aqueous humour of a woman with irido-cyclitis in the course of the early secondaries, also in the scrapings from three cases of Keratomalacia in syphilitic infants. Babs found the spirochæta pallida in the eyes of three syphilitic still-born fetuses, and finally we have the finding of the spirochæta pallida in the case here reported. A mucous patch of the conjunctiva is a rare condition and, while the spirochæta pallida has been found in a number of eye conditions, I would not be surprised if this were the first report of its demonstration from a secondary lesion of the conjunctiva. On this point the translator in Axenfeld's books says: "Until the present, syphilitic lesions of the eye, hard sore, secondary and tertiary affections, have given no opportunity for their bacteriological examination. If the spirochæta pallida is confirmed as the cause of syphilis and the signification of the silver impregnation methods be established the determination will be of enormous value to the ophthalmologist." The patient was put upon anti-syphilitic treatment and made satisfactory progress. No local measures were applied to the conjunctiva which cleared up quickly.

A PLATE FOR THE RELIEF OF PAIN IN THE FIRST METATARSO-PHALANGEAL JOINT.

BY

J. APPLETON NUTTER, B.A., M.D.

During the past year I have had referred to me a number of cases of disability in the feet where pain in the metatarso-phalangeal joint of the great toe was the distinguishing feature. These were treated according to their etiology by foot-plates, strapping, baking and other orthodox methods. To my chagrin I experienced great difficulty in effecting a cure, and indeed many of the cases failed to respond at all. After persevering for some weeks I was driven to adopt new tactics, and the idea occurred to me of affording rest to the painful joint, but without confining my patients to bed. Such relief seemed possible by the use of a foot-plate made with a high inner arch, which would thus bear more than its accustomed share of the body weight. The plan seemed logical, but before committing myself to it I sought the advice of one of my former teachers in a distant city. On receiving his endorsement and advice I had the plates made which are being passed around. The results obtained by mechanically protecting the painful joints have been so thoroughly satisfactory wherever they have been tried, that I have thought the matter worth bringing before your attention. In each case a cure is being effected by giving rest to the painful joint, and relief is being obtained after many years of pain and discomfort.

As you know, the head of the first metatarsal bears a large proportion of the weight which comes upon the front of the foot. This weight-bearing function naturally resists any effort to relieve an inflammatory condition of the joint. Hence a plate that will relieve the painful joint of its burden of weight-bearing will aid materially in its cure.

Chronic pain in the first metatarso-phalangeal joint is met with frequently.

Shoes which are too narrow, and which crowd the metatarsal bones together laterally, have furnished a majority of the cases which have come under my observation.

Hallux valgus, generally the result of too narrow shoes, is itself often accompanied by pain in the joint. When severe and especially when paroxysmal it is generally attributed by the patient to gout. Mechanical treatment of this deformity, as by applying splints to bring the toe into line, is seldom satisfactory, as the apparatus generally causes more discomfort than the deformity itself. Under the heading of mechanical

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treatment is not meant to be included the protection of a painful bunion from the irritation of the shoe. In such a case the pain is periarticular, and not in the joint itself.

Weakness in the longitudinal arch has been a frequent cause, and in fact the pain from such a weak foot may be largely confined to the region of the great toe-joint. In some cases simple support to the arch will cause all pain to disappear, in others, where the inflammatory process is more deeply rooted, the joint in question needs individual attention.

In another group of cases we find this joint picked out for the attentions of rheumatism, rheumatoid arthritis, and gout. Sometimes cases of rheumatoid arthritis are so severe as to lead to a suspicion of tuberculosis of the first metatarsal.

Inflammatory conditions of this class are frequently combined with weakness of the foot, and the two conditions must be carefully differentiated. The most common example is an infectious arthritis in young adults with weak feet, causing nearly constant pain in the great toe-joint, and a pronounced limp, associated with similar pains elsewhere, as in the shoulder or fingers. This may or may not show swelling of the periarticular soft parts.

In the case of weakness of the transverse arch, the cause of Morton's metatarsalgia, the pain is commonly referred to the distal extremities of the outer metatarsals, and seldom attacks the first.

As regards diagnosis, it is most essential to be able to estimate how much of the disability is due to so-called rheumatism, and how much is the result of weakness of the longitudinal arch. Now weakness in the longitudinal arch manifests itself perhaps earliest by two signs. The first is a bulging or convexity on the inner side of the foot over the region of the head of the astragalus and the navicular bone, seen when the foot is bearing weight. If this bulging be marked, and especially if it be present when the foot is *not* bearing weight, the longitudinal arch is probably giving way.

The second sign is limitation of voluntary inversion of the foot. This action takes place largely in the mediotarsal joints, and when the longitudinal arch is being flattened it is mechanically restricted.

In making a diagnosis of rheumatic or rheumatoid conditions it is important to find other manifestations of the disease. If, for instance, bad weather brings on pain in the great toe-joint of a patient with a weak foot, and if this is accompanied by an aching finger which shows a Heberden's node, we can be fairly sure that we have to deal with more than static disturbance in the foot. At times, however, it is necessary, as a therapeutic test, to have recourse to strapping or even a foot-plate.

In designing a support to afford relief to the first metatarso-phalangeal joint, a cast of the foot must be made. Upon this plan a comfortable plate extending from the centre of the heel to the heads of the metatarsals, with the following essential additions, (1) a quick rise just behind the head of the first metatarsal, so as to raise this from the ground; (2) a doming up of the plate under the heads of the second and third metatarsals. When placed in the shoe and walked upon the patient at once notices that the affected joint is bearing no weight, and as a rule experiences relief immediately. It may take a day or two, however, before walking can be indulged in freely. If properly made they are quite comfortable. The plate must, of course, be regarded as a crutch, to be discarded when no longer absolutely necessary. After a month or two of freedom from pain the patient should be allowed to walk an hour or more daily without it, this period to be gradually increased until its use may be entirely discontinued. While being worn, appropriate exercises for a weak foot should be practised, if such a condition co-exists.

As a rule the shoes worn by the patient are too tight across the front of the foot, and are all the more so when the plate is in the shoe. For this reason it is usually necessary to procure new shoes, made very broad and roomy.

Although these plates suggest a blacksmith and a workshop more than they do a pathological laboratory and microscopical technique, yet I feel sure that they are none the less valuable on this account. Should you meet with a case of obstinate pain in the metatarso-phalangeal joint of the great toe, have a plate made that will give the joint a rest, and I am sure you will be gratified by the result.

THE SURGICAL TREATMENT OF NON-RESILIENT DIVERTICULA OF THE BLADDER.

BY

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The comparative infrequency of large diverticula of the bladder has prompted me to report in detail a case which I have observed, and to review the methods employed in the surgical treatment of this affection.

While cystoscopists of experience are apparently agreed that diverticula of the bladder associated with urethral or prostatic obstruction or the presence of stone are relatively frequent, such sacculations, whether single or multiple, are usually unassociated with peridiverticular adhesions and tend to disappear after the removal of the cause of increased intravesical pressure. In this connection I wish to deal only

with that form of diverticulum, usually of large capacity, which, owing to the existence of adhesions to the surrounding organs or the paucity of the muscular element in the sac wall, is characterized by the absence of expulsive force. From the point of view of pathogenesis one should not include as true diverticula those cases which are a sequence of perivesical suppuration, although from the point of view of diagnosis and treatment they are indistinguishable from such as result from attenuation of the bladder wall through pressure.

Varieties. Large diverticula may be either congenital or acquired. I am not aware of any case in which a diverticulum has been found post-mortem in infancy; Pean's[1] case, however, strongly supports the congenital theory, as does a case reported by Hofmokl and Ghon,[2] especially as in the female the conditions chiefly considered as causative factors, such as urethral stricture and prostatic hypertrophy, do not exist. Nor was there found in these cases any evidence of spinal injury or disease.

Symptomatology. The variations in the symptom complex in vesical diverticula are so numerous that I have given somewhat in detail the symptomatology in each case of the series reviewed. A case reported by Murchison[3] illustrates in a striking way the occasional obscurity of the urinary relation and the difficulties of diagnosis where cystoscopy cannot be carried out. Generally speaking, however, the symptoms complained of are those of an acute cystitis, that is pain, frequency of micturition, and the passage of cloudy, malodorous urine. Micturition may be associated with severe tenesmus. The frequency with which a tumor has been found, generally situated to one side of the median line, is noteworthy. Possibly, however, the most characteristic symptom is the ability of the patient to repeat the act of micturition after a short interval. In such cases the introduction of a catheter after voluntary urination usually evacuates a large residue. While the stoppage of the stream in the first act is no doubt due to the passage of the vesical contents in the direction of least resistance, that is into the diverticular sac, a reversal of this process is initiated as soon as the expulsive efforts of the bladder cease, and continues until the pressure in the two cavities is equalized. Where the diverticulum occupies a dependent position there is always residual urine, and one generally fails in attempts to wash the bladder clean,—which adds greatly to the difficulties of the cystoscopist. The writer's case illustrates very well this latter point, as upon first examination, owing chiefly to the fact that the distending fluid was cloudy, the presence of a diverticulum was overlooked.

In the majority of cases there is a history of recurring febrile attacks

associated with chills, with or without symptoms of renal involvement.

Where the diverticulum replaces an abscess cavity, there is, of course, a history of the sudden evacuation of a large amount of purulent urine. This symptom of urgency is also associated with those cases in which a sudden evacuation of the diverticular contents follows periodical occlusion of the orifice.

Complications. The burden of the literature on this subject deals with post-mortem findings, the cardinal complications observed being severe vesical or diverticular inflammations, displacement and dilatation of the ureter, pyonephrosis, perivesical abscess, peritonitis and femoral thrombosis. Pressure upon and deflection of the ureter above its intramural course is a frequent complication and leads eventually to dilatation of the ureter and of the renal pelvis. With the advent of infection there follows in consequence of the ureteral obstruction widespread renal suppuration and impairment or destruction of the renal function. In the author's case the renal symptoms were decidedly the most striking when the patient first came under observation, the presence of a diverticulum remaining unrecognized for some time. In cases III, V and VII of the series reviewed the diverticular orifice was found to occupy the normal site of one of the ureters, and the ureter of the corresponding side to discharge directly into the diverticulum. Careful perusal of the cases reported strongly substantiates Young's [4] opinion that this condition of affairs is due to a gradual inversion of the ureteral orifice through extension of the diverticulum and not to sacculation of the ureter itself.

Treatment. Catheterization. The use of the catheter for retention and irrigation is at best a makeshift, as, owing to the fact that the communication with the bladder seldom provides dependent drainage, irrigation cannot possibly give permanent relief or even free the urine from pus. There are no successful results recorded from this method of treatment.

Drainage. Suprapubic cystostomy undoubtedly gives temporary relief and is properly undertaken in weak individuals. The absence of resiliency in the diverticulum, however, deprives this method of treatment of any permanent value. In a case reported by Burckhardt [5] a perineal drain was inserted but the patient died.

Enlargement of the orifice. In considering this form of treatment the position of the diverticulum must be one's chief guide. Where the accessory sac is found to underlie the trigone of the bladder, or where the most dependent portion of the diverticulum is on a lower level than the base of the bladder, treatment by this method cannot be expected to

yield a cure. Where, however, the diverticulum is in the course of the urachus, or is so placed that the incision may be carried to its lowest level and still be above the base of the bladder, it is conceivable that the result might be satisfactory, provided there remained no obstruction in the course of the urethra, either from enlarged prostate, spasm of the sphincter, or urethral stricture. As the reflection of the diverticular wall upon the outer surface of the bladder may extend for only a short distance around the opening of communication, the corresponding cut edges of the bladder and diverticulum should be carefully approximated by sutures in order to forestall the danger of an extravasation into the pelvic cellular tissue. A case reported by Young [4] in which this method of treatment was followed, resulted in the re-establishment of voluntary micturition but a residual urine of 300 c.c. necessitated the use of the catheter at bedtime.

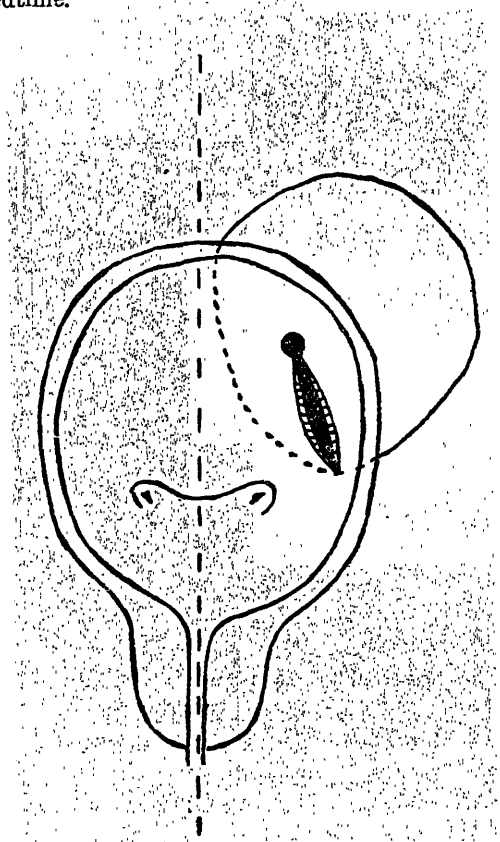

Diagram I.—Illustrating Operation of Enlargement of Orifice.

