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ON THE COMPARATIVE ANATOMY OF THE LYM-PHATICS OF THE UTERUS. By George Hoggan, M.B. (Edin.), and Frances Elizabeth Hoggan, M.D. (Zurich), M.K.Q.C.P. Ireland. (Plates I. and II.).

ALTHOUGH nearly two hundred years have elapsed since Nuck first observed the lymphatics on the peritoneal surface of the pregnant uterus of some of the lower animals, and the same vessels were afterwards studied by Méry, Mascagni, Cruickshank, Winslow, and other later anatomists upon the pregnant or puerperal uterus of woman, yet the whole history of the intimate or microscopical investigation into the lymphatics of the normal uterus might be comprised within the last twenty years. During that short period no other organ has perhaps been made the subject of so many special researches with regard to its lymphatics; and yet the most important part of these are not only unknown, and their existence denied, but even as regards the remainder the greatest ignorance or misconception exists. Nevertheless, perhaps no organ is more exposed to injury and denudation of its internal surface and, consequently, to the dangers following morbid absorption from that denuded surface than the uterus. Nowhere, therefore, is it more important that the relation which the lymphatics bear to that surface should be intimately and completely known. The disasters so often following parturition, clearly shown to be due to morbid infection, and to which nearly one-half of the human race are exposed at some period or other of their lives, make our ignorance of the channels of absorption from the interior of the organ a scandal to obstetrics in particular, and to scientific medicine in general.

In our English text-books the compilers appear to have derived all their information upon the present subject from no more modern an authority than Mascagni. Even special writers seem, with one or two exceptions, to know only of the so-called subserous lymphatics, a division which we shall hereafter show to belong, both anatomically and physiologically, to the musculature. If we go back as far as the time of Cruickshank

we are informed by that observer (Anatomy of Absorbent Vessels, p. 143): "In the gravid uterus (i.e., human) the trunks of the absorbents are large as a crow-quill, and the vessels so numerous that when they only were injected with quicksilver one would have been tempted to suppose that the uterus consisted of absorbents only. In the unimpregnated uterus they are not so easily detected, but when the viscus has been injected by the arteries and veins, and has afterwards been macerated in water by putrefaction, air gets into the absorbent vessels and makes them perfectly distinct."

Coming down to our own day, we find that Kölliker mentions only these subserous lymphatics, with the remark that "the lymphatics which *probably* begin in the mucosa are numerous, and form coarse and fine networks under the peritoneal surface."

Chrobak, who writes the article on the Uterus in Stricker's well-known *Handbook*, in 1871, frankly confesses that "the lymphatics in the interior of the uterus are as good as unknown."

Sappey, a veteran practical investigator of the lymphatic system, states in his Anatomie Descriptive, in 1869, p. 761: "The lymphatic vessels of the vesical and uterine mucosa have not yet been injected;" and again, p. 826: "The lymphatics of the uterus arise from the musculature of the organ; probably some come out of the uterine mucosa, but on this last point observation has established nothing up to the present time." Later still, however, in the third edition of his Anatomie Descriptive, published in 1876, p. 801, Sappey, speaking of the smooth mucous surfaces which are destitute of lymphatics, says: "With the foregoing mucous surfaces we may include the mucosa of the body of the uterus, and that of the Fallopian tubes, upon which no one has ever been able to discover any trace of lymphatics. But in studying the vesical and urethral mucosa, by the light of the unsuccessful character of all the investigations that have hitherto been made at different parts of their course, we find them differing from those of the uterus and tubes in the conclusions to be drawn from this want of success. We must, in fact, consider that the latter are not so easily adapted for this kind of investigation as the mucosa of the urinary

apparatus, that they have been very much less explored than these, and that the lymphatics arise in great numbers from the body of the uterus. Now, there is nothing to prove that they do not come, in part at least, from the sides of its cavity; that is to say, from the mucosa which lines it. Far from denying their existence in the thickness of that mucosa, I believe, on the contrary, that it is very probable. Thus, while the latest scientific researches appear to promise nothing, on the other hand they permit us to hope for better results."

In 1867 an article appeared on the structure of the uterus by Hjalmar Lindgren, which deserves especial notice, for several reasons. It is written in Swedish, and published in the Medicinskt Archiv of the Carolinska Institute of Stockholm, and although apparently well known to the Germans, not a single copy seems to exist in London, where all the principal and scientific libraries were ransacked for it in vain. It was only by the kindness and careful searching of our friend, the late Professor Georgii, at Stockholm, that we were able to procure a copy of the article.1 To the whole history and question of the lymphatics Lindgren devotes scarcely two pages, but he gives drawings of lymphatics, most of which are apparently incorrect, one of which, however, bears the stamp of truth, and deserves greater consideration than Lindgren has bestowed upon it. This is to be found in the centre portion of fig. 1, Plate IV., which represents what are virtually only blue casts of small portions of the lymphatics of the mucosa of the neck of the uterus; but as neither cells, vessels, glands, nor other tissues are represented, one is left to guess the relationship these lymphatics bore to the tissues in which they are supposed to lie. And yet we believe that little portion partly to bear out Lindgren's claim that they are portions of the lymphatics of the mucosa of the neck, as stated in his modest conclusion, p. 36: "On the lining mucous membrane the lymphatics extend themselves principally upon the mucous membrane of the neck of the womb. I have not succeeded in making a true injection of the lymphatics of the body of the womb." Unfortunately for Lindgren's claim, he gives in fig. 2 of the same plate a much enlarged drawing of two

¹ This copy has now been deposited by us in the library of the Royal College of Surgeons of England.

of these injected lymphatics, with their relation to the branched connective tissue cells of the locality, and shows in this drawing the blue injection passing from the cavities of the supposed lymphatics along the cavities in which the branched cells of the connective tissue are supposed to lie, as bearing out the theory that the origins of these lymphatics are in these cavities. There is no doubt that this drawing is copied correctly from the original, but it shows also in the clearest manner possible that the whole injection there is a mistake—an artificial production which can easily be repeated and recognised by a method

already explained by us in this Journal.

In short, it is evident that at one part Lindgren has hit a lymphatic, but he has so far missed his good fortune as afterwards to offer an artificial production as his typical example, under high power, of a lymphatic in its relations to the branched cells of the part, while of its relations to other tissues, or even its precise locality, he says nothing. It is evidently such considerations which cause Leopold, in his special article written five years afterwards, to reject entirely all Lindgren's conclusions and figures, although Frey, in his Histology, 1870 edition, accepts Lindgren's conclusions as far as regards the neck of the uterus, adding (p. 540): "While for the lymphatics of the mucosa of the body of the uterus further investigations are necessary." These further investigations were shortly afterwards undertaken by Leopold, who also (apparently for the first time) investigated the course of the lymphatics of the musculature of the organ. His article,1 as the last and most complete one on the general lymphatic system in the normal uterus, will be specially and constantly referred to by us; but as we disagree with by far the greater part of his views, we shall merely quote for the present his conclusions on the lymphatics of the mucosa, which are remarkable as coming after those of Lindgren, and with the results of that investigator before him. At p. 31 he gives the following conclusion strongly emphasized :- "The results of my investigations are as follow: IN THE MUCOSA OF THE UTERUS OF THE AFORE-MENTIONED ANIMALS (i.e., sheep, swine, rabbits, &c.) AND OF WOMEN, THE LYMPHATICS ARE

¹ "Die Lymphgefässe des normalen, nicht schwangeren Uterus," im Archiv fur Gynækologie, B. 6, für 1874, p. 1.