Suture of the orifice of the diverticulum without excision of the sac has been practised by Pousson,[6] who reports a case in which after the mucosa of the diverticulum had been thoroughly curetted and the margin of the orifice freshened, closure was effected by means of catgut sutures. The operation is said to have been successful, but the procedure, for very patent reasons, is not to be recommended.

Complete excision of the diverticulum. This would appear to be the only method yielding permanently satisfactory results. Where obstruction is present it should be dealt with primarily, or at least at the same time that the excision of the diverticulum is carried out. Further, in cases where pyonephrosis exists as a complication, and examination of the segregated urine shows extensive impairment of the renal function, it would seem rational to deal in a radical way with the complication before attempting bladder suture in the presence of a constant inflow of purulent material.

The literature contains the reports of ten cases treated by complete excision, which owing to the varied symptomatology and different operative methods employed are, in addition to the author's case, given somewhat in detail.

(1) *Author's Case,* 1906. R. F., aged 32, was first seen on October 27, 1906. His complaints were pain in the right loin, frequency of micturition, interruption of the stream and attacks of fever. His family history was negative.

Personal History. Since adolescence he had experienced difficulty in emptying the bladder, the act requiring as a rule several minutes. In 1897 he contracted a severe urethritis, which became chronic and was complicated at first by cystitis and later by what was diagnosed as pyelitis. Subsequently there was marked impairment of health; the urine from time to time became extremely cloudy and fœtid, and frequent attacks of cystitis, occasionally complicated by retention, necessitated the use of the catheter. Throughout this period a marked irritability of the sphincter urinæ led to frequent interruptions in the act of micturition. In 1902 the patient was sent to Arizona for one year, where he subsisted largely on milk diet with beneficial results. After his return to work he was from time to time interrupted in his vocation by attacks of cystitis, necessitating bladder lavage and the use of urinary antiseptics. In August, 1906, a severe febrile attack intervened, associated with pain in the right side. In September a second and in October a third attack similar in every way occurred. It was during convalescence from the last attack that the patient came under my observation.

On examination there was found tenderness on deep pressure in the

right flank. The bladder dulness extended above the symphysis halfway to the umbilicus. The urine was cloudy, specific gravity 1.018, acid, and contained albumen, casts, and a large quantity of pus. The residual urine amounted to 200 c.c. The act of micturition was prolonged by pressure upon the lower abdomen. The evening temperature was 103°F., falling to 99° in the morning.

Digital examination of the rectum showed the prostate to be normal; the seminal vesicles were slightly thickened and somewhat tender. Above the prostate extending to the right could be felt a large, boggy mass which was considered to be a dilated, atonic bladder.

A cystoscopic examination by Dr. R. P. Campbell on October 30 revealed the following facts:—

The bladder held 350 c.c. with but a slight feeling of distention. The bladder wall was hypertrophied and trabeculæ were everywhere visible; some cystitis was present, most marked about the trigone, but not sufficient to account for the quantity of pus present. The urethral orifice appeared normal and the ureters were easily catheterized. The right ureteral terminal was displaced towards the median line. The urine from the right ureteral catheter flowed steadily drop by drop (evidently from a dilated ureter) filling two test tubes, while the secretion from the left side, flowing at a normal rate, filled one-half a test tube. The urine collected by catheter from the bladder and from the two kidneys when compared showed:—

	COMMON	RIGHT	LEFT
	Turbid	Turbid	Clear
	Acid	Acid	Acid
Sp. G.	1010	1009	1025
Albumen	Present	Present	Trace only.
Urea	—	0.8%	2.0%
	Pus	Pus	No pus.
	Bacteria	Bacteria	No bacteria.
	Blood cells.		
CULTURES			
	B. Pyocyaneus	B. Pyocyaneus	An occasional Colony
	B. Coli.		of B. Coli.

Diagnosis. Spasm of the sphincter, hypertrophy and dilatation of the bladder, chronic cystitis, dilatation of the right ureter (above the ureteral sphincter), chronic suppurative pyelonephrosis.

Rest in bed and lavage of the bladder effected within a few days a

marked improvement in the patient's general condition, the evening temperature falling to 99½°. An attempt was made by means of vaccines prepared from devitalized cultures to induce a bacterial immunity to both B. Pyocyaneus and B. Coli Communis under strict opsonic observations. Before inoculation with composite vaccine the index to B. Pyocyaneus was 1.25 and that to B. Coli 2. On November 18 the indices were 2.5 and 6 respectively. At this time the temperature showed an increase in the evening registration, and fearing a recurrence of the former severe febrile symptoms with attendant toxæmia, I decided to remove the right kidney.

On November 22 a nephrectomy was performed under ether anæsthesia. As was expected the ureter, pelvis and calices were found greatly dilated. Secreting tissue remained in isolated areas, chiefly at the two poles, and there could be seen macroscopically numerous small abscesses throughout the gland. Cultures from the pelvis of the kidney upon agar slants yielded within twenty-four hours pure growths of B. Pyocyaneus. Following the operation there was an immediate cessation of the pyrexia. As, however, in spite of daily irrigation of the bladder the urine continued to be cloudy, on December 5 under a general anæsthetic a suprapubic drain was inserted. On exploration of the interior of the bladder a small opening was observed to the outer side of the right ureteral orifice through which purulent material exuded. A probe thrust into this opening could be felt per rectum to pass to the posterior wall of the pelvis. The orifice of communication was found to admit readily large blunt forceps, through the open jaws of which a drainage tube 1 c.m. in diameter was inserted. The anterior extremity of the tube was then sutured to the margin of the suprapubic wound.

Following this procedure the urine showed a very marked decrease in the amount of pus present. At the end of ten days the diverticulum tube was removed and at the end of three weeks the suprapubic opening was allowed to close. The temperature maintained an afebrile course. During the next two months the bladder was irrigated daily and upon several occasions the suprapubic wound closed only to open again in from four to six days. Throughout this period it was noticed that although micturition could be readily initiated, the stream rapidly declined after the passage of 240-280 c.c. A few minutes later the patient was able to pass a similar amount, this state of affairs being due evidently to the passage of the urine on contraction of the bladder into an accessory cavity offering less resistance than the via naturalis. It was further observed that if catheterization were employed, the instrument if re-introduced in ten or fifteen minutes evacuated a further amount of 180-250 c.c.

A cystoscopic examination was again undertaken and the existence of a large diverticulum demonstrated. The opening from this into the bladder was found about 2½ c.m. to the outer side of the right ureter. This cavity was further determined to be of large dimensions, probably capable of holding 200-250 c.c., as it was possible to introduce the cystoscope through the opening (1 c.m. in diameter) into a cavity which appeared to be almost as large as the bladder itself.

Operation, February 28. Extravesical, extraperitoneal excision of the diverticulum; re-establishment of suprapubic drainage.

Under ether anæsthesia a vertical incision was made through the lower segment of the right rectus muscle. The peritoneum was readily stripped back to the upper margin of the diverticulum, but owing to the close adhesion of the wall of the accessory cavity to the outer surface of the bladder for some distance from the opening of communication, it was found impossible to isolate the neck of the sac without re-opening the suprapubic wound. With the tip of the left forefinger passed through the orifice of the diverticulum and used as a retractor and guide, the separation of the diverticulum from the bladder was readily effected. After the neck of the sac had been divided, the bladder was closed extravesically by means of a purse-string suture. This was re-inforced and the bladder wall further inverted by a continuous catgut suture. The enucleation of the sac presented little or no difficulty. It was found to extend below for a considerable distance undermining the trigone, behind to the posterior wall of the rectum and laterally to the pelvic wall. Drainage of this cavity was provided by means of a rubber tube passed behind the prostate and through the perineum without communicating with the urethra. Complete closure of the lateral suprapubic incision and partial closure of the suprapubic wound after excision of scar tissue concluded the operation. Intravesical pressure was provided against by means of a small suprapubic syphon. Convalescence was rapid and uninterrupted. The perineal drain, which was apparently unnecessary, was removed on the third day, and at the end of three weeks, after I had determined by cystoscopic examination through the suprapubic wound that the diverticular opening was firmly united, the suprapubic syphon was removed.

A miscroscopic examination of the excised diverticulum showed the wall to consist of several layers of flattened cubical epithelium; a well-defined submucosa; muscle bundles running in various directions, and externally a layer of loose connective tissue.

Owing to the recurrence from time to time of a suprapubic fistula, the patient was given an anæsthetic on May 18, and the sphincter urinæ

dilated to 42 F. with a Kollmann instrument. The suprapubic wound closed finally within ten days.

On June 15 the patient was discharged well. The urine at this time was clear and contained but few pus cells and bacteria. The residual urine varied between one and two ounces.

Subsequent History. Apart from a mild attack of prostatitis in May, 1908, at which time there was a residual urine varying between one-half and two ounces, the patient has been free from urinary symptoms.

Remarks. In reconsidering this case in detail, I am of the opinion that the diverticulum was most likely congenital in origin, although I am aware that this is not capable of proof; the early symptoms, however, support this view. With such a condition existing an infection alone was necessary to produce the subsequent train of symptoms; this in time arrived. It is further probable that infection of the kidney was favored by the pressure of the diverticulum upon the ureter at some little distance from its vesical orifice. This theory would also account for the extreme dilatation of the ureter without involvement of its vesical terminal.

If the diverticulum were of recent development, the spasm and hypertrophy of the sphincter must be considered the etiological factor, as they furnished sufficient obstruction to produce sacculation. As an illustration of the degree of obstruction produced by the sphincter, one has only to recall the repeated failures to close the suprapubic wound.

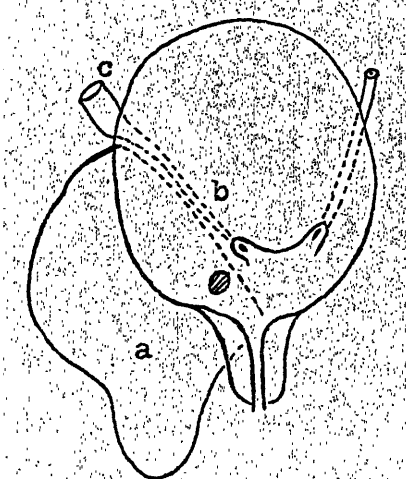

Diagram II.—Illustrating Author's case. (a) Diverticulum, (b) Displaced Ureter and Ureteral Orifice, (c) Dilated Ureter above intramural course.

Abstract of cases. (2) *Pean's Case,* 1895.[1] Congenital vesical

diverticulum and supernumerary urethra in a girl aged fifteen. There had been incontinence from birth. On examination there was found on the anterior wall of the vagina a median protrusion the size of a nut. On digital pressure over the tumor urine was seen to escape from a narrow opening placed in the median line 3 mm. below the external orifice of the urethra. On obstructing with the finger the supernumerary external orifice and again exerting pressure, there was a gradual diminution in the size of the tumor, and the patient complained of a desire to micturate. Under a general anæsthetic an incision was made over a director along the anterior wall of the vagina, the diverticular tract excised, and the opening into the bladder sutured. The patient was cured.

(3) *Czerny's Case*, 1896.[7] A young man, aged 31 years, developed after traumatism a stricture of the membranous portion of the urethra followed by retention, cystitis, and pain in the region of the left kidney. On examination there was found to the left of the median line a tumor the size of a child's fist which on compression discharged its contents into the bladder. Suprapubic cystostomy disclosed a greatly thickened bladder with a finger-shaped prolongation towards the navel. In the region of the left ureteral orifice a large diverticulum was demonstrated, the opening of communication admitting the finger. The accessory sac completely filled the small pelvis, and contained foul urine and epithelial detritus. Suprapubic drainage was continued for a fortnight without freeing the urine from pus, and excision of the diverticulum was decided upon. The left rectus was incised transversely. Many adhesions were encountered especially in the region of the rectum and in the hollow of the sacrum. During the operation the peritoneum and the left ejaculatory duct were injured. The left ureter was dilated and passed obliquely through the wall of the diverticulum. It was divided and implanted into the bladder wall. The wall of the excised diverticulum contained muscular and epithelial elements. Convalescence was retarded by the formation of a ureteral-abdominal fistula. Four months later the left kidney, the seat of pyonephrosis, was extirpated. At the time that the patient was discharged, the bladder held 150 c.c. and he was able to retain his urine from two to three hours.

(4) *Riedel's Case*, 1903.[8] The patient, aged 61 years, was admitted to the Surgical Clinic in Jena December 20, 1902. He had experienced difficulty in urinating for three years. Latterly the use of a catheter had been necessary. On examination there was found marked enlargement of the prostate. Prostatectomy was performed. Five months later, in May, 1903, symptoms of obstruction returned with pain

in the right side above Poupart's ligament, for the relief of which a perineal section was performed. On June 13, 1903, suprapubic cystostomy revealed the presence of a large diverticulum communicating with the bladder through an opening 2 c.m. in diameter. The bladder was closed and a second incision made through the right rectus muscle. The accessory sac was excised and the communication with the bladder closed with catgut suture. Perineal drainage was re-established. Collapse and death occurred on the following day.

(5) *Pagenstecher's Case,* 1904.[9] The patient, a male aged 33 years, was seen in August, 1903. During the preceding winter he had suffered for two or three days from pain in the bladder and on micturition. Five weeks later the pain had returned with strangury and tenesmus every half hour. On admission the distended bladder could be felt above the pelvic brim. After evacuation with a rubber catheter, a solid instrument when introduced withdrew a further amount of turbid, bloody urine, with the disappearance of the abdominal tumor. On subsequent irrigation the bladder was found to hold as much as one litre. Cystoscopy was unsuccessful and on August 30, 1903, suprapubic exploration was undertaken. In the position of the left ureter was found the opening of a large diverticulum.

As there was no improvement in the patient's condition following drainage, extirpation of the diverticulum by the sacral route was carried out on December 16. The left ureter, which opened into the accessory cavity, was implanted into the bladder at the former opening of communication. A self-retaining catheter was placed in the urethra. The excised sac contained in its walls bundles of smooth muscle fibres running in various directions and a well marked submucosa. Of the epithelial lining only a few fragments were preserved. In addition to a sacral fistula the suprapubic wound continued to discharge for some time. In February both fistulæ had healed, but in March the sacral fistula reopened, urine escaping during micturition.

(6) *von Eiselsberg's Case,* 1904,[10] *reviewed by Christel.* In the discussion upon Pagenstecher's paper, von Eiselsberg reported a case of vesical diverticulum which had come under his observation, in which a palpable suprapubic tumor disappearing under pressure was followed by a desire to micturate. The presence of a diverticulum was confirmed by cystoscopic examination, the orifice of communication with the bladder being situated at the base. Excision of the sac was successfully practised. Details as to operative procedure and histological examination of the sac wall are not given.

(7) *Young's Case,* 1904.[4] Male, aged 30 years, was seen in Janu-

ary, 1904, complaining of frequency of micturition and pain in the back. There was a history of severe attacks of urethritis in 1893 and 1898. During the last attack a tight stricture in the bulbo-membranous region was found to exist, for the relief of which a combined external and internal urethrotomy was performed. During the next three years the patient was free from urinary symptoms. About April, 1902, he had an attack lasting one week characterized by obstruction and frequency of micturition. Three months later a second attack similar in every way occurred. In September, 1903, a third attack supervened, and in October a fourth attack with pain in the right side of the pelvis and severe tenesmus culminated in the sudden passage of a quantity of pus. It was thought that an abscess had ruptured into the bladder. Although retention occurred, a catheter could be passed without meeting with obstruction. Bladder lavage was practised without diminution in the amount of residual urine. On December 9 pain and tenderness developed in the right flank beneath the costal margin. On January 4, after coming under observation, the patient had a similar attack lasting several hours, necessitating the use of morphia. At this time fever, nausea and the presence of muscular rigidity over the right kidney were observed. Examination showed the prostate to be slightly harder than normal, but there was no evidence of stricture. There was a residual urine of 350 c.c. The bladder was washed clean with difficulty. Pressure on the lower abdomen was necessary to evacuate completely the bladder contents. The cystoscope revealed a large diverticulum with an orifice of communication 2-3 c.m. in diameter, situated in the position of the right ureteral opening. The left ureteral orifice was found displaced towards the left, with the opening of a second and smaller diverticulum lying above and to its outer side. The right ureteral orifice, of course, could not be seen, but it was subsequently found to open upon the inner wall of the larger diverticulum. For six weeks catheterization and lavage were practised, but without diminution in the size of the diverticulum or in the quantity of residual urine.

Operation, February 10. Suprapubic extravesical excision of the large diverticulum and intravesical enucleation of the small diverticulum with closure of the orifices was carried out; also drainage of the bladder through a perineal urethrotomy and drainage of the retrovesical space by means of a tube passed behind the prostate and through a posterior perineal incision without entering the urethra. The intradiverticular emplacement of the right ureteral orifice was brought forward into the plane of the bladder wall by means of a flap operation.

Owing to the failure of the suprapubic wound to heal, the presence of

30 c.c. of residual urine, and the recurrence of a small pouch at the site of the excised diverticulum on the right side,—all indicating obstruction,—a Bottini operation was performed on August 4.

Examination of the wall of the excised diverticulum showed the presence of an epithelial lining and numerous layers of smooth muscle bundles running in various directions. There was also present the usual evidence of chronic inflammation.

Five months after operation the patient reported his urine to be clear and the function of urination normal.

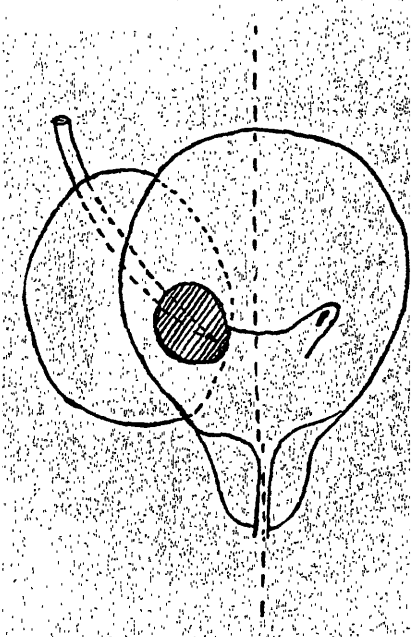

Diagram III.—Illustrating Case VII. (After Young).

(8) *Young's Case*, 1904.[4] Male, aged 34 years, was admitted to the Johns Hopkins Hospital on January 18, 1904. In March, 1899, the patient jumped from a moving locomotive striking upon the buttocks. Following the accident he felt severe pain in the lower portion of the abdomen, and on examination found a lump about the size of a hen's egg below and to the left of the umbilicus. This swelling gradually subsided. There was, however, a return of the pain at the site of the tumor if the bladder were allowed to become distended.

On cystoscopic examination there was found in the region of the vertex the small orifice of a diverticulum. The bladder wall was not trabeculated.

Operation, January 28. Excision of a small diverticulum lying within a dilated urachus. On February 23 the patient was discharged well.

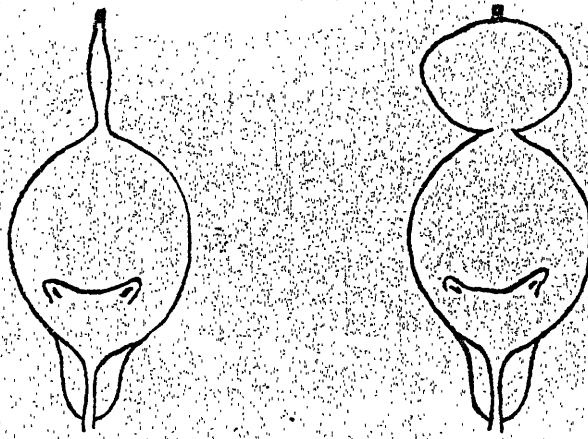

Diagram IV.—Diverticula in course of urachus. (After Young).

(9) *Young's Case*, 1903.[4] Male, aged 63 years, was seen in February, 1903. In 1901 the patient first noticed frequency of urination and difficulty in starting the stream. At the time of admission urine was voided about every fifteen minutes. The patient had never had complete retention and a catheter had never been used.

On examination the urine was found to be normal. The prostate was moderately enlarged. On passing a catheter 1200 c.c. of residual urine was withdrawn. Cystoscopic examination showed intravesical prostatic hypertrophy, moderate trabeculation of the bladder wall, and on the right side anteriorly the opening of a diverticulum.

Operation, February 22. Suprapubic extravesical extraperitoneal excision of the diverticulum with suture of the orifice of communication; perineal prostatectomy. Enucleation of the diverticulum was effected without difficulty owing to the absence of dense adhesions. The capacity of the diverticulum was estimated at 500 c.c. The bladder itself was not opened. The patient was discharged well on the 27th day following operation.

Microscopically the mural elements consisted of well defined mucous, sub-mucous and muscular layers. There was no evidence of inflammation.

(10) *Porter's Case*, 1907.[11] This patient, a male aged 34 years, first came under observation in April, 1906, complaining of difficulty in starting the stream, of frequency of micturition, and of the passage

of foul urine which occasionally contained clotted blood. On examination the bladder was found to extend to the umbilicus. The residual urine varied from 19 to 24 ounces. Treatment at this time was declined. When the patient returned one year later digital examination of the rectum showed the prostate to be moderately enlarged and cystoscopy revealed the presence of three (?) diverticula, one of which was especially large, with its orifice of communication situated at the right side of the base of the bladder.

On April 30 suprapubic drainage was established. On May 21st the bladder was re-opened suprapubically, and the sphincters of the diverticula widely dilated. The patient was discharged in August, but leakage still occurred from the suprapubic wound.

He returned in September suffering from epididymitis and pain in the region of the left kidney.

Operation, September 8. An incision was made parallel with Poupart's ligament. The peritoneum was opened and an elastic swelling the size of a banana, extending backward and to the left of the base of the bladder, was found. In order to separate the accessory sac from the rectum, the bladder was again opened and the forefinger inserted into the diverticulum as a guide and retractor. In this way the sac was isolated. The orifice was closed with two layers of catgut sutures. Suprapubic drainage was provided and a rubber catheter placed in the urethra. At the end of October the patient was reported to be much improved in health, but, in the absence of urethral drainage, leakage still occurred at the site of the bladder suture.

(11) *Wulff's Case*, 1904.[12] The patient, a male aged 34 years, first experienced difficulty in micturition in May, 1903. In July, while confined to bed, he suddenly lost the power of voluntary urination. A large quantity of urine was withdrawn by catheter. Although voluntary micturition was subsequently restored, there remained a residue of one litre which, however, did not produce discomfort. The condition was at first thought to be due to a disturbance of the sensory nerve supply. On examination some months later there was found in the right lower quadrant a large tumor, which catheterization failed to reduce, but which, on pressure, suddenly discharged into the bladder a large quantity of fœtid, brownish-yellow fluid. Cystoscopy showed the presence of a diverticular opening on the right side.

Operation. An incision was made parallel with Poupart's ligament, the peritoneum stripped back, and the diverticular sac opened and evacuated. The cavity was then tamponed.

Three weeks later the sac was resected and the orifice of communica-

tion with the bladder sutured. Intravesical tension was provided against by means of a permanent urethral catheter.

Several weeks later, owing to the failure of the bladder suture line, the opening into the bladder was again exposed and the edges freshened and re-sutured. At the end of a further period of several weeks the patient was discharged. The wound had healed. The urine, voided spontaneously every three hours, was for the most part clear. There was a residue of 150-200 c.c. On cystoscopic examination the mucous membrane at the site of the suture was found to be firmly united. Whether the presence of the residual urine was due to atony of the vesical wall following the prolonged distension, or whether due to defective enervation, had not been determined.

The wall of the excised sac contained epithelial and muscular elements.

Etiology. Of the series of 11 cases reviewed, I, II, V, VIII, X and XI belong to the congenital variety, although positive evidence of congenital origin can be said to exist only in Case II, reported by Pean.[1] In this connection it is fallacious to lay too much stress upon the presence of bladder epithelium and muscular tissue in the wall of the accessory sac, as these elements may be present in cases where prostatic hypertrophy has been considered the etiological factor (IX), and also in cases in which a urethral stricture has existed (III and VII).

To prostatic enlargement may be ascribed the development of the diverticulum in Cases IV and IX. Porter's [11] case may belong to this category. The note on the prostatic condition is not very definite. While the age would suggest a congenital origin, it does not exclude a prostatic causation.

Urethral stricture was present in Cases III and VII. Owing to the persistence of obstructive symptoms (that is pouching of the suture line and residual urine) after extirpation of the diverticulum, a Bottini operation was performed in Case VII with permanently satisfactory results.

The etiological factor in the case reported by the writer must remain in some doubt; the history on the one hand suggests the possibility of the diverticulum having been congenital, while on the other the presence of hypertrophy and spasm of the sphincter urinæ cannot be left out of consideration.

Traumatism was undoubtedly the exciting cause in Case VIII. The urachus had probably remained patent from birth.

Perivesical suppuration has to be considered as possibly the precursor of the diverticulum in Case VII, in view of the history of a sudden evacuation of a large quantity of pus. Opposed to this theory are the

facts that a stricture had existed in the bulbo-membranous portion of the urethra and that the diverticulum was lined with epithelium and contained muscular elements in its wall.

While no case of diverticular formation secondary to congenital stricture of the meatus urinarius has been reported, the possibility of this condition figuring as an etiological factor should be borne in mind.

Phimosis was associated with the formation of a vesical diverticulum in a child 21 months old, observed by Lennander [13] and cited by Young.[4]

Spinal injury or disease as an etiological factor was first suggested by Hale White.[14]

von Eiselsberg's [10] case (VI), owing to the absence of details, cannot be classified.

Age. It will be seen from the foregoing that, apart from Cases IV and IX (prostatics aged 61 and 63 years respectively) and the case reported by Pean,[1] all those included in our series occurred in individuals between the ages of thirty and thirty-four. This fact is most striking and suggests the possibility that they were all congenital in origin; that is to say, even the two cases with a history of pre-existing stricture present features which bring a congenital hypothesis within the limit of reason.

Prognosis. Out of the 11 cases reviewed the operation of excision of the diverticulum was followed by the restoration of the normal function of urination in eight instances. In two cases urinary fistulæ persisted at the time of their being reported, and in one case the operation was followed by collapse and death. The age at which the majority of these cases occur imposes a grave responsibility upon the surgeon. With modern methods of investigation, physical, biological and chemical, applicable to the urinary tract, a correct diagnosis should practically always be made early in the affection, and with a method of procedure well established these cases should be accorded a favorable prognosis.

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PERFORATIVE APPENDICITIS: VENOUS THROMBOSIS, PARATYPHOID, INTESTINAL OBSTRUCTION.

BY

JAMES BELL, M.D.

The patient was a young farmer of 23 years of age from the Eastern Townships, who came to the Royal Victoria Hospital on the night of the 30th December, and was operated upon for an acute typical perforative appendicitis on the following morning, December 31st.