NOT, AS IN THE SUBSEROSA AND MUSCULARIS, TRUE ROUND VESSELS, BUT IN THE MUCOSA THERE IS A COLOSSAL SYSTEM OF CAVITIES OR HOLLOW SPACES (LYMPH-SPACES), WHICH EXTEND FROM THE EPITHELIAL LINING OF THE UTERUS TO THE LYMPHATICS OF THE MUSCULARIS, THE FRAME-WORK OF THE MUCOSA BEING FORMED BY BLOOD-VESSELS, GLANDS, AND CONNECTIVE TISSUE ELEMENTS. Or, in other words, the uterine mucosa is to be considered as a spreadout lymph gland, permeated by glands and blood-vessels—a superficial covering of lymphatic gland tissue, which possesses consequently no special lymphatic vessels, but consists of hollow cavities (lymphsinuses) lined by an endothelium." We shall afterwards explain but not repeat the above remarkable conclusion.

About and before this time appeared two other articles, which we mention only to show that we have not forgotten them. One of them is a work in Russian, by Fridolin, which we have failed to obtain, as it does not seem to exist in any scientific library in London, all of which have been searched for it. We are therefore forced to rely on a reviewer's (Schwalbe's) abstract of it, which states that "Fridolin has not specially followed the lymphatics into the mucosa; nevertheless, he has made this much certain, that the lymphatics which come upon the surface (i.e., peritoneal) from the deeper structures, have their special origin in the mucosa." Well may Leopold ask with amazement how so certain a conclusion could be found if he had never followed the lymphatics into the mucosa.

The second work we referred to is by Dr Lucas Championnière.² These writings have obtained much prominence, both in France and in one of the ablest English text-books on Obstetric Anatomy, but for what reason it is difficult to say. In his earlier writings the author specially gives his attention to Lymphangitis, and grafts upon this some speculative opinions about the lymphatics. Thus he states, at p. 12: "All the lymphatics begin equally in the muscular tissue and the mucous surface. Although here direct demonstration is imperfect, we have a right to expect, from the development of these vessels parallel to

^{1 &}quot;On the Lymphatics of the Pregnant Uterus," Journal of Military Surgery, St Petersburgh, 115 Division, part ii. p. 105.

² Lymphatiques Utérines et Lymphangite Utérine, Paris, 1870; Les Lymphatiques Utérines et leur rôle, Paris, 1875.

those of the placenta, their presence and their abundance in the mucosa."

The easily-written sentences which we have quoted from the two last-named authors are samples of the guesses by which non-investigating writers continually seek to discount the future ascertained facts of investigators. From the text and drawings of Dr Championnière's work it appears that his field of investigation was the superficial or subperitoneal and pus-filled lymphatics of half-contracted uteri of fatal parturitions. Some of these he endeavoured, but failed, to fill completely with quick-silver, and these partial puro-mercurial distended localities furnished him with the above information.

In his later brochure, written after the publication of Leopold's article, Dr Championnière takes credit for certain of his predictions, which Leopold had verified, and continues to form elaborate deductions from the presence of stomata and similar mythical structures.

Finally, we have to direct attention to the last special research on our present subject, an article by Dr Vladislas Mierzejewski on the "Subserous Lymphatics of the Uterus." This little research has been apparently conducted principally on the normal uterus of the sheep, and is illustrated by a plate, which appears to be perfectly correct and natural. The writer specially draws attention (p. 216) "to the extreme richness of the subserous portion of the uterus in lymphatic vessels." This, although partially true of the sheep, would give a very incorrect idea in relation to comparative anatomy, for in the mare not one lymphatic is to be seen in that locality, and in most animals the supply is extremely irregular, plentiful at one place, and perhaps altogether absent from the rest of the subserous surface. To this, however, we shall afterwards recur, remarking merely in the meantime that Mierzejewski's drawings are more acceptable to us than his conclusions, insomuch that we feel inclined to appeal to the former to disprove the latter.

Of the foregoing historical sketch we have now to remark that all the conclusions were obtained by injecting, or attempting to inject, the lymphatics with mercurial or coloured injection masses. Leopold, in one case, gives a drawing from an injection

¹ Journal de l'Anatomie, 1879, p. 201.

of silver solution; and both he and Mierzejewski show lymphatic endothelium treated by silver. None, however, show distinct lymphatic vessels obtained by imbibition of silver solution; and in certain cases the latter repudiates the process. We, however, have obtained nineteen-twentieths of our results by imbibition with salts of silver. Specimens thus prepared gave fairly satisfactory results, as those who have seen our preparations and the photographs taken directly from those preparations under the microscope, when exhibited at the Obstetrical Society on the 12th of January 1881, will be able to testify.

According to our hitherto almost invariable custom, we took the opportunity of there submitting the drawings which illustrate this research, for comparison with the preparations from which they had been taken, along with a very short account of the progress already made. At that time our studies were so far incomplete that we had not had an opportunity of applying our methods to the still living tissues of the human uterus. We had indeed been able to verify by modified injection the similarity existing between the lymphatics of the mucosa of the human uterus with those of the uteri of some of the lower animals, and more especially with that of the mare; but we had not been able to obtain a human uterus so shortly after death that we could make a superficial preparation of the mucosa by the method of silver imbibition, which would show the exact relations of the lymphatics with the blood-vessels, glands, and general cell-elements of the locality. It was for this reason that we only gave a short résumé of the progress we had made, reserving ourselves for a future occasion, when we should be able to include the results of our methods on the human uterus in our more complete account. In the meantime, many of our obstetrical brethren promised to procure for us, if occasion offered, a fresh human uterus; but as more than six months have elapsed since then without any such occasion offering itself, we deem it advisable to present our interim account, even with the incompleteness referred to, accompanied by the present explanation of the cause of it.

Hitherto it has been the practice in treating of the lymphatics of the uterus to separate these, for the sake of convenience, hypothetically into three divisions, corresponding to the anatomical structure of the uterus. Thus we have had those, 1st, of the subserosa; 2d, of the muscularis; 3d, of the mucosa. We have already intimated that the first belong, both anatomically and physiologically, to the lymphatics of the outer surface of the longitudinal layer of muscle, and not to the subserous tissue. Consequently we have to divide these lymphatics into only two divisions: 1st, those of the muscularis; 2d, those of the mucosa; leaving altogether out of consideration those of the subserosa as a separate division. Before directing special attention to either, it may be advisable that we should first give a description of the technique employed by us in the preparation of the various tissues of the organ in the different classes of the Mammalia to which we have given our attention.