His illness had begun on the night of the 26th after serious dietetic indiscretions during that afternoon and evening. The appendix was removed and the wound drained. The patient did well for eight days when he had a severe chill on the 8th of January, one on the 9th and another on the 13th, the temperature rising to 104° and 105° following these chills. The temperature remained high, although the wound had healed and the condition of the abdomen was quite satisfactory.

I suspected a portal thrombosis, but no definite evidences of such condition developed. I then began to suspect typhoid fever, and 15 days after operation a positive Widal was obtained. On the 22nd of January, organisms of the paratyphoid variety were obtained from blood smears and on that day he was transferred to the medical side under care of Dr. Hamilton.

Up to this time, the bowels had moved regularly and freely, and there were no indications of deranged digestion. But, on the 23rd, he began to vomit and had an unsatisfactory and imperfect evacuation of the bowels. On the 24th, he appeared to be suffering from obstruction and on the 25th I saw him and found him apparently in an almost moribund condition, signs quite definitely indicating obstruction of the bowels, and, as I had already suspected thrombosis or some form of interference with the circulation on account of the previous chills. I was inclined to believe that it was a mesenteric thrombosis causing paralysis of the intestine.

I decided to operate in the afternoon, although I felt that he would probably not survive the ordeal. I found a definite mechanical obstruction. The omentum had become adherent at the brim of the pelvis and

encircled a loop of small intestine,—the lower part of the ilium. The obstruction was easily overcome, and the distended upper small intestine was evacuated by puncture. By the administration of intravenous salines and stimulants, the patient rallied well. His bowels moved; fæces and flatus were passed freely and the obstruction was completely relieved. The only unsatisfactory sign, however, was that he still had a weak and rapid pulse. He had no pain, declared that he felt well and had no elevation of temperature.

He died rather suddenly at 3.40 on the morning of the 28th, *i.e.* three days after operation.

Autopsy: The autopsy showed that there had been typhoid fever, healed and healing ulcers of the small intestines, appendectomy, septic thrombosis of the inferior vena cava, iliac and pelvic veins.

At the operation for obstruction, as soon as I had opened the abdomen, I immediately examined the portal and mesenteric veins, but did not think of investigating the inferior vena cava or the iliac veins, and so concluded that my suspicions of thrombosis based upon the series of chills had been unfounded.

I was unable to explain the death until autopsy revealed these conditions of thrombosis.

There were also evidences of nephritis and acute ulceration of the rectum which was probably due to repeated enemata. This, therefore, was a perfectly healthy young man developing a typical appendicitis after indiscretions in diet. The appendix would seem to have perforated thirty-six hours before operating, judging from the symptoms.

I did not consider that there was any evidence of typhoid fever clinically, and, even when 15 days after operation a Widal reaction was found, I still doubted the diagnosis. From the fact that his chills began on the 8th day after operation and the first evidences which were demonstratable of typhoid were found on the 15th day, it would seem that he must have developed the typhoid after coming to hospital.

Another extraordinary complication was the development of intestinal obstruction 22 days after operation. There were absolutely no signs prior to that time.

Altogether his case presents a series of pathological conditions which is quite unusual and until the diagnosis was cleared up by autopsy, it was very puzzling.

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ARGYLL ROBERTSON.

It is with much regret that we have to chronicle the death of Dr. Argyll Robertson, the celebrated Scottish ophthalmic surgeon, which occurred on January 3rd, at Gondal, India, whither he had gone on a pleasure trip in November last. Although Argyll Robertson had retired from active practice, some five years ago, he will nevertheless be greatly missed in Scotland, where his charming personality as well as his great professional abilities had made for him a host of friends and admirers. He was born in Edinburgh in 1837, his father being a noted surgeon and teacher, who practiced to a limited extent the, at that time, new specialty of ophthalmology. Dr. Argyll Robertson after graduating in Medicine from St. Andrews devoted his attention to ophthalmology, being a pupil of the celebrated Von Græfe, in Berlin. Shortly after returning to Edinburgh he became attached to the Royal Infirmary from which he retired in 1896, at the same time resigning his teaching appointment in the University.

He enjoyed wide popularity and had a large practice, which may have accounted for the comparatively small amount of writing he produced. In his earlier days, he wrote an article on the use of Calabar bean, and another on the loss of the pupillary reaction to light in locomotor ataxia, now so well known as the Argyll Robertson phenomenon. Later he described trephining the sclera as a new treatment for glaucoma, and a few years ago reported a case of filaria loa in the eye. As a teacher, he was

remarkably lucid, but gave his attention rather more to treatment than to pathology. It was as an operator that he excelled; he was neat, deft, resourceful. Dr. Robertson was of splendid physique, and was endowed with the most charming, old-world courtly manner, a courtesy unfailingly exhibited as much to the poorest patient in the hospital as to the titled people who thronged his waiting room. Professionally, he had honours showered on him, was surgeon oculist to the late Queen and the present King, was president of the Royal College of Surgeons of Edinburgh, and President of the Ophthalmological Society of the United Kingdom.

Outside of his professional life, Argyll Robertson was a devotee of golf, and carried off for several years the gold medal at St. Andrews; he was also a noted curler, and a member of the Kings Royal body-guard of Archers, the *corps d'élite* of Scotland. He was an art connoisseur of a high order being one of the judges of the Royal Scottish Academy. As a result of his wide literary attainments, he was a delightful speaker, the well-rounded sentences, the splendid diction, and fine delivery completely fascinating his hearers. It is hard to think that this fine personality is gone for ever. He had his day, he did his duty nobly and well, and the world is much the poorer for his passing.

Reviews and Notices of Books.

PUBLICATIONS OF THE MASSACHUSETTS GENERAL HOSPITAL, BOSTON. Selected Papers by the Staff, Volume II, No. I. October, 1908. Boston, The Barta Press.

This is a pamphlet of 390 pages, containing about thirty papers upon subjects widely diverse but interesting and practical. There seems to be such a wide range of subjects treated in the various contributions that every medical man can find something that will interest him. Illustrations are introduced where necessary.

HIGH-FREQUENCY CURRENTS. By FREDERICK FINCH STRONG, M.D., Instructor in Electrotherapeutics at Tufts College Medical School. Boston, with 138 illustrations in Text. Cloth, $3.00. New York: Rebman & Co., 1123 Broadway.

The author has divided this book into twenty-six chapters and a copious index.

He begins in the first chapter with a historical introduction and goes on in the second to describe what electrons are and their connection with

the various forms of vibratory energy and the waves of radiant energy, showing the relation existing between waves of the slower and larger volume of waves which we recognize as sound waves, and how they increase in rapidity from .16 per second the lowest note we can recognize as a definite note, and how the rapidity increases in frequency by double in rapidity in each succeeding octave and so on till we reach eight octaves, when the rapidity is so great, between 4 and 5 thousand in the second, that the sound emitted reaches the highest note we can recognize as a note, and beyond which the sound loses appreciation by our auditory apparatus and passes on through the heat effects till we reach the vibrations of light varying from 140 millions of millions in the lowest red light visible to the eye to 176 millions of millions per second of the violet ray, and beyond to the X-ray, and ultra violet ray reaching to 200 millions of millions per second: these figures are almost inconceivable by the finite mind.

That these enormously rapid vibrations should produce a profound effect upon the changes which we recognize as life is demonstrated to us every day in the white stalks and leaves of vegetable life wher deprived of light and grown in the dark and the energy of life in the spring when the ordinary day light is richer in the violet and ultra violet light at the more rapid moving waves of the spectrum and the changes which take place in the latter part of the summer when the red ray predominates and heat produces the ripening of the fruits and the conversion of the glucosides into sugar. Dr. Strong points out the methods of producing these rapid vibrations by electricity, and describes in a clear and lucid manner the different apparatus made use of for their production, and the different methods of their application to the different cases in which they have been found to be of use.

The text is illustrated throughout with clear drawings and diagrams of the different kinds of apparatus in use. He promises us a second volume which, he says, will be a corollary to the present volume, giving the results of the application of these vibratory movements in actual cases of disease. The present volume is a clear exposition of the facts so far as known and the modes in which the applications are made.

The type is clear and readable, and the book, although well illustrated, not too heavy to read with comfort. To any one wanting to know about high-frequency currents we cordially recommend the book as a good addition to the knowledge of the subject.

G. P. G.

ESSENTIALS OF MEDICINE. A textbook of medicine for students beginning a medical course, for nurses and for all others interested in

the care of the sick. By CHARLES PHILLIPS EMERSON, M.D.; illustrated. Philadelphia and London: J. B. Lippincott Company, 1909.

What Dr. Emerson says in his preface about the confusion of mind of the average student in his fourth year is probably correct, and his book is an attempt to remedy that condition by giving him a better perspective. The author does not err on the side of attributing to his reader too great a profundity of knowledge; indeed the book may be read pleasantly by any intelligent person who will gain some notion, if not an entirely accurate one, of the function of organs from the frequent comparisons which are drawn between them and brick walls, pumps, steam-engines, and furnaces. The permanent value of this method is open to question; since, although it is quite true that "the cell somewhat resembles a steam-engine," it differs from it in so many important particulars that the comparison loses much of its force. The book might be read with profit by a person who intended, but has not yet begun, to study medicine in a school where first-hand information is difficult or inaccessible, and by nurses who "often know a great deal in a general, indefinite, inaccurate way." The teaching of nurses is approximating that of students, and students are being taught as if they were nurses. Eventually they may be taught in one class, and these essentials would make a very good text-book. Our own belief is that medicine must be taught, one thing at a time. Apparently Dr. Emerson's belief is to the contrary, that a general impression should precede the acquirement of precise details. Both cannot be right.

PRACTICAL GUIDES TO THE DISEASES OF THE THROAT, NOSE, EAR. By WILLIAM LAMB. Published by Baillière, Tindall & Cox, Edinburgh and London, 1909.

This is a concise, thorough manual for the student and general practitioner. The examination of the throat, nose, ear, and larynx are illustrated by plates.

The treatment of the commoner diseases of the mouth, larynx, nose and pharynx is clearly outlined. Some very valuable selected formulæ for the therapeutics of these diseases are given at the end of the book. The work is admirably illustrated by some clear and beautiful plates on the different subjects.

AIDS TO OBSTETRICS. By SAMUEL NALL and C. J. NEPEAN LONGRIDGE, London. Published by Baillière, Tindall & Cox.

This is a small, handy volume of the Aid series on Obstetrics for the

use of students and practitioners similar to those of the series which have already been reviewed. Briefly the authors deal with the anatomy of the female pelvis and the process of development and physiology of the fœtus, the care and treatment of the mother during pregnancy and labour, the diseases during gestation and the management of all the different forms of difficult labour, the puerperium and the abnormal conditions found in both mother and child. Different operations such as version, forceps, craniotomy, embryotomy, Cæsarean section, and the choice of anæsthetics are then discussed. Puerperal infection and pelvic cellulitis, phlegmasia alba dolens, pulmonary embolism and puerperal insanity receive mention.

MEDICAL GYNÆCOLOGY. By SAMUEL BANDLER, M.D. Published by W. B. Saunders & Co. Philadelphia and London, 1908. Original illustrations.

This work of some 650 pages is devoted entirely to the consideration of the treatment of diseases of women by means other than the knife. When the operation is necessary, the author does not hesitate to say so, but he confines his remarks to the statement that some form of operation is required. In the opening chapters, the different methods of examining the various sexual organs, as well as the bladder, are well described and there is a short and useful section on the various bacteria found in the genital tract, together with information regarding the modes of culture of these organisms. The treatment of deviations of the uterus by means of the pessary is clearly and conservatively handled, not too much being promised in the way of cure. Abdominal massage, with its indications, is well described, as are also the various kinds of baths, medicated and plain. The work is well got up, contains a sufficient number of illustrations which are good; and, while the pathologist may complain that his subject receives scant attention, it can be recommended to either the general practitioner or specialist.

F. L.

TUBERCULOSIS IN INFANCY AND CHILDHOOD, ITS PATHOLOGY PREVENTION AND TREATMENT. By various writers. Edited by T. N. Kelynack, M.D. Publishers,—Baillière, Tindall & Co., London. Canadian Agents: J. A. Carveth & Co., Toronto, Ont. Size, demyo 8vo. Price, $3.75.

The interest in tuberculosis is perennial, and no matter at what age the disease may fasten upon the tissues, its development always attracts attention. The present volume, devoted to the study of the disease in

infancy and childhood, has been prepared, the editor states, as an expansion of the symposium in the "British Journal of Tuberculosis," and also in view of the great gathering in America, of the representatives of all nations, which must stimulate scientific inquiry, and develop new powers for practical service in the interest of infants and children throughout the world.

The treatise is a collection of studies. The list of contributors to it contains 41 names, and the subjects discussed by these writers are those of greatest interest in the matter of infection of the various tissues, the treatment of the disease both from the individual and the social standpoint, and features of this disease as it is found in children in the various countries of Europe, and in America.

An important feature of this work, is the reference system. Almost every page of the book contains numerous foot references, thus enhancing the value of each article and making the book not only "a comprehensive and authoritative survey" of the subject of tuberculosis, but readily helping those to the original article, when more details are desired. A few of the names of those who have contributed, might emphasize the authoritativeness of this work. L. Emmett Holt, R. W. Philip, John Thomson, A. Calmette, K. F. Andvord, Sir John Byers, A. D. Blackader, T. N. Kelynack, D. J. McArthur,—familiar names to every one who has read diseases of childhood.

The book is well printed, and contains a full index of names of persons, of places, and of subjects. We highly commend it to all who are interested in the subject of which it treats. It contains in all 376 pages and 27 illustrations.

W. F. H.

SOURED MILK AND PURE CULTURES OF LACTIC ACID BACILLI IN THE TREATMENT OF DISEASE. By GEORGE HERSCHELL, M.D., London. Second impression, ninth thousand. London: Henry J. Glaisher; Chicago: W. T. Kenner & Co., 1909. Price, 1s. 6d.

This little book of 32 pages deals with the value of lactic acid ferments in the treatment of disease. It is really an amplification of a scientific paper upon the same subject by Dr. Herschell which was published more than a year ago. The discussion is extremely interesting and aims to put upon a reasoned basis the practice of administering milk of varied kinds and degrees of sourness. Cases are cited in which benefit was received from the treatment, from which it would appear that the method has a wide range of usefulness.

WHY WORRY? By GEORGE L. WALTON, M.D., Consulting Neurologist to the Massachusetts General Hospital. Philadelphia and London: J. B. Lippincott Company, 1909.

This book is dedicated by the author to his "long-suffering family and circle of friends, whose patience," he says, "has been tried by his efforts to eliminate worry." That is often the effect of efforts at amelioration no matter how well-meant, but the confession is not an encouragement to reading the book. The present reviewer having nothing to worry him, and therefore feeling incompetent to offer an opinion upon the value of the book, procured a patient for the experiment, a man to whom "the grasshopper is a burden," and the decision was that the process "did him good." The philosophy of the author is cheerful and sound. His illustrations and comment are refreshing and profoundly true, especially those which have to do with golf in its relation to life. One would say that the book will serve admirably to assist one in bearing another person's troubles.

PAIN, ITS CAUSATION AND DIAGNOSTIC SIGNIFICANCE IN INTERNAL DISEASES. By DR. RUDOLPH SCHMIDT, translated and edited by Carl M. Vogel, M.D., and Hans Zinsser, A.M., M.D. Philadelphia and London: J. B. Lippincott Company, 1909. Cloth, $3.00 net.

Pain is universal amongst sentient creatures. It is the subject of all literature, the origin of religion, and the inspiration of medicine. It has remained consistently with created beings since the appearance of a motor mechanism by which the organism might remove the source of it. Originally pain was intended to warn the organism against harm, and it still serves that useful purpose, although life is full of instances in which the pain is out of all proportion to the necessities of the case. But this merely emphasizes the fact that laws which are just and useful in their general application may be unjust, useless and harmful in special cases. The alleviation of pain is the business of the physician and the priest, indeed of all humane men; and when this is done by the removal of the cause we have entered the sphere of modern, scientific medicine. This book of Dr. Schmidt's is an attempt from Neusser's clinic to analyse the various painful sensations that occur in internal diseases, their mode of causation, and correct interpretation. The author discusses the manner in which they are affected by positions of the body, motion, pressure, the ingestion of food, remedial agents, functions of organs, their topography, and especially their relations to the different diseases and their diagnostic indications. In the first section the subject of pain in general, and of its occurrence in various regions of the

body, is set forth, while in the second each organ and organ-system is taken up at length, and detailed discussions are devoted to the pains accompanying the various diseases. We agree entirely that a reading of this volume will prove a revelation of the possibilities inherent in the careful analytical study of this single symptom, and that there is no department of medical practice to which its teaching cannot be applied with profit. We look upon this book as the most important which has appeared upon the subject since Hilton's "Rest and Pain."

A TEXT-BOOK OF GENITO-URINARY DISEASES. By DR. LEOPOLD CASPER, Professor in the University of Berlin. Translated by Chas. W. Bonney, B.L., M.D., assistant demonstrator of anatomy, Jefferson Medical College. Second edition, revised and enlarged. Philadelphia: P. Blakiston's Son & Co. Price, $5.00.

It is but three years since the first edition of Prof. Casper's text-book first appeared in English and was noticed in this JOURNAL. To the very favorable criticism, which then appeared in these pages, it is perhaps unnecessary to add more than a further word of commendation. It is difficult, however, to let the occasion pass without remarking the completeness with which Prof. Casper has presented his subject: in every instance that long experience meets us, which adds so much weight to the resulting, carefully drawn conclusions, while the personal touch, which is to be found throughout, brings home many a fact a more elaborate if less impersonal work might fail to do.

The article on hypertrophy of the prostate is especially deserving of praise. It is short and complete and very conservative, though the author's personal experience with the newer radical operations is limited as compared with that seen in other fields. The chapter on gonorrhœal urethritis is one which has brought order out of chaos for many a student and will, we doubt not, continue to do so.

The author, as is almost self-evident, has personally gone over much of the translated work; small additions have been added by the editor, who has done his work thoroughly and well.

The book is but slightly enlarged though the material is somewhat rearranged, most notably in those sections dealing with chronic urethritis, cystoscopy and prostatic hypertrophy. One notices also an occasional new illustration. Altogether we can quite understand why the first edition is followed by a second at so early a date.

R. P. C.

Medical News.

MONTREAL GENERAL HOSPITAL.

At the annual meeting of the Montreal General Hospital the ordinary income was reported to be $101,848 and the current expenditure $128,909.

The total number of indoor patients treated to a conclusion was 3,087, or a decrease of 260 over the previous year. Of these, 188 remained over from last year, 3,103 were admitted during the year, and 204 remained in the hospital at the end of the year. There were discharged from the hospital 2,795, and there died in the hospital 292. The percentage of mortality was 9.4 or 4.8 exclusive of deaths occurring within three days of admission. The average number of patients in the wards per day was 200. The average number of days in the hospital per patient was 23.3, and the aggregate number of days in the hospital by all patients was 72,038, or an increase of 1,152 as compared with the previous year. The average daily cost per patient was $1.79.

The indoor patients treated to a conclusion numbered 3,087. In the out-patient department the total number of patients treated was 15,078, and the total number of consultations was 52,980. The treasurer stated that the committee of management intended to spend about $400,000 on the first part of the proposed changes. Towards this they hoped to be able to use the Alexander fund of $210,000, and the hospital's share of the receipts from the Orkney estate should value out about $100,000, making a total available amount of $300,000. It was thought that the committee could presume on the generosity of the people of Montreal for the remaining $100,000, and so proceed with a building clear of debt.

Twenty-two nurses graduated during 1908, bringing up the number to 331 who had passed through the training school since its establishment.

Officers elected were:—President, James Crathern; vice-president, H. Stikeman; treasurer, F. W. Evans; secretary, Dr. F. G. Finley.

Physicians—Drs. W. A. Molson, A. D. Blackader, F. G. Finley and H. A. Lafleur.

Surgeons—Drs. F. J. Shepherd, G. E. Armstrong, J. A. Hutchison and J. M. Elder.

Specialists—Oculist and aurist, Dr. G. H. Mathewson; gynæcologist, Dr. F. A. L. Lockhart; laryngologist, Dr. H. D. Hamilton; neurologist, Dr. D. A. Shirres.

The following having been nominated by the medical board for the outdoor department, and as assistant specialists, were appointed for one year:

Physicians—Drs. G. Gordon Campbell, S. Ridley Mackenzie, C. A. Peters, A. W. Gordon, A. G. Nicholls, A. C. P. Howard.

Surgeons—Drs. Kenneth Cameron, E. M. von Eberts, A. T. Bazin, A. R. Pennoyer, W. L. Barlow, R. P. Campbell, A. Mackenzie Forbes.

Specialists—Assistant oculist and aurist, Dr. S. H. McKee; assistant gynæcologist, Dr. H. M. Little; assistant laryngologist, Dr. R. H. Craig.

The following compose the committee of management:—Messrs. James Crathern, H. Stikeman, F. W. Evans, Dr. Shepherd, J. B. Learmont, David Morrice, James R. Wilson, Abner Kingman, Sir Hugh Graham, Sir Montagu Allan, Hugh Paton, Bartlett McLennan and George R. Hooper.

TYPHOID FEVER IN MONTREAL.

The authorities of the Montreal General, the Royal Victoria, and the Notre Dame Hospitals have addressed to the Board of Health the following communication:—

"The governors of the hospitals of this city desire to draw the attention of the City Council to the alarming prevalence of typhoid fever. During the recent epidemic, hospital accommodation has been insufficient to meet the demands for admission made by citizens suffering from this dread disease. Numbers of patients requiring treatment were turned away daily during its height. It is the duty of the city immediately to trace the cause of the outbreak and to take the necessary steps to prevent its recurrence, and to find means to alleviate the situation.

"The hospital authorities having been advised by the medical men of the city, and civil engineers, are convinced from the widespread character of the disease that impure water is the cause. Typhoid fever is a water-borne disease, and results from drinking contaminated water containing typhoid germs; when conveyed through milk, the milk has been contaminated by water containing the typhoid poison.

"Typhoid is a preventible disease, and should not become epidemic in any well-governed city.

"The proper filtration of water has in many other cities proved an efficient means of preventing typhoid, and some well-known system to bring about the desired result should receive your immediate consideration.

"The governors of the hospitals deem it their duty to present an urgent demand upon the Mayor and Council to take prompt action and protect the citizens against this scourge."

Retrospect of Current Literature.

SURGERY.

UNDER THE CHARGE OF DRS. ARMSTRONG, BARLOW, ARCHIBALD, AND CAMPBELL.

W. Simon. "The Experimental Study of Transverse Nephrotomy." *Beiträge zur Klin. Chir.*, Bd. LIX, Heft 2.

Simon, in this article, brings out certain points in the anatomy of the kidney with reference to the blood supply. These points he uses in order to strengthen his arguments in favour of the transverse nephrotomy. His anatomical work consisted in injecting, with a suspension of mercury, the arteries of the kidney and then having the organ skiagraphed. His findings were these: The renal artery divides into anterior and posterior branches; these again dividing so as to send branches into the lobules and on to the cortex.

Thus one has an arrangement by which there exists a considerable space, in which run no important vessels, lying between the two large main branches, anterior and posterior, and their ramifications; and this space runs longitudinally from pole to pole. Now it has been generally taught for a number of years that this longitudinal space lies a little posterior to the longitudinal mid-line of the dorsum of the kidney, and that in consequence the nephrotomy incision should be made a little posterior to the mid-line.

Simon finds that this view of things is somewhat erroneous; that the line of separation is situated in many cases exactly in the mid-line; and that in any case it is an extremely narrow one. Further injections showed him that with the usual longitudinal nephrotomy incision, large arterial branches were often cut, and, these being end arteries, large areas of the kidney were thus actually cut off from their blood supply, and were therefore functionally useless. Such considerations suggested the idea of the transverse as opposed to the longitudinal nephrotomy incision.

Next, he studied kidneys subjected to transverse nephrotomy and found the following:—A transverse incision could be made mid-way between the poles, commencing about 1 cm. on the posterior surface, passing across the dorsum and down into the pelvis on the anterior surface, without serious hæmorrhage or the cutting off of the blood supply to any large area of the kidney substance. This seems to be a considerable advance in the operation of nephrotomy, if one is to judge from his review, in the first part of this article, of the work of the older surgeons who have used the longitudinal incision; many of these, as well as himself, have come to the conclusion that the old operation is not as conservative as used to be generally considered, and this because of the frequency of

large anæmic infarcts and of serious, even fatal, secondary hæmorrhage. There have been already a few cases operated on by this method with very slight hæmorrhage and no untoward consequences.

The essence of this article, therefore, lies in this, that the transverse method on the one hand offers less danger of hæmorrhage than the longitudinal, and on the other an equally good exposure of the kidney pelvis.

W. H.

MEDICINE.

UNDER THE CHARGE OF DRS. FINLEY, LAFLEUR, HAMILTON, AND HOWARD.

THE THYROID GLAND.

In the matter of simple goitre, it has long been known that the disease was local or endemic, but just what was the offending cause has led to no small speculation.

An interesting communication dealing with this question came from Captain McCarrison of the I. M. S., in 1906, upon the occurrence of goitre in the Chitral and Gilgit valleys on the northwestern frontier of India.

In the Chitral district the water supply comes from springs fed by melting snow. In the notoriously goitrous portions of the district the water passes through a limestone formation. In these districts goitre was very frequent among young children as well as adults. Seventeen Hindus—members of the expedition, from non-goitrous regions of India, after four months residence developed enlargement of the thyroid.

In the Gilgit valley, goitre was found in all of the villages but one. In this one, the water supply was from a source different from the others, though analysis of the two waters gave practically the same result.

A point of interest exists in reference to a village called Nagar. This village was closed to outsiders until a sharp frontier "little war" in 1893. Before this no cases of goitre had occurred in the village. After the unpleasantness, three persons came from Gilgit with goitre and inside of two years four others in the same house developed enlarged thyroids. In another house one member of the family brought home a goitre and later two others in the same house contracted the disease.

The first family lived at the head of the village water supply, and during McCarrison's stay, 12 children in different parts of the village were brought to him with goitre.

From these facts he suggests the probability of goitre being infective and the infecting agent thriving best in a lime-containing water. Charlton's observations on the goitre-bearing areas in the Montreal dis-

trict, made in 1901, showed that on the island of Montreal, simple goitre was found in a percentage of the inhabitants from 1.5 in the east at Pointe-au-Trembles, to 7 at Ste. Anne's, a steady increase occurring in a westerly direction along the river front, excluding the city proper. In the central parishes of St. Laurent and Sault-au-Recollet it was almost absent. He found that where it was least common, the water supply was from deep wells tapping blue clay; where most common, it was from more superficial wells in sandy soil. At Pointe-aux-Trembles, when well water was used, the incidence was 4%; since the installation of a municipal river supply it had dropped to 1.5.