We have stated already that to our knowledge no investigation into the lymphatics of the uterus had been made as yet by silver imbibition. It was consequently our first object, in endeavouring to utilise that method, to devise a suitable technique for our purpose; and, after many trials, we arrived at a very simple one, which can be explained in few words. As in the great majority of the Mammalia, the uterus is formed of very distinct layers of different tissues, it was evident that the arrangement of the lymphatics would almost certainly be in planes parallel to the layers or surfaces; and we considered that they ought to be specially investigated as such, a course which had not hitherto been employed, only transverse sections having been studied, in addition to the appearances given by the injections on the outer and inner surfaces of the organ. Stated generally, our plan was as follows:-In the case of all animals, whether of the size of a mare or of a mouse, the uterus having been extracted was laid open alternately, either along its attached or free border, and the tissue distended as a membranous sheet. When the uterine wall was thin enough to be transparent, it was at once mounted on our histological rings, and the surface of the mucosa denuded of its epithelium and mucus by shaving it with a sharp scalpel to a greater or less depth, according to the animal class which it belonged to. This having been done, a one per cent. solution of nitrate of silver was quickly poured upon, and as quickly poured off, one or both sides of the tissue, as considered advisable. After a few minutes' exposure to a dull

light this was carefully washed, and a one per cent. solution of chloride of gold allowed to remain in contact with the washed surface or surfaces for a couple of minutes. Then the membrane was washed and exposed to light until the desired reaction had taken place. This would be verified by continual examination under the microscope of the tambourine membrane thus formed. If successful, it could be clarified in the usual way with alcohol and oil of cloves, the disc excised, and mounted as a permanent preparation.

In addition, however, to the foregoing general directions, almost every class or size of animal requires special precautions or manipulations, for there are the widest possible differences in the arrangement of the tissues in the different classes of animals, and some of these must be mentioned seriatim. Let us take for example the uterus of a mare or ass, with a wall too thick to be transparent. In such a case the uterus, having been laid open, is tightly stretched across a wooden board by nails inserted at the edges of the sheet. With a very sharp-pointed scalpel the mucosa can be easily dissected off the musculature, some little care being taken not to cause undue distension or injury to it while dissecting it off. If this is skilfully done it will be found unnecessary to cut the surface, but one may simply snip across with the point the vessels which here and there pass from the musculature to the mucosa, and attach the two together. When a sufficiently large sheet of the mucosa has been dissected off (being grasped by the fingers merely at the edges without touching the surface of the centre of the sheet) it is gently laid upon the lower of the pair of histological rings (which may be 2 inches in diameter), and the upper ring is gently applied and forced upon the lower, taking care not to tear the delicate membrane, the epithelial surface of which must be uppermost, which is thus stretched like the head of a tambourine upon it. The mounted portion may now be severed from the rest of the sheet.

It is to be particularly observed, in the present case of the chevaline race, to scrape the epithelial surface of the mucosa with the utmost care and lightness, only apparently sufficiently to get rid of the mucus lying upon the surface, for the lymphatic vessels lie and ramify so closely beneath the lining epithelium that the cells of that one layer can scarcely be removed suffi-

ciently to allow the silver solution to penetrate more deeply, without injuring at the same time the crenated cells forming the endothelial wall of the more superficial lymphatics. The shape and arrangement of the glands, lymphatics, blood-vessels, &c., of the mare are widely different from those of most other animals, and approach nearer to those of the human uterus than those of any Mammalian class lower than the monkey. For that reason we shall give more prominence to them in the following pages.

When the epithelium and mucus of the outer surface has thus been lightly and carefully removed, the silver and gold solutions are to be equally applied to both surfaces of the tambourine membrane, and thus a complete and beautiful demonstration of the lymphatics, as they appear differentially on the two surfaces, may very readily be obtained. Of these drawings are given in figs. 1 and 2, both being drawn under the same low power of the microscope. Without going at present into a minute description of the character and relations of these lymphatics, we may add that while the same methods of preparation are applied to the uteri of cows, sheep, and goats, the scraping or shaving of the surface of the mucosa must be very deep and effectual in them before we can arrive at the more superficial lymphatics of the mucosa; in other words, the most opposite treatment, as far as removal of the surface is concerned, must be applied respectively to the mucosa of such animals as the goat and the mare.

The mucosa having been carefully dissected off and disposed of as described, the remaining portion of the uterine wall may be unnailed and treated in the same way, when a separate arrangement or layer of lymphatics will be found lying on the mucosa side of the musculature, and the subserous surface may be equally prepared in portions of the same uterine wall, but in the mare no lymphatics will be demonstrated within the subserosa. In other cases it will be found possible and advisable to dissect the inner circular layer off the outer longitudinal layer of muscle, and to treat the respective surfaces with silver, &c., which will complete the demonstration of the whole of the lymphatics of the organ.

When the uteri of smaller mammals are to be examined, other precautions are necessary, more especially as the musculature is apt to contract to such an extent on exposure to the air that, without special manipulation, it is impossible to distend the uterine wall on the histological rings. In the case of the mouse, whose unimpregnated uterus is so delicate and small that it cannot well be placed on rings at all, it will generally be found advisable to distend the organ with air by means of an injecting-nozzle or canula fastened into the vagina. When thus distended and ligatured at the neck and Fallopian tubes, the organ may be treated externally with the solutions of silver and gold, and clarified with glycerine before being opened into. This, however, will at most only show the arrangements of the outer portion of the organ. For the inner surface it had better be laid upon a thin dry sheet of cork, and the uterine tube having been laid open by a pair of fine-pointed forceps is spread out carefully upon the cork, to which the peritoneal surface adheres sufficiently to allow the mucous surface to be denuded, treated with the solution, and fixed and clarified in glycerine. For the pregnant uterus of the mouse at term, and for the unimpregnated uteri of rabbits, guinea pigs, &c., other precautions are necessary; and the following plan is of very general and satisfactory application. In a slab of cork (a piece of an ordinary cork sole is what we always use) circular holes are cut that admit of the passage of the respective sized histological rings through them. Choosing a ring of a suitable size, the portion of pregnant uterus containing one fœtus is laid across the corresponding sized orifice in the cork slab, and fixed at each end by small pins. With fine pointed scissors a small incision is made into the distended bag, at each extremity, which is then pinned out on either side of the originally fixed pins, and in this way, by cutting and pinning a small portion alternately, the whole uterine wall may be stretched across the hole in the cork slab. The lower ring may now be applied from below the slab upon the stretched out tissue, the upper ring fixed upon it, the pins taken out, and the whole tambourine removed by pushing it up through the hole in the cork, when it can be treated as before described. This use of the cork slab is very convenient, as it dispenses with the help of an assistant, which is often necessary to keep a contractile membrane distended upon the lower ring while the upper ring is being affixed to it. With the application of the various modified manipulations we have enumerated, the various tissues

of the organ in question may be prepared in almost all classes of animals.