There is now no necessity of stating that myxœdema is due to an absence of the thyroid secretion, but it is interesting to note that MacCallum and Fabyan, in an autopsy lately on the body of a myxœdematous idiot, found the thyroid glands represented by small fibrous nodules with only a suggestion of proper thyroid tissue. On the other hand, to indicate that the matter is not monotonously simple, Samuel West, among others, reports the onset of an acute myxœdema in the course of exophthalmic goitre.

In the matter of the ultimate causation of Basedow's disease there is not much to be said, no one theory having a safer standing ground than another. That its immediate cause lies in the thyroid gland there is now but little question, though from this point another division of views takes place, namely:—(a) That its manifestations arise from a metabolic poison unhampered by an insufficient or inert thyroid secretion; or, (b) that the production of thyroid substance has run riot and itself acts as a body poison. The first theory has some support from the observation of Hunt, who found that mice fed on thyroids were able to stand larger doses of acetonitrile without fatal effect than controls. Blum held that a toxic globulin arising in the course of metabolism was detoxicated in the thyroid by chemical combination with the iodin, and that therefore the colloid was an excretion, and the more perfectly iodized it was the less toxic it became. This theory he based upon the observation that thyreoglobulin lost its physiological properties when iodine was added to it; but if followed to its conclusion, this view would contradict the fact that physiologically active thyreoglobulin does contain iodine, and more, that its activity is in proportion to its content of iodine. Oswald's chemical studies of goitres showed an excess of globulin poor in iodine, and Beebe found in exophthalmic goitres a very great increase in the nucleoproteid as compared with normal glands; in the fatal cases, this increase was excessive. The hypersecretion theory has these facts in its support, as also the well known appearance of individual signs of Basedow's disease

after thyroid feeding; though it must be said that so far, the complete clinical picture has not been reproduced by this means.

An instructive case in this connection is reported by Matthes, who removed a thyroid from a patient suffering from exophthalmic goitre with a curative result, and then fed to him his own dried gland with return of his old symptoms. But if hypersecretion be the cause,—why the hypersecretion? Pawlow's work upon the digestive glands and their change of function from psychic causes, gives colour to the idea that it may be of nervous origin.

"Did the hen come first or the egg?" Is the goitre nervous or is the nervousness goitrous? It seems most likely the latter.

Another reasonable supposition is that the altered secretion of the gland has been brought about by an acute infection. In favour of this are Gilman Thompson's 80 cases in which forty had recently tonsillitis, influenza, or other acute febrile illness.

There have been long recognized four cardinal signs of Basedow's disease, beside a number of accessory ones.

First, the goitre, which is almost always present, and is also nearly always vascular, giving pulsation, thrill and murmur on examination: its surface as a rule is apparently granular to the touch.

Second, tachycardia, which is perhaps, the most important and most constant sign. It is not only a sign of the disease, but the degree is an indication of its severity.

It is probably due to direct sympathetic cardiac stimulation, as the blood pressure is as a rule higher than normal.

Third, exophthalmos, which is said by Barker to be absent in one-third of the cases. It is much the most obvious sign on casual inspection. Early in its course it may be reduced by the finger temporarily, but later this is impossible. In fact, as Möbius states, a "fat pillow" is found behind the eyeball in late cases, which would indicate an organic adaptation to its presence.

Fourth, tremor, which is fine and rapid, not increased by voluntary motion, but is increased by excitement.

In this connection one might mention the greatly diminished muscular power—about one-fifth of the normal, and also the observation of Shaffer that the kreatinin output is greatly lessened, the latter possibly being associated with diminished muscular metabolism. In comparison with this we have the greatly increased output of total nitrogen and phosphates, which facts go hand in hand with the rapid and severe emaciation characteristic of the disease.

The ocular signs aside from exophthalmos have been much described and much named. Of these, Stellwag's sign, the widening of the palpebral fissure, is the most valuable. Möbius states that it is the earliest sign to appear and is never completely absent. It may be present on only one side, and may vary from time to time. He states also that a strip of uncovered conjunctiva above the iris is always pathological. The other ocular signs may be simply mentioned:—Von Graefe's, failure of the upper lid to follow the eye ball; Stellwag and Dalrymple's, retraction of the upper lid on straight vision; Stellwag's, incomplete winking; Giffard's, difficult eversion of the upper lid; Jalinek and Rosin, pigmentation of the upper lid; Joffroy's, failure of the forehead to wrinkle; Möbius', insufficiency of convergence. Möbius states that internal ophthalmoplegia does not occur, but explains the sign called by his name as a weakness of the external muscles.

One is struck by the resemblance of the eye signs of Grave's disease, except for the state of the pupil to the results after stimulation of the sympathetic in an animal. In a bird there follow protrusion of the eyeball, retraction of the nictitating membrane, widening of the palpebral fissure, and dilatation of the pupil—all and sundry an apparent demand for more light.

Fever is often present to a slight degree, but Thompson has laid stress on what he terms an acute form of the disease simulating an acute septicæmia. I quote his report of such a case:

"A woman of 39 entered the hospital with the following history:—She had been in good health up to six weeks previously, never having noted any goitrous symptoms. At that time she had a severe cold and cough, became extremely nervous and restless, and complained of violent palpitation. Two weeks later she noticed that her neck was much swollen, and there were marked tremor of the hands, abdominal pains and œdema of the legs. On admission there was no exophthalmos, but there was a large soft pulsating goitre with a thrill and bruit. The heart apex was five inches from the midsternum, with loud systolic murmurs at apex and base. There was a leucocytosis of 20,000. Sweating was active, vomiting frequent, and the tongue dry and red. There was much abdominal pain. For ten days the temperature ranged from 101 to 104, the maximum pulse rate was 144. Theere was marked dyspnœa without any pulmonary lesion. Insomnia was constant; jactitation, mental distress and complaint of excessive pulsations in the neck were painful to witness. The legs were greatly swollen with a tense œdema, a smooth shining skin with extensive erythema. This, with fever,

leucocytosis, and sweating and the typical appearance of a general infection led me to call upon a surgeon for advice as to free incision. I fortunately decided to postpone the procedure and became more and more convinced that the case was one of unusually acute Grave's disease. The subsequent history and the complete cure under the Rogers-Beebe serum proved the correctness of the diagnosis." Such cases one would think must be rare.

In the treatment of Basedow's disease, there are few drugs in the pharmacopæia which have not had their turn. Looking at the number used on this side of the water, Möbius says: "America must be an Eldorado for the apothecary." He, himself, on the recommendation of Sahli and Kocher, has made use of sodium phosphate 2-10 grm. per diem with satisfactory symptomatic results. As to iodine, he states that he teaches his patients, "Iodine is poison for you." Forcheimer has for a long time made use of quinine hydrobromate gr. 5, thrice daily, over long periods and is so pleased with his results that he continues using it. The use of static electricity and the x-ray have had their advocates, and especially the latter has shown in some cases a diminution in size of the goitre with some amelioration of the symptoms. The most hopeful form of medical treatment has been that by some form of serum.

Broadly speaking, this method has been followed along two lines: First, an "antitoxic" serum, which had its origin in the supposition that the thyroid was producing too much of the substance normally employed in neutralizing the toxic globulins of metabolism. Myxœdema being the antithesis of exophthalmic goitre, blood from a myxœdematous patient was injected into a Grave's disease patient with apparently beneficial result. Enriquez and Ballet, in 1895, then used serum from dogs, whose thyroids had been removed, also with favourable results. Lanz, in 1899, used the milk of thyroidectomized goats. Möbius, in 1901, used the serum of sheep treated similarly, in doses by the mouth of 10-30 minims three times a day. Writing in 1906, he still considers that this is the most satisfactory form of treatment yet brought forward; a fair proportion of his patients were cured and a number improved, but in some there was no effect. Second, Rogers and Beebe proceeded along the line of producing a cytolytic serum. This they produced by extracting from thyroid glands (preferably of exophthalmic goitres removed at operation), the nucleo proteids and thyroglobulin, injecting these into rabbits and using the rabbit serum for human injection. They tested the cytolytic serum by agglutination with an emulsion of thyroid gland. The object in using both nucleoproteid and thyreoglobulin, is that the former

produces the cytolytic agent which inhibits the production of poison by the gland cells of the thyroid, while the latter stimulates the production of a direct antitoxin. This serum was found much more efficient in acute cases than in more chronic ones.

In September, 1906, Rogers reported having personally treated 55 cases, of whom 20 were cured of all symptoms of thyroidism, 24 were improved; 7 failed to show benefit and 4 died.

A. H. G.

PATHOLOGY.

UNDER THE CHARGE OF DRS. ADAMI, KLOTZ, AND NICHOLLS.

THE THYROID GLAND.

Abnormalities of development of the thyroid are frequent and these can in almost all cases be traced to a persistence of the fœtal stricture in part. Such are the small thyroid to be found at the base of the tongue, the small collections of fluid with occasionally solid masses that develop in the median line at or just below the hyoid bone due to a persistence of the thyroglossal duct with at times a small portion of attached thyroid. Portions of the thyroid are frequently found misplaced, that is, they may occur outside the capsule of the gland proper and even further removed as in the thymus or other structure of the neck or mediastinum. Occasionally a marked enlargement of the gland occurs in fœtal life and hinders birth. Complete absence of the thyroid is almost certainly incompatible with life and is therefore never seen, while over-development is thought to be always due to some disturbance of the gland function.

The thyroid gland may be the site of any of the inflammatory processes met with in the body, such as syphilis, tuberculosis and typhoid or pyæmic abscess. Very rarely the thyroid has shown temporary enlargement during an attack of mumps.

Changes in the thyroid gland are seen in two or at the most three diseases that appear to affect the body very widely, but the relationship of the alterations of the gland to these diseases is by no means clear. We will first consider that disease where the secretion of the normal thyroid is supposed to be insufficient for the body needs, chiefly because a supply of extraneous thyroid to that body proves beneficial.

This disease, that in its slighter form appears as myxœdema and in its severe form as cretinism may be endemic or sporadic, and is supposed to be due to a toxin in the water supply affecting most severely a weakened system. It is almost always associated with macroscopic and microscopic changes in the thyroid. In endemic cretinism the gland is

usually enlarged, and a study of its minute structure shows that the gland acini are widely dilated and filled with colloid material. There appears to be a formation of new glands and the stroma is marked and often shows a myomatous change. This condition of the thyroid is known as colloid struma or as parenchymatous degeneration of the thyroid. Again in these cases of endemic cretinism or myxœdema the gland may be atrophied and the vesicles are few and small, while the stroma is markedly increased.

This is the condition of the gland usually seen in the case of the so-called sporadic cretinism or myxœdema, and very rarely the gland appear to be entirely absent.

We now come to the second special disease that is supposed to depend upon an increase of the thyroid function, beyond the body need, Graves' or Basedow's disease, also often termed exophthalmic goitre. In this disease, as can be understood from the last mentioned name, the thyroid is almost always enlarged; but still a few cases are on record where the gland remained of normal size, and there are even a few cases of Graves' disease in old persons where the gland, as would be expected from normal involution, was atrophied or even absent.

MacCallum, Lubarsch and many others hold that in true Graves' disease, the thyroid is always enlarged and that the minute structure of the gland in part or whole will show definite and constant changes which are as follows: the gland lumen is usually dilated and often tubular or convoluted. There is an absence or diminution of the stainable colloid. The lining epithelium tends to change from cubical to tall columnar often with papillary-like projections into the lumen. There is an increased vascularity and an increase in the fibrous stroma with numerous areas of small celled infiltrations. These changes are found, however, only in those cases of Graves' disease that occur in young people from about 14 to 30 years of age, where the toxic symptoms and the enlargement of the thyroid have occurred at one and the same time. At times the enlargement of the thyroid has antedated the toxic symptoms and here the gland shows dilated acini filled with stainable colloid and lined by flattened or cubical cells. Here the general disease is supposed by some to be secondary to the enlarged thyroid. At times in the thyroid in these, small areas are found showing the epithelial hyperplasia described as occurring in the typical cases. Dock thinks the enlarged thyroid will always show these areas if it is searched carefully enough, but the weight of evidence appears to be against him. Again, where a thyroid adenoma has been present for a long period, the toxic symptoms of Graves' disease may develop and the excised gland may

show no change other than the presence of the above tumor. Again a hæmorrhage into an otherwise unaltered gland or into a gland showing colloid degeneration or into an adenoma of the thyroid, appears to cause the onset of Graves' disease. Again patients who die with the severe symptoms of Graves' disease may show perfectly normal thyroids, and occasionally in old persons who died with this disease, the thyroid tissue may be completely absent, and lastly hyperplastic changes of the thyroid as described by MacCallum to be met with in Graves' disease may, as pointed out by Kocher, be found in excised thyroids where there was not a single toxic manifestation. From the above one can easily see that Graves' disease has not an approximately constantly altered thyroid.

The parathyroids in cases of Graves' disease are usually unaltered, but at times show extensive fatty infiltration of the stroma. The thymus is also occasionally found persistent and enlarged and often contributes markedly to a lethal termination.

As Graves' disease is supposed to be connected with disturbance of functions of the thyroid so tetany is supposed to be due to diminution or absence of function of the parathyroids. From their small size and also from the difficulty in finding them, the parathyroids have been relatively rarely studied from a histological standpoint.

Their supposed connection with tetany rests mainly on the fact that very occasionally after complete extirpation of the thyroid, tetany has developed. This is supposed to be due to removal of these glands or to interference with their blood supply. Gley and MacCallum found that if the parathyroids are removed in animals, tetany develops, while Vincent and Joly state that this is not so; and Forsyth, the latest investigator, states that the parathyroids are really thyroidal in nature, have no special function, and are not essential to life.

Other observers state that the parathyroids are related to calcium metabolism, and when tetany occurs as it often does in cases of lactation or rickets or osteomalacia where a disturbance of calcium metabolism is suspected, the glands show change from aplasia to atrophy. This view is not generally accepted.

The thyroid gland may be the site of tumors which may take origin from any of the cells of this structure and may show any degree of reversion to a fœtal type. The most frequent tumor is the well known adenoma of the thyroid which may be single or multiple. Apparently at times adenomata that are benign as far as one can judge from the sections may give rise to metastatic tumors which seem to have a special predilection for bones. These thyroid tumors in bones have been found when there was no tumor of any kind in the thyroid and are then supposed to spring from foci of misplaced thyroid tissue.

These metastases have apparently the power of performing the usual function of thyroid cells, but apparently never give rise to the toxic symptoms of Graves' disease.

Tumors arising from parathyroid cells have been described, both from the parathyroid glands, and from parathyroid cell groups misplaced in the thyroid gland as they frequently are. These are characterized by the presence of the three types of cells met with in these glands, that is large, clear, fat—and glycogen—containing cells with small round nuclei, large oxyphile cells with eccentric small round nuclei where the cytoplasm shows eosinophile granulations and lastly multinucleate cells.

C. B. K.

Society Proceedings.

MONTREAL MEDICO-CHIRURGICAL SOCIETY.

The sixth regular meeting of the Society was held Friday evening, December 18th, 1908, Dr. J. M. Elder occupied the Chair in the absence of the president.

PATHOLOGICAL SPECIMENS.—HEART DISEASE.—TYPHOIDAL LESION IN A MECKEL'S DIVERTICULUM.

OSKAR KLOTZ, M.D. The first three specimens that I shall show you illustrate three types of heart disease, occurring at different ages.

The first specimen is the heart of an infant, one month and sixteen days old, in which an acute septic aortic endocarditis is found, affecting particularly one valve. This valve, the anterior cusp, has its aortic surface and the sinus of Valsalva almost completely covered with fresh exudate, from which streptococci were obtained. This was the only lesion in the heart.

In this case, the heart only served as a secondary distributing point of infective material. The primary site of infection was found in a suppurative middle ear, from which the same organisms were obtained. The heart lesion can thus be considered to be only one of the manifestations of a septicæmia.

The second specimen is that taken from a man of forty-five years, who, on the day previous to his death, was transacting his usual business. During that day, however, he developed anginal attacks which continued with increasing frequency for the next twenty hours. He sought the Hospital for treatment, but died shortly after reaching it. The autopsy disclosed an interesting and rather unusual lesion in the nature of a small and recent pedunculated thrombus attached to the

upper margin of the anterior coronary orifice. This thrombus was in such a position that every now and again the blood pressure forced it into the mouth of the coronary artery. The fatal turn resulted from the thrombus being forced into the mouth of the anterior coronary, and not being relieved by the subsequent pulsations. The coronary arteries of the heart, as also the aorta of this man, were in relatively good condition, while the heart valves too showed little change. Just why this small and recent thrombus found its origin at the mouth of the coronary artery is difficult to explain.

The third heart specimen was obtained from a man aged thirty-four. He had been a sufferer of heart disease, possibly a rheumatic, for some time. The particular lesion of this heart is also located on the aortic valve. Here I find evidence of old sclerotic processes with fusion of the heart cusps, while there is also a recent and progressive ulcerative process of the valves. The anterior cusp is remarkably thickened by the deposit of organizing exudate. Besides this, we find attached to this valve a long ribbon-like thrombus extending freely into the aorta. When the specimen was obtained, this thrombus was floating freely in the blood of the aorta. The length of the thrombus is rather unusual, having been in the fresh heart 8 cm.

The last specimen is part of the intestinal tract, taken from a patient suffering from typhoid fever. Typhoidal ulcers were met with in the large and small intestine, the appendix and the rectum, but more unusual than this, was the presence of typhoidal lesions in a Meckel's diverticulum, whose perforation had led to peritonitis and death. The ulcers in the small bowel were of the usual appearance seen at the end of three weeks' illness. The ulcers, however, immediately before the ileo cæcal valve were extensive and had led to severe hæmorrhage. The Meckel's diverticulum was situated 40 cm. from the valve, and itself was 9 cm. in length. The diverticulum had its own mesentery, but was not attached to the umbilicus. It was roughly divided into two portions: the proximal portion communicated freely with the intestine and its mucosal lining was very similar to that of the ileum. The distal portion was separated from the proximal by a constriction giving it an hour-glass appearance. The distal part was globular and contained fluid, while its lumen did not communicate freely with the other portion. The distal part was lined by a necrotic membrane, in which the mucosa had been entirely destroyed. There were several deep ulcers through it, which allowed leakage of the contents. It is probable that the original shape of the diverticulum was hour-glass, and that the inflammatory swelling of the bowel led to a closure between the proximal and distal portions of the

diverticulum, thus converting the distal portion into an infected sac.

W. F. HAMILTON, M.D. The third cardiac specimen is of peculiar interest from a clinical standpoint inasmuch as one feature, to me at least, was entirely exceptional. The patient came into hospital for treatment of a very marked acute hæmorrhagic nephritis, and, in the examination of his circulatory system, the first thing that struck me was the peculiar second beat or wave in the pulse which impressed itself upon the finger. A second wave we are all accustomed to feel more or less frequently in typhoid fever, but it is rather remarkable to have this dicrotism in this condition. In this case we were led to look a little further into the case and analyse it by the aid of tracings which Dr. Moffatt made for me. Not only could one feel this second beat in the distal arteries, but one could see distinctly in the carotids a distinct second jog. In analysing that under the finger one thought it is not like dicrotism, because it comes too close to the summit of the wave, and I was thus nonplussed to make a decision concerning it. Looking up MacKenzie, he says that such pulses are instrumental, but here it was certainly not instrumental and we have concluded that it was an unusual second wave corresponding to the so-called systolic, predicrotic or elastic wave which appears to be found most frequently in aortic regurgitation with stenosis. We therefore go back to what some physiologists teach that the heart muscle in its systole consists of two distinct efforts, the first when the muscle tackles the load and the second when it accomplishes its effort. It would appear therefore to be an unusually high predicrotic wave occurring in systole, and associated with a very marked disproportion between the muscle of the heart and the load it had to bear. The blood pressure was from 130 to 145. The second case of angina is that definitely associated with what was taught many years ago, namely ischæmia of the heart muscle.

RIDLEY MACKENZIE, M.D. I am glad to hear the case of thrombus in the coronary vessel. I think this condition explains a case I had of repeated attacks of intense dyspnœa which passed off after a time. There were about six attacks in all and the only explanation I could think of at the time was the infarcts of the lung. The heart was not much enlarged and though blood pressure was high, angina pectoris did not account for the attacks—the specimen here presented gives an explanation of the attacks, which in my case eventually caused the patient's death.

J. M. ELDER, M.D. I understood Dr. Klotz to say that he thought that the diverticulum had been always probably of the "dumbbell" or "hour-glass" shape. I should like to ask Dr. Klotz if, in his post-

mortem examinations, he has ever found diverticula of this particular shape? My own experience of diverticula was largely got from the dissecting room, and I cannot remember having seen there any of such shape. That a diverticulum should have become ulcerated in typhoid is, I fancy, what has occurred before.

DR. GURD: I would like to ask Dr. Klotz if it is not a rather unusual place for a Meckel's diverticulum to occur.

OSKAR KLOTZ, M.D. In regard to the Chairman's question I may say that I do not remember having seen an hour-glass Meckel's diverticulum before, the nearest approach to this which I have seen was a Meckel's with an attachment to the umbilicus and along which occurred a little sac, entirely separated from the Meckel's itself, but containing mucous membrane within it. It did not form a true hour-glass organ, in that the communication between the Meckel's and the sac was obliterated.

As Dr. Gurd points out it is unusual to have a Meckel's diverticulum arising so far to the side of the bowel. On the other hand, the falciform mesentery attached to the diverticulum, rather than opposing the view that this is a true Meckel's, suggests it. Every Meckel's has a main blood supply along one side, and the blood vessels are usually in a more or less marked mesentery. On the other hand, the diverticula occurring along the mesenteric border of attachment of the bowel consist of small sacs, without such a definite blood supply to them. These latter diverticula are usually of the nature of small hernias of one or more coats of the bowel.

THE CHEMISTRY OF THE URINE IN DIABETES MELLITUS.

C. P. HOWARD, M. D.

W. F. HAMILTON, M.D. I have been a member of this Society for many years and this is the first paper of this kind, and it speaks of the nearness of touch we are gaining to the laboratory, and at the same time it speaks for the kind of men we are gathering round us who do such laborious and careful work as this. I have been very much interested in diabetes and during the last year have treated three cases which came directly under my notice, but in only one instance did I have such a severe case as this. In three instances I was able by careful grading of the carbohydrate content of the food to arrive at a tolerance for that element of the food and in two cases a fair amount was borne, that is an amount in which the patient could do work and be confortable. In one case the subsequent history showed a very pronounced glycosuria. He was a clergyman, passing 4 per cent., who had recently fallen ill with all the signs of diabetes. In 6 to 8 weeks we are able to get him free from

sugar and to tolerate 1 to 2 potatoes, some egg and a little toast. He went abroad and returned after several months; on the resumption of his duties his physician finds that he is again passing sugar. It appeared to me that he belonged to the light cases and one that would do well under ordinary circumstances with a light diet. I never saw coma in diabetes begin without ending fatally or even threaten without it went on to death. I have tried the bicarbonate of soda and have given the patient for weeks at a time from three to four hundred grains a day and yet in the midst of this she lapsed quickly into a coma and died.

F. M. Fry, M.D. I would like to add my gratitude to Dr. Howard for bringing before us such painstaking work. I was hoping that he would emphasize that we have to deal, roughly, with two kinds of patients, 1. the one who is well past middle age and stout, and 2. the patient who is young (about the age of Dr. Howard's), and thin. Our forefathers knew perfectly well that the prognosis in the former is favourable; we all know, too, that the prognosis in the lean class of patients is very grave. As to tests for acidosis: we have in Legal's test a delicate means of recognizing the first note of warning—the presence of acetone in the urine. The test (sodium nitroprusside and ammonia) can be carried out in a minute's time and I am accustomed to use it in a busy out-door department where more elaborate and quantitive tests are impossible.

H. M. Little, M.D. In looking over the figures of Dr. Howard, I find that in three or four instances a low output of urine was accompanied by a high specific gravity, and a high specific gravity has a low output of sugar. I would like to ask what may be drawn from this.

C. P. Howard, M.D. As regards the question as to the various methods for ammonia. The one that I used was at that time the best one available, viz: von Schlössing's method, which is rather an elaborate one and requires three to four days before one can get one's result. However, as Dr. Gilday no doubt knows, Folin, of Boston, has introduced a much more accurate method and one which takes but a few hours instead of a few days. At that time I had no experience with the method, but since then I can get very accurate results. It depends upon the driving off of the ammonia by means of an air current and collecting it in a decinormal hydrochloric acid solution. It is a method which can be recommended to all and is the simpler one. As regards Dr. Hamilton's remarks, this case was a very severe one and was taken on this account; for my purpose was not to see the benefits but rather to watch the chemistry of a severe case. The object of any dietry is to increase the carbohydrate tolerance. Many cases will never be free of the glycosuria, but many will have their carbohydrate tolerance increased and the import-

ance of that can best be realized by saying that the carbohydrates are the saving factor. If one can do this one lessens the chances of coma. This will answer Dr. Peter's remarks that it is not practical for a man in ordinary practice to do this hospital routine: but I would say watch rather your acetone than your sugar, the sugar, authorities now believe, is of less importance than the acetone. When you have a low sugar output, as for instance in the last stages of diabetic coma, you may have a very high acetone output, which is the real danger point and not the sugar that is being lost. The percentage of the sugar is of absolutely no importance as compared with the amount in the 24 hours. A clinician who satisfies himself with reading the percentage of sugar and not knowing the amount in the 24 hours, is wasting his time and is falsely scientific, because the amount of sugar varies considerably. The percentage may improve and the sugar may increase. Hence, if you only take the reading of the percentage of sugar you are no wiser, in fact you are probably misled. As to Dr. Hamilton's remark of never having seen a case of diabetic coma, or even threatening coma, recover: this is in part quite true. In my own case coma was threatening several times, that is she became drowsy and the urine showed then an increased acidosis. In these cases clinicians have got improvement with large doses of sodium bicarbonate, but when the coma has once become established, as in the three cases I have attended, this has had no benefit. But, I feel that we use the alkalies too late and then in not heroic enough doses. It should be given intravenously; there is no use dallying with subcutaneous or rectal injections and 1 litre or 1500 cc. in as brief a time as possible should be given. Of course, this is not a clinical paper and I could not pretend to discuss the clinical aspect of the whole subject. As to the practical test mentioned by Dr. Fry I did not discuss the qualitative tests but only the quantitative ones.