Sometimes, instead of the circular histological rings we have so often referred to, we use narrow oblong arrangements of the same nature, with corresponding oblong holes in the slab of cork. These are particularly suitable for the narrow elongated uteri of rats, rabbits, &c. We have recommended that the organ should be sometimes opened out along its attached border, sometimes along the free border. This is advisable from the fact that there is often a great difference between the arrangements of the glands, lymphatics, &c., at these opposite points on the tube, due apparently to the fact that the placenta in some of the lower animals without cotyledons is attached as a rule against the attached border only.

In order to understand the comparative general arrangement of the lymphatics of the organ, we must begin our study with the simplest forms in the smallest mammals, and pass gradually to the more complex forms in the larger mammals, and to the more minute arrangements in the special tissues and layers. Beginning, therefore, in the mouse, and passing backwards against the lymphatic stream, we find one or two large efferent lymphatic trunks accompanying the main artery and vein within the broad ligament, lying nearly parallel to the respective horn of the uterus, or approaching gradually nearer to it at its extremity. From this main lymphatic branches pass off nearly at right angles, generally accompanying corresponding branches of the artery or vein passing directly to the uterus. As soon as these lymphatics reach the uterine tube, they (unlike their behaviour on the intestinal tube) at once pierce the outer longitudinal layer of muscle, and divide into two or three main branches, which pass respectively on either side of the tube, and after running parallel to the fibres of the inner or circular muscular coat, but at right angles to the fibres of the outer layer, they finally anastomose at the unattached border of the uterine tube. While coursing circularly round the tube, between the muscular layers, many branches are given off nearly at right angles to the main vessels which ramify between the layers. Other branches pierce the longitudinal outer layer, and after a short course on the subserous aspect of that layer, again pass down through it to anastomose with branches in the intermuscular layer, as in fig. 9. These are the branches which have hitherto been erroneously described as the lymphatics of the subserosa, with which structure, however, they have no absolute anatomical or physiological connection. The number of branches given off in this direction in different localities varies extremely. Fig. 9 shows the most extensive group we have yet met; on the other parts of the subserous surface of the same uterus scarcely a single branch was to be recognised; and in many other uteri we failed at times to find any lymphatics on the subserous aspect of the muscle. As shown in that figure, it is perfectly evident that they are only the lymphatic twigs ramifying between and around the various muscle bundles in the longitudinal layer, but to this question we shall recur later on.

While in the mouse a certain number of lymphatic twigs pierce and ramify on the outer muscular layer, they do not do so to the same extent in the circular inner layer. In fact, in this animal (and the arrangement seems similar throughout the Rodentia) the lymphatics seldom show any ramifications on the mucosa surface of the inner muscular layer, the general arrangement being that here and there villous-like processes or culsde-sac pierce the circular layer, through sphincter-like openings, which remain gaping under the ordinary circumstances of preparation; and this seems to be the only relation of the lymphatics to the mucosa, in those little animals. It will, however, we hope, be borne in mind that, although we have specially examined great numbers of such small uteri to obtain evidence on this point, the great damage done by removing the mucosa on such minute and delicate organs, makes the chances of success in tracing lymphatic ramifications infinitely rarer and less complete than in the uteri of larger animals.

Taking, therefore, the smaller mammals as a whole, the rule is that almost the whole lymphatic system of the uterus is comprised in one layer, lying between the two layers of muscle; that ramifying twigs are given off, more or less irregularly, to ramify on the peritoneal surface of the outer muscular layer; that very few branches ever pierce the inner circular layer; and that these never ramify in the mucosa as in the larger mammals.

The changes induced by pregnancy in the lymphatics of the

uterus of these little animals, are exceedingly simple. On the mucosa side of the circular muscular layer, the changes are almost nil. There is no additional development of lymphatics, and the villous-like processes, piercing the muscular layer, are not appreciably enlarged. Of the outer or subserous surface almost the same may be said. There is no further development of lymphatics, and the existing twigs are scarcely doubled in size, although the whole of the subserous surface has become at least twelve times greater. As it happens, and as shown in fig. 9, the lymphatics appearing on the subserous aspect of the outer muscular layer are of the same general calibre, and this is true equally of the non-pregnant and of the pregnant condition. Consequently, although it is impossible to show the same lymphatic as it appears in the pregnant and non-pregnant states respectively, it gives a very fair conception of either if we draw a lymphatic belonging to this layer from different animals of the same class in the pregnant and non-pregnant conditions, as has been done in figs. 10 and 11, from the mouse. Both have been drawn under the same magnifying power. Fig. 10, from the normal uterus, is shown under a low power in fig. 9; while fig. 11 is from a uterus at term, where all the other twigs on the same surface were of similar calibre, although separated from each other by greater distances, corresponding to the increase which pregnancy had caused in the whole surface of the organ.

The difference caused by pregnancy is, in the superficial lymphatics, seen to be very slight indeed, and in no way corresponding with the general increase of the surface. Very great changes, however, occur in the lymphatics lying between the two muscular layers. The main trunks, lying alongside of the arteries, increase to eight or ten times their former calibre, chiefly by an addition of the crenated endothelial cells, and very slightly by increase in the size of these cells themselves, which alone form the lymphatic walls. These lymphatics, of course, lie parallel to the circular fibres, but the branches connecting them have now developed into great valveless sinuses, lying parallel to the fibres of the longitudinal layer of muscles, and to each other; lying specially between the more or less distinct bundles which pregnancy, by separating them, makes very evident, in the longitudinal layer, as well as in the circular layer.

These longitudinal sinuses or ditches are the true collecting lymphatics of the organ, and the increase they have undergone, both in calibre and length, is perhaps the best marked change caused by pregnancy in any part of the lymphatic system of the organ. These sinuses are similar in position and function to the parallel drains dug along the slopes of a tilled field, joining, at right angles, the main drain which lies at the lowest side of the field, that main drain being represented in the uterus by the huge valved efferent lymphatics which lie one on each side of the main arterial and venous trunks which encircle the organ, between the muscular layers.

Notwithstanding the great increase in the size of these lymphatics, there is no addition of any strengthening elements to their walls. Both in the pregnant and non-pregnant states, these walls consist only of the one layer of crenated endothelium, without any muscle fibres whatsoever. In the pregnant mouse, the outer muscular layer is so thin that these collecting and efferent lymphatics can often be made evident from the outer side of the longitudinal layer, if the serous endothelium have been previously removed in order to permit the silver solution to penetrate through the layer and make the lymphatics evident. When we reach an animal the size of the pregnant guinea pig, this is no longer possible, but here we observe great lozengeshaped gaps between the bundles of muscle forming the outer longitudinal layer. In many cases, the whole of the floor of such gaps appears to be filled by a lymphatic vessel large enough to occupy the whole field of the microscope under a power of fifty diameters. In fact, the gap seems paved with crenated lymphatic endothelium, which is really the wall of an intermuscular lymphatic, made evident in consequence of the separation of the special muscular bundles in the longitudinal layer caused by the great distension undergone during the progress of pregnancy.

It may give us an idea of the physiological importance, as a whole, of the uterine lymphatics, to compare them with the lymphatics of similar hollow organs in the same animal, as, for example, the ileum, which in general appearance and anatomical structure (barring the villi) much resembles the uterine cornua. Tracing, in the case of the ileum, the efferent lymphatics of the mesentary backwards, we find that these, on reaching the intes-

tine, divide into two or more large branches, which, passing up equally on either side of the intestine, but lying as great streams in the subserosa, there, after spreading like a tree, divide into numerous branches which pierce both layers of muscle, to join the colossal system of comparatively less valvular lymphatic vessels lying in the mucosa. Between the two layers of muscle, we have no lymphatic arrangement comparable to that in the uterus, for we find there only anastomosing vessels between the perforating branches. It is, however, the comparatively speaking regularly arranged plexus of colossal lymphatics forming small meshes, which lies in the mucosa, having cul-de-sac prolongations extending into the villi on the one surface, and joined by the efferent branches on the other, which forms the chief feature of the intestinal lymphatics, and make it clear that the adaptation of the lymphatics in that organ is directed towards one surface, from which absorption of the nutrient material of the chyme takes place.

As we have no such arrangement in the muscular tube of the uterus, we feel bound to consider that there the lymphatics are only adapted to the periphery of a bag, having, it is true, minute orifices, above and below, more or less closed by the nature of the organ. In the pregnant uterus, each fœtus indeed seems to form its own bag, like spherical sausages in a string, without distinct pervious communication between them. In short, in the intestinal tube, the lymphatics are directed to the most minute points of the internal surface; in the uterine tube, they are not directed to points on either surface, but adapted generally to its periphery, regarded as that of a tube or bag. As we ascend the scale in size of animals, we find considerable modifications in arrangement and by the formation of additional layers of lymphatics, but nevertheless the same physiological plan that we have just described in the case of the mouse, is traceable throughout the series of mammals.

In the uteri of middle-sized animals, such as sheep and swine, the intermuscular layer still remains the principal one, and the branches, passing through and ramifying upon the outer muscular layer, become much more numerous and more complex in their arrangements, and more evidently the special lymphatics of the muscle and not the lymphatics VOL, XVI.

of the subserosa. That intermuscular layer, now, however, sends great offshoots through the inner circular layer of muscle, and these offshoots not only pass round the mucosa surface of the inner circular layer of muscle, in streams parallel to its fibres, but give off, in turn, great branches, which pass on to the deeper or muscular surface of the mucosa. These again give off loops extending as convex bows towards the epithelial surface or cavity of the uterus. In the pig, these branches of the submucosa run comparatively straight, and still parallel to the circular muscle fibre of the inner layer, but in the sheep, goat, mare, &c., we have a complete system of continually anastomosing vessels, forming junctions with each other at almost every valvular dilatation, as seen at figs. 1 and 8, which show the plexus of lymphatics as a layer on the plane of the deep surface of the mucosa.

Here and there the branches seem to stop short with a greatly dilated circular end. This, however, merely marks the point where the lymphatic passes into the substance of the mucosa, going towards its epithelial or free surface, the increased circular enlargement being caused by the penetrating link (if we may so speak of the short intervalvular portions of lymphatic) passing off, at right angles to the general plane of the deep surface plexus; and being seen flattened or compressed in the direction of its axis, it thus presents the appearance seen at the extremities of the vessels in figs. 1 and 8. The forms taken by the ultimate superficial loops of the plexus in the mucosa is particularly well shown in figs. 6 and 7, from the sheep. These loops lie with their convexity towards the free epithelial surface amongst the coils of uterine glands, to the greater part of which they lie superficial, as seen in fig. 6. In the centre of the arc, however, the lymphatic dilates into a wide sinus where the vessel lies nearest to the surface. In other words, we have a number of dilated lymphatics forming sinuses that are connected with each other by comparatively narrow or slender lymphatics, which also establish anastomoses with the deeper and larger lymphatics of the mucosa.

In none of the middle-sized animals we have been considering does the lymphatic system obtain the complete development, as a surface structure, that it afterwards does in the mare, for, as we have already mentioned in treating of methods of preparation we must penetrate pretty far beneath the epithelial surface of the mucosa in these animals before we reach the lymphatics, removing, in most cases, the whole of the superficial regular arborisations of blood-vessels and capillaries that characterise the free surface of the uteri of the bovine and porcine races, and which are absent in the chevaline race, this being due, apparently, in great part, to the great difference in the anatomical structure and arrangement of the uterine glands in these animals, respectively.

In the mare we have immense lymphatics covering almost the whole of the mucosa surface of the internal muscular layer, lying closely packed and parallel to each other. The valvular dilatations are so close and enormous that each lymphatic looks like a string of huge eggs. On the deep surface of the mucosa we have cactus-like ramifications of the lymphatics, as shown in fig. 1, which are similar to those seen in the goat, in fig. 8. These, after innumerable subdivisions and ramifications in the substance of the mucosa, finally appear as terminal vessels, greatly decreased in size, that arrive immediately under the epithelium of the free surface of the mucosa or cavity of the uterus. The great difference in size of the lymphatic vessels as they appear on the respective surfaces of the mucosa is well seen in figs. 1 and 2, drawn under the same power from opposite sides of the same preparation. The terminal superficial twigs of the lymphatics reach the surface either as dilated cul-de-sac endings, like that seen in fig. 3, or as the ramifying sinus shown in fig. 4, descriptive words which are almost identical with those used by Lindgren to describe the lymphatics of the neck of the uterus, and corresponding also tolerably well with his drawings.

All we have described bears not the slightest relation to Leopold's views, to which we may now direct attention under the special heading of

The Lymphatics of the Uterine Mucosa.—Leopold's views on this question are specially interesting from the fact that he is the latest investigator who has put the results of his own practical investigations on record, investigations which he conducted under the great advantage of having Lindgren's results, by the same process of preparation, before him to guide or

control his opinions while seeking to verify or disprove the facts put on record by Lindgren. The conclusion he arrived at as to these is definitely stated at page 30, as follows:—"Lindgren has only demonstrated the lymphatics in the cervix uteri, and describes them as loops from which cul-de-sac offshoots with sinuous borders stretch towards the epithelium. These results I cannot confirm, and I shall give my reasons for disagreeing with them further on, when I enter into the other very interesting results of Lindgren in connection with the mucosa."

These reasons subsequently given consist really in the different results Leopold has had from his injections into the mucosa; and as he minutely describes the various steps and appearances of that technique, his descriptions are well worthy of being reproduced, as they not only explain the errors he has fallen into, but fully demonstrate the untrustworthiness of the technique employed for investigating the lymphatics by means of injections. This technique is responsible for nine-tenths of our erroneous conceptions of the lymphatics, two-thirds of what is accepted at the present day, in connection with the lymphatic system, really consisting of the misconceptions due to that method.