DREAMY STATE WITH TUMOUR OF THE TEMPORO-SPHENOIDAL LOBE.

C. K. Russell, M.D. This case report appears on page 75 of the February Journal.

E. W. Archibald, M.D. Dr. Russel referred the case to me for operation and I first did a decompressive operation intended as the first stage of the radical operation. It was hoped that the decompression might accomplish something for her very severe neuralgia. At the second operation, which was undertaken on account of no relief to the neuralgia, I had my finger practically into the middle line and palpated the whole tempro-sphenoidal lobe upwards, but I could feel no growth. It is very

instructive, looking back now in the light of the autopsy, to find that the tumor was really larger than had been expected. As it looks now from the specimen you could imagine it a very easy matter to palpate, yet it was impossible to detect it. It is very difficult, except with certain kinds of tumor, to palpate in this region. There is no possibility of doing bimanual palpation, and it is only bimanually that one can actually feel a tumor in this position, unless it be especially resistant. This was an irremovable tumor by virtue of the fact that it had penetrated the base of the skull. As to the point mentioned concerning the diagnosis of these lesions by aurae of taste or odour, referable of course to a lesion of the uncinate gyrus, I remember one case where a spicule of bone had deeply penetrated the temporal lobe in which the cardinal symptom of the fits was that they were ushered in by a foul taste in the mouth.

C. K. RUSSEL, M.D. With regard to the fits I would say that aurae of smell and taste are not uncommon as evidence of lesions in the uncinate gyrus and are often associated with these dreamy states, but it is just these latter that I wish to emphasize to-night as of localising value in tumors of the temporo-sphenoidal lobe.

PYELO-NEPHRITIS COMPLICATING PREGNANCY.

D. J. EVANS, M.D.

E. W. ARCHIBALD, M.D. I think Dr. Evans is to be congratulated on presenting such an admirable paper. The general surgeon sometimes comes across these cases and may be much puzzled by them. I have had three cases of pyelonephritis with abscess in women, of whom two were pregnant, the first being in the very early months and the second in the sixth month. The last was a very severe case, but got well. Two were referred to me with the diagnosis of appendicitis, because of the pain in the right flank. They are extremely important cases, I think, for that one reason, that it is very necessary for the general surgeon or practitioner to distinguish them from appendicitis.

R. P. CAMPBELL, M.D. It is some time since I saw these cases and I can only vouch that they were undoubted cases of pyelo-nephritis. There is some doubt as to the manner of infection in all these cases; that it is an ascending infection in the urinary tract always seems to me to be open to question. Experimentally it is practically impossible without the additional factor of urethral obstruction, hence pyelo-nephritis in women is a rare event. The nature of the infection is an extremely interesting point, in most of my cases it was the bacillus coli. This, I think, must be far the most common cause and it seems to me it must come from the gastro-intestinal tract through the blood, though a direct

passage from the bowel to the kidney is perhaps possible. I was interested to hear that the gonococcus was found in a case of pyelo-nephritis; I have tried to discover cases in the literature where the kidney was infected by this organism. It has never been found to my knowledge in smears or in culture, either in the kidney or pelvis itself.

J. M. ELDER, M.D. I cannot, from a practical surgical standpoint, agree with the opinion that this condition can possibly be due to the occlusion of the ureter by pressure. One must have some other etiological factor associated with pressure. My reason for such opinion it that it is well known in surgical literature that a complete occlusion of the ureter has another effect, viz: to produce an acute hydronephrosis and secondarily complete atrophy of the kidney. It has occurred quite frequently, in operating, that the ureters have been ligated by mistake, and the above has been the result. I do not think, therefore, that occlusion of the ureter alone will be sufficient: there has to be some added infection; and I think that an ascending infection is not an uncommon cause of pyelonephritis. That would exploit, to some extent, the ingenious theory of the Frenchman, namely, that if you occlude the ureter and produce thereby an acute hydronephrosis, then you would expect, if the bacillus coli got through, to get a pyelonephritis. I should think a certain amount of pyelonephritis in a woman, pregnant or otherwise, might be due to temporary occlusion of the ureter by a calculus.

D. J. EVANS, M.D. I think there was no doubt of the diagnosis in the cases I have reported though only one of them could be verified by autopsy.

When a woman late in pregnancy complains of pain and tenderness over McBurney's point it is very much more likely to result from pyelonephritis than from appendicitis. To clear up the diagnosis in such cases, the urine should be carefully examined daily for at least four days before pyelitis is excluded.

The bacillus coli is extraordinarily prominent as the infective agent in these cases. In an overwhelming proportion of those cases examined bacteriologically this has been the infecting organism.

In my own experience in every single case of pyelonephritis that I have seen, there has been more or less abnormal vaginal discharge. Two or three of my cases complained of irritable bladders, some days before any evidence of nephritis developed. These two facts have led me to rather favour the view that the condition present in my cases resulted from an ascending affection.

In reply to Dr. Campbell's question as to my authority for the presence of gonococcus in the kidney, I may say that I have simply stated that

these among other organisms are stated to give rise to the condition.

In regard to dilitation of the ureters in consequence of pressure of the uterus during pregnancy I know, as Dr. Elder has said, that recent writers tend to oppose this theory, but again my own personal experience must affect my opinion, because I have seen several post-mortems on women who have died from accidental causes during advanced pregnancy, in whom there has been most marked hydronephrosis, and always on the right side. Another thing that may account for the tendency for this condition to be associated with the right kidney is that possibly pyelonephritis in pregnancy is the result of twisting of the ureter occurring in women who are the subjects of "floating kidney." This combination of causes, pregnancy, plus floating kidney, probably act by reducing the resistance of the ureter and pelvis of the kidney on that side and thus favour the infection by the colon bacillus.

The seventh regular meeting of the Society was held Friday evening, January 8th, 1909, Dr. J. Alex. Hutchison, President, in the Chair.

Dr. G. E. Armstrong read the report of the committee appointed to look into the question of the water supply to the City of Montreal.

This report was adopted after discussion by Drs. Shepherd, Roddick, England and the President. It was resolved that a copy be sent to the press and that the committee of this Society be asked to act in conjunction with any committees of other societies which may be appointed to take up this particular question with a view to interviewing the civic authorities and demanding a better water supply.

ABSCESS AND GANGRENE OF THE LUNG.

G. E. Armstrong, M.D., read the paper of the evening. This will be found on page 83 of the February number of the Journal.

F. J. Shepherd, M.D. Dr. Armstrong is to be congratulated on the excellence of his paper. He has left us very little to say on this subject. I remember the first case I saw was one following excision of the tongue many years ago, the patient rapidly dying of gangrene of the lung. There was a post-mortem and the gangrene was found to be confined to one lobe. I have seen quite a number of cases since; one I mistook for a localised empyema with adhesion of the parietal pleura. With regard to the fact that foreign bodies sometimes cause these I remember one case where one of our graduates swallowed a piece of nut shell and finally died from an abscess formed from this foreign body. Another such case was in the hospital lately, but here the foreign body was coughed up.

J. ALEX. HUTCHISON, M.D. I would like to add in conclusion that no case would appear too advanced to have one hope for a successful result. I had a case a few years ago where the patient was almost unconscious. He had been advised not to submit to any operation and his friends were also against any operative interference, though his family physician and myself had advised it for some time. Against this opposition, however, we opened the cavity and drained it without an anæsthetic as the patient was unconscious, and the case made an uninterrupted recovery. This would show that the gravity of any particular case should not prevent one endeavouring to drain the cavity just like an abscess elsewhere. We are all indebted to Dr. Armstrong for his excellent paper.

E. HAMILTON WHITE, M.D. I was much interested in Dr. Armstrong's reference to foreign bodies as the etiological factor of importance in some of these cases. Such cases furnish a very important field for the use of bronchoscopy, both as a means of diagnosis and in suitable cases for treatment: Professor Killian reported a case last year which illustrated some important points. The patient had had symptoms of a chronic lung abscess for five years. No history pointing to foreign body aspiration was obtained until after an X-ray showed a nail in one of the bronchi. It was then explained that the man was an epileptic and had once taken a seizure while at work with some nails in his mouth. The case presented special difficulty owing to a stenosis of the bronchus above the foreign body. The nail was removed by means of the bronchoscope and the result very good. I had an opportunity of seeing a case in Siebenmann's clinic where the symptoms were somewhat similar and with a history of aspiration of a piece of nutshell some four of five years before. A thorough examination with the bronchoscope failed to reveal any foreign body. The case was operated on later by a surgeon, but he also failed to locate any foreign body.

G. E. ARMSTRONG, M.D. Dr. Shepherd's remarks recall a case that was really of great interest, one which Dr. Molson and Dr. Gordon sent over from the medical side with a diagnosis of pulmonary abscess. The diagnosis seemed to be pretty definitely made with the aspirating needle which brought away a small quantity of pus. On opening into this area, I came into a space which I was subsequently able to define pretty distinctly as situated between the middle and lower lobes of the lung on the left side, the space containing a small quantity of sero-purulent matter, perhaps a couple of ounces. The abscess was not, strictly speaking, within the lung and therefore was hardly a true lung abscess. Neither was it in the pleural cavity but located between the lobes of the lung, an interlobular abscess. Such collections may be found

between the lower lobe and the diaphragm. The condition immediately followed the extraction of teeth under a general anæsthetic. I drained this space for a week or ten days when it closed up and she went home. She did not, however, seem to get well. There remained a feeling of discomfort in the side and an irritable hacking cough. A few days after her return home she coughed up a tooth and since then, I understand, the symptoms have entirely disappeared.

PANCREATITIS, ACUTE, SUBACUTE, AND CHRONIC RELAPSING.

E. W. Archibald, M.D., and A. A. Bruère, M.D.

F. M. Fry, M.D. If this lipase is found in the liver, in the subcutaneous tissue, and elsewhere, why would not disease in these tissues lead to the presence of lipase in the urine and prevent one being absolutely certain that the disease is in the pancreas.

F. J. Shepherd, M.D. I should like to express my pleasure in hearing this paper and the interesting cases that have been reported. The fact that they have been diagnosed without operation is important. I think myself it is always well to drain the gall bladder, as there may have been a stone which has escaped, as Dr. Duval has said, into the ampulla of Vater. I remember a good many years ago we thought a hard pancreas indicated malignant disease. I operated on a case of supposed gall stones and found nothing but the head of the pancreas quite hard. I thought I felt some nodules here and compressed them with my fingers and they seemed to disappear, the gall bladder was opened and nothing found and then sutured. I thought that these nodules were stones in the duct of Vater and that in compressing these nodules I had moved them on or broken them up. The man got perfectly well from that time on. Of course I have seen many cases of chronic pancreatitis with gall stones and also without and I have found many get better after drainage. I have had no recurrences in any cases that I know of.

E. W. Archibald, M.D. In reply to Dr. Fry, it is true that lipase is found normally in other organs, such as the liver and subcutaneous fat, and that lipase might possibly come from these places rather than from the pancreas. Yet, of course, in these cases the pancreas is the organ definitely at fault; we are not dealing with any inflammation of the subcutaneous fat or of the liver, except possibly in certain cases of severe biliary infection. We must conclude, therefore, that it is the disturbance of the pancreas that is causing the exit of lipase into the urine. With regard to Dr. Duval's remarks that the chronic relapsing form may be due to a ball-valve stone in the ampulla of Vater, that, of course, is perfectly sound. I had one case in which this condition of affairs was

present. and Dr. Garrow's case was one of that sort. Yet the same type of pancreatitis does occur without any apparent evidence of stones at all; and I assume that, just as in the appendix, so also in the pancreas, as the result of fibrosis from preliminary inflammation there may develop a series of secondary inflammations, giving the relapsing type.

Dr. Shepherd advises draining the gall bladder as a routine thing. Certainly one would always be inclined to operate in these cases (if only in an exploratory way), because after all one can never be quite sure that the pancreatic lesion is not dependent upon a stone which might be removed. or adhesions round the pancreatic head, which might be separated; but if in the course of such an operation one does not find any of these conditions, the etiology remains unclear and draining would seem to me to be hardly indicated. I prefer to give Urotropine, upon the offchance of the lesion being due to infected bile. This is a less serious form of therapy than a cholecystostomy or cholecystenterostomy.

OSTEOMYELITIS: RECOVERY OF TYPHOID BACILLUS 20 YEARS AFTER PRIMARY INFECTION.

A. H. MacCordick, M.D.

J. M. Elder, M.D. I would like to say that, though I operated upon this case, mine was merely the mechanical part; the presumption that this was possibly an old typhoidal lesion was due entirely to the physician who had charge of the case and who worked it out, namely, Dr. Lafleur. The wound healed by primary intention. The history was that these attacks would come on, apparently after she walked a little more than usual, the pain being very violent. This condition, off and on, persisted for a good many years. I do not think there is another case where a pure typhoid culture has been recovered from the bone after twenty years. Keen reports a case of, I think, seven years, and I remember one case from Dr. Blackader's wards which I operated on four or five years ago; and, if I remember rightly, she had been in the hospital eleven years previously with a history of typhoid fever and more or less trouble with a typhoid node on the tibia ever after. Here we got a pure typhoid culture also.

The case under discussion gave a positive Widal reaction of the blood, and an interesting question would arise whether typhoid bacilli were present in the stools, and whether, therefore, she would be capable of conveying typhoidal infection all these years. I regret that we did not settle this point in our investigations of this very interesting case.