Leopold used for his injections a watery solution of Berlin blue, either simple, or mixed with a little gelatine. This he injected, by means of a syringe and fine canula, into the substance of the mucosa, and he describes how, instead of filling distinct lymphatic vessels, as in the case of the muscularis and subserosa, the injection mass became regularly diffused throughout the mucosa, appearing as a circumscribed extravasation. Thus he states, at page 40:- "The mucosa swells up evenly over the point of injection, whether one has entered direct into the mucosa, or between both layers of muscle, and this constantly recurring appearance leads one to suppose that the blue mass has not flowed into separate distinct vessels, but has penetrated completely through the whole tissue of the mucosa. Thus, in the most carefully conducted or repeated injections, a real extravasation takes place, which, however, depends entirely upon the above-mentioned structure of the mucosa. The injection fluid forces its way from the muscularis into the first and nearest spaces formed by a colossal network which might be compared to the framework of a great labyrinthine cavernous

tumour. It forces its way on gradually, from cavity to cavity, till it reaches the surface epithelium, extending itself also laterally; and in this manner are seen in their transverse section injection images corresponding to each other in their chie features, and which only vary in certain points, according to the kind of fluid used."

From the foregoing appearances, Leopold has framed the conclusion in italics which we gave at page 54 of this paper and he explains further on that the mucosa in man and animals consists of a mass of funnel-shaped cavities, having their wide mouths immediately underneath the epithelial clad surface, and gradually tapering to a narrow orifice where they join the lymphatics of the muscularis, the funnel-shaped cavities being longer (or deeper) in man than in other animals. With the drawings of our preparations which accompany our paper, before us, it is almost needless to repeat that all Leopold's conclusions, like the results of the technique upon which they are founded, are nothing but one long series of errors. While in the comparatively firm tissue of the cervix one might not be surprised to learn that Lindgren had some successes together with his mistakes, it is difficult indeed to conceive any result from injection into the delicate, soft, and even plastic, embryonic tissue forming the matrix of the mucosa of the body of the uterus, other than that obtained by Leopold. Even although that mucosa is thoroughly permeated by the normal-valved and endothelium-formed, roundwalled lymphatics, as we show it to be, the injection of fluid would at once close all the lymphatics, and form a true extravasation in the tissue, serving very well to lead astray, but not to demonstrate the truth. That there are numerous cavities in the mucosa, we shall afterwards show to be the case; but these cavities have no relation with the ones described by Leopold, and although lined with epithelium, they have no connection whatever with the lymphatic system.

There is this peculiar distinction between Lindgren and Leopold, the only two investigators who profess to have specially investigated the lymphatics of the uterine mucosa, that whereas the latter gives no drawing of his funnel-shaped cavities, his description fully illustrates the grave errors into which he has fallen, while the description of the former probably

represents the exact truth, although his drawings (vide his fig. 2) show erroneous conceptions.

While our camera lucida drawings of the lymphatics of the mucosa might be safely left to give a correct idea of their condition in different animals, some little description may be necessary to account for their different relations to corresponding structures in these different animals. In the absence of the fresh human uterus, we have given our special attention to the uterus which (the monkey tribe apart) most resembles it in the structure of its mucosa, namely the uterus of the mare. In the various species the chief differences in the lymphatics of the uterine mucosa are due principally to the great variations in the shape and arrangement of the uterine glands. In the sheep, goat, and pig, these glands may be called compound, as a number of glands open into the one main orifice, and each gland is composed of an immense number of diverticula or cul-de-sac terminations, as shown in figs. 6 and 8. The main orifices referred to open at a considerable distance from each other into the cavity of the uterus, where they appear large enough to be detected sometimes by the naked eye.

In the mucosa of the mare we have a very different condition. The glands are merely single tubes, as in the human subject, and these are so numerous, and open so close to each other into the uterine cavity, that when a lymphatic lies immediately under the epithelium it is in a manner compressed between the glands, and its sides are impacted upon, and distorted in shape by the pressure of the individual glands upon the endothelium-formed walls, whether the lymphatic lies superficially in the plane of the surface, as in fig. 4, or reaches the surface as a villous process or cul-de-sac termination, as shown in fig. 3. At the attached border of the uterus, or, in other words, the side where the broad ligament joins each uterine tube, and where the placenta becomes subsequently attached, the gland tubes or openings are so closely packed that it is almost useless to seek between them for superficial twigs of the lymphatics; but at the opposite or unattached border they are not packed so closely, and consequently the superficial lymphatics are more easily and plentifully found in this locality. The cotyledonous areas in the sheep, cow, and goat, also interfere considerably with the arrangements of the lymphatics; and the great difference in the arrangement of the blood-vessels in the animals we have mentioned must cause corresponding modifications in the arrangement of the lymphatics. In those animals, owing to the great distance between the openings of the glands, comparatively large portions of the general surface of the uterine mucosa are left unbroken and undisturbed, so that the blood-vessels which pass as large trunks towards the surface, break up there into a regular meshed network of capillaries, similar to the capillary plexus upon the air-vesicles in the lung. In the mare, however, we have not this extensive and regular capillary plexus, on account of the broken up character of the surface of the mucosa, caused by the innumerable closely packed openings of the uterine glands, and the blood capillaries ramify in a thoroughly irregular manner amongst and between the glands and their openings.

Finally, in the horned ruminants there is a considerable amount of tissue intervening between the superficial capillary plexus we have described and the bulk or secreting portion of the glands; and although, as shown in fig. 6, from the sheep, the lymphatic loops lie superficial to the mass of the gland tubes yet even then they are some little distance from the surface epithelium. In the mare, however, we have no appreciable layer of tissue intervening between the epithelium and the lymphatics, the consequence being, as already stated, that it is almost impossible to remove the surface epithelium without at the same time injuring the endothelium-formed walls of the lymphatics, which lie immediately underneath the epithelium.

It will, of course, be understood that although in the mare the gland tubes by their pressure upon the wall of the empty lymphatic probably distort the natural appearance of the lymphatic, yet when the latter is full of lymph that distortion may not exist. In the most superficial portion of the lymphatics of the uterine mucosa of most other animals, we do not observe the irregular sinuous borders we see in the mare, as in them the glands are not, so to speak, so crowded upon the lymphatics as to produce any such effect. In the sheep, the irregularity in the shape of the lymphatics seems purely due to functional requirements. The more superficial portion of the loop becoming dilated, and these dilatations being joined together at a

deeper level by narrow portions of the lymphatic vessel, a peculiar appearance is given to the whole plexus when viewed from the cavity side of the mucosa. In the pig, again, we have a similar series of circular loops with the convexities turned towards the epithelial surface of the mucosa, but the arrangement of dilated and constricted portions does not show itself so well as in the horned ruminants. In general, these loops have a distinct thickness of tissue interposed between them and the epithelium, or the superficial capillary plexus. In rare cases, however, the curved loop may approach close enough to the capillary plexus to almost touch it, as seen in fig. 5, where, although the plexus has been removed immediately above the lymphatic loop, yet the points where the various vessels are breaking up into the capillary plexus are still shown in the preparation.

The character of the villous or cul-de-sac projection of the lymphatics, reaching up to the surface epithelium in the mucosa of the mare, is often made clearer by a lucky accident which very often happens when the mucosa of that animal is being prepared for examination. When the mucosa, having been dissected off the muscularis, is being mounted upon the histological rings, the smallest amount of undue distension serves to crack or rupture the sheet of epithelium lining the cavity surface of the mucosa, without tearing the elastic or embryonic tissue which forms the subjacent portion of the mucosa. Where a number of the villous processes referred to penetrate the mucosa in a line with each other, that line forms the weakest part of the surface, and just as riveted iron plates, when forcibly torn apart, give way first at the line of rivet-holes, so does the sheet of uterine mucosa give way in the line of the penetrating lymphatics, showing under the microscope like a deep gash upon the epithelium-formed surface. When the silver is applied after this very common accident, it makes the tissues forming the sides of the fissure very evident, and in this way the blindending lymphatic tubes are seen lying upon the side and continuous with the horizontal lymphatics at the bottom of the fissure, a view appearing all the clearer when seen by the binocular microscope.

The changes caused by pregnancy in the lymphatics of the mucosa in the larger animals seem to be very slight and unim-

portant when compared with the changes which take place in the size of the lymphatics lying between the two layers of muscle; in fact, like the other structures in the mucosa, they appear to be pretty much disordered and disarranged owing to the amount of attention given to the part where the placenta is attached. In the non-pregnant uterus the mucosa is comparatively thick, the glands are plump, and the small embryonic or branched cells appear like stars in a clear firmament or matrix of embryonic tissue; the lymphatics also look plump and regular. With the advent of pregnancy important changes occur. The whole of the surface layer of epithelium begins to proliferate, each cell breaking up into several new cells, in order to form the chorion as a sheet of embryonic tissue. The small branched cells become greatly increased in size and elongated into contractile cells that form an irregular felting of cell-fibres of the mucosa; the clear matrix between the cells disappears to a great extent; the blood-vessels increase in size and number; the uterine glands now appear shrivelled and drawn out into very irregular shapes and positions, while the lymphatics appear to be little increased in size or number, although from the great increase in the uterine surface, and from the fact that the lymphatics seem to have the same relative number and size, occupying the same extent of surface, we must conclude that there has been a very great increase in their size, as they became extended over the increasing surface, notwithstanding that in the same sized field of the microscope they appear individually to have increased very little in size. No doubt the lymphatics occupying the whole thickness of the mucosa of the non-pregnant uterus, have, by the thinning of that structure in pregnancy, become compressed and extended into a thin plane which seems to occupy the space between the thin mucosa and the muscularis. Indeed, the mucosa has become so very thin that in the pregnant sheep, from which figs. 13 and 15 were drawn, the silver solution when applied to the free surface penetrated right through to the inner surface of the circular muscular layer, making all the tissues in that thin sheet perfectly distinct as we have just described it.

From what we have said, it would appear that during pregnancy the uterine glands are quiescent, and the embryonic cells

formed into contractile cell-fibres. It seems equally probable that the lymphatics of the mucosa have very little function to perform during pregnancy, for the sheep having a cotyledonous placenta, the lymphatics examined by us lay between the cotyledons, and therefore within the area of the placental functions, although not upon the cotyledons themselves, where we failed to trace superficially the presence of lymphatics. In the pregnant uteri of rodents, being mono-placental animals, we examined at term the site of the placenta for lymphatics; but none were to be seen there, although at the very edge or ridge external to the placental border, a solitary twig, somewhat increased in size, might be observed at rare intervals. Between the muscular layers, however, opposite to the placental attachment, in mice, the intermuscular lymphatics had greatly increased in size, as formerly described. As far, therefore, as these little animals are concerned, parturition can cause little injury to the lymphatic system, but it must constitute a very serious and dangerous condition to those higher animals in whom separation of the placenta may readily injure and lay open those lymphatics lying between the placenta and the muscular wall of the organ.

There is another structure existing in the mucosa which merits attention, and although it is closely allied to many structures that have been described by others, it seems to be, as far as we have been able to discover, hitherto undescribed. It resembles bursal sacs or surfaces interposed between the mucosa and the muscularis of almost all the animals in which we have looked for it. It is not to be detected in transverse sections of the tissue, where it would only appear like the longitudinal section of a uterine gland. To see it properly one must separate the mucosa very carefully from the muscularis, using no cutting of the tissue further than snipping across the blood-vessels, &c., which pass across from the one layer to the other. When this has been done, and either layer or sheet is mounted on the rings, and the surface treated with silver which corresponds to the separation between muscularis and mucosa, it will be observed that large portions of these surfaces are covered with a sheet of epithelial cells. We have found this condition more prominent in the non-pregnant uterus of the pig than anywhere else, and

wherever this covering of epithelium is present it prevents the silver solution from passing through it to act on the tissue underneath. Where there are breakages in the surface or sheet of cells, the solution naturally penetrates for a considerable distance, and renders the matrix very dark in comparison with the white cell-covered portions. These cells are seen to be placed directly upon blood-vessel and lymphatic walls as well as upon the embryonic matrix which forms the bulk of the mucosa; consequently, where it covers these vessels, their endothelium can be no longer seen, although the breaks here and there in the sheet of cells enable one to mark the course and condition of these vascular walls. Similarly, even in a smaller mammal like the guinea pig, these bursa-like sacs appear, more especially during the earlier stages of pregnancy, as oval-shaped sacs or cavities lined by epithelium. The cells themselves resemble in appearance the cells lining the cavity of the uterus, except that they are a little smaller, as if younger. To show the comparative character and size of these cells we have drawn them at c, fig. 19, as well as the cells, b, lining the cavity of the uterus, and d, the cells lining the uterine glands, while e and a represent respectively the endothelium of the veins and lymphatics of the same locality, all drawn under the same magnifying power by the camera lucida.

These bursal cavities are certainly not funnel-shaped cavities in connection with the lymphatics, or rather forming the mucosa portion of the lymphatic system according to Leopold, for they are flat, collapsed, bursa-like sacs, and not funnel-shaped, extending across the mucosa. They have no connection whatever with the lymphatics, and the characters of the cells lining these cavities are the very opposite of the cells belonging to the lymphatic endothelium. At the same time it is very possible that these were the cavities injected by Leopold; in fact, he could scarcely avoid them, and if injected into they would certainly give the distinctly circumscribed borders that he has referred to. We have already shown abundantly that Leopold's conclusion that the lymphatics of the mucosa were not really the round vessels that one meets with everywhere else, is entirely erroneous, for the lymphatics in this structure are exactly like the lymphatics elsewhere in the body. In short,

we must come to the conclusion that Leopold had really injected these bursal cavities or sacs, and endowed them with the attributes of the lymphatics, when he failed to find the real lymphatics of the locality. At the same time, we have still to find a function for such sacs. It is possible that they really have the function of bursæ, to allow of the mucosa gliding upon the muscularis for some purpose or other, although the shape of the cells does not correspond with that of cells usually lining bursal sacs. We are, however, of opinion that there is still another reason for their presence, and that it is from these sacs that the new epithelium is derived with which to line the cavity of the involuted uterus after parturition. This opinion is merely advanced as an hypothesis, but it seems to us to be a very probable one under the circumstances.

The Lymphatics of the Uterine Muscularis forms the second of the two divisions under which we class the uterine lymphatics, and, as we stated at the commencement, we include under that head those lymphatics which have hitherto been described as the subserous lymphatics. Under that head is really comprised also all that was definitely known of the uterine lymphatics prior to the researches of Lindgren and Leopold. Lindgren, however, does not enter into the consideration or give any description of any others than the lymphatics of the mucosa of the neck, so that Leopold ought to be considered as the first, and indeed the only, investigator who has offered a systematic description of the lymphatics of the muscularis. As mentioned in our historical resumé, many writers speak of the superficial lymphatics on the peritoneal surface of the organ as coming out of the muscular substance, but their character or relationship there, like the question of their existence on the mucosa beyond, could only be hypothetically discussed in the complete absence of ascertained facts.

Following Leopold, we have, five years afterwards, another investigator, Dr Vladislas Mierzejewski, already referred to, who, under the title of "Investigations into the Subserous Layer of Lymphatics of the Uterus," really gives an excellent description of the lymphatics of the superficial or longitudinal muscular layer of the normal-sized organ in the sheep. Our first task

will therefore be to show that such a division as the subserous lymphatics is erroneous, and that the division ought to be absorbed into that of the muscularis.

Commencing with Mierzejewski as the latest investigator, we have first to observe that his drawings and descriptions are singularly opposed to his conclusions, even when the two latter are given in the same paragraph, which we quote verbatim, in order to allow our readers to judge for themselves. If, in addition, they have access to the article in question, one glance at the drawing he gives of the lymphatics, as seen in transverse section, ought to convince any one that we have there to deal with the lymphatics of the superficial muscular layer, and not with those of the subserous tissue only, for they form a special and regular plexus of enlacement of the muscular bundles constituting that layer. With respect to this, he states, p. 220: "In successful examples of subserous injections, it is seen that the subserous lymphatics having been filled, the injection mass passes into the lymphatics which are distributed to the muscular layer, and it is from these latter, and not from the subserous lymphatics, that the great lymphatic trunks arise which pass towards the broad ligaments. It is generally admitted that the uterine lymphatics have their origin in the mucous layer, and go from there towards the superficies of the organ, from which they pass downwards, as great trunks, into the broad ligaments." After this remark, with the correct description which precedes it, comes now his conclusion in the opposite direction: "It cannot be considered that the lymphatics of the subserous layer are in continuation (forment suite) with the lymphatics of the muscular layer. They appear rather to constitute a separate plexus which joins the lymphatics of the muscular layer at the level of that layer, and the lymph thus mixed descends towards the broad ligaments." It is difficult to understand this self-contradictory conclusion, which is entirely at variance with the previous description and the drawings given, and, we may add, equally at variance with the facts of the case, as we have ascertained them to exist in the same animals by the silver process, which coincide more or less with the drawings already referred to. In short, as drawn by Mierzejewski, the so-called subserous lymphatics are evidently only

the superficial portion of the lymphatic plexus which encircles and embraces the muscular bundles of the longitudinal muscular layer. It is much to be regretted that he only offers one complete mesh of the subserous lymphatics in his fig. 1. Such a drawing may show the size of the lymphatics, and proves that he actually saw them, but it gives a false idea of the general distribution, a point indeed always left vague by the injection method, which may either multiply the supposed lymphatics by extravasation, or fail to show any where many may exist. It is for this reason that we show the lymphatics on a comparatively large portion of the surface, but even then it is to be borne in mind that the portion has been specially selected as showing the largest number of lymphatics in the specimen, and that in the same specimen there are areas, equally large, where not a single lymphatic appears in the subserosa.

When, next, we turn to the long chapter which Leopold devotes to the lymphatics of the subserosa, we find that he too gives descriptions which lead us to suppose that he clearly understood the relationship between those of the subserosa and muscularis, but takes it for granted that they are to be described separately, although no reason for doing so is apparent. With respect to this he distinctly states: "From the periphery of the uterus the lymph passes through the muscular lymphatics in order to reach the trunks in the parametrium." Nowhere does Leopold seek to prove that the lymphatics of the subserosa are a plexus apart. While he recommends the injection method for investigating the lymphatics, he dwells strongly upon the tendency to cause extravasation that he has experienced-a caution not out of place, seeing that some of his best drawings are from extravasations, and unconnected with the lymphatics. All the drawings in his first plate are devoted to the subserous lymphatics; but as these figures are only of the natural, or even half the natural dimensions, it is difficult to trace the exactitude of the partial injection represented. We are of opinion, however, that these injections are incorrect as compared with the results we have obtained by the silver process, and if his fig. 7, the only drawing of the subserous lymphatics in transverse section which Leopold gives, is to be considered as a

portion of either of the uteri shown in the first plate, then there can be no doubt that these figures are incorrect, and that the greater number of the lymphatics of the subserosa and superficial muscular layer represented there are only extravasations. From numerous silver preparations made by us on the same animals, both in the normal and pregnant uterus, we feel inclined to hold that no such lymphatics exist as are shown in the upper portion of his fig. 7. On the other hand, his drawing of the subserous lymphatics of the uterus of the rabbit, as shown by injection of silver solution, seems to be quite correct; but the numerous short trunks, disappearing as they pass downwards through the muscular layer, show that we have in that plexus only the superficial portion of a plexus which exists equally dense between and below the bundles of muscles forming the superficial layer. In short, it is almost possible to prove from the researches of those who profess to describe the lymphatics of the subserosa as a system apart, that those lymphatics are not anatomically those of the subserosa, but of the superficial muscular layer.1

When we turn to Leopold's special references to the lymphatics of the muscularis, we find them distorted by the mistakes made by the injection method. He carefully distinguishes between the lymphatics of the regularly arranged double layer of muscles in the lower animals and the irregular musculature in man, and his fig. 8 is supposed to represent the lymphatics

1 After the plates and text of the present article had been arranged, and were on the point of being sent off for publication, one of us while in Paris, and through the kindness of Professor Ranvier, of the Collège de France, in placing the use of the laboratory of histology at our disposition while there, had an opportunity of applying our methods of preparation to the human uterus a few hours after death. In it, notwithstanding the unfavourable condition of the tissues caused by the intense heat of the season, we were able to investigate fully the condition and relations of the so-called subserous lymphatics, and to recognise the presence of those of the mucosa. These subserous lymphatics are to be found most plentiful where the peritoneal tissue is loosely attached to the neck of the uterus, but as we approach the upper part of the body of the organ where the peritoneal tissue becomes, so to speak, firmly incorporated with the uterine tissue, the lymphatics are not found at all superficially. Further down on the neck, where the loose peritoneal tissue may be easily dissected off the organ and suitably prepared, the lymphatics form an intricate network intertwining irregularly with the plexiform arrangement of long narrow bundles of smooth muscles, which pass in every direction across the surface of the organ, and give so special an appearance to the subserous tissue of the human uterus and broad ligaments.

of the musculature of a young woman. With regard to this drawing we desire to record our conviction that it does not show a single lymphatic, and that the beautiful plexus of supposed lymphatics shown there is the result of extravasation, and has no connection with the lymphatic system. For our part we show two drawings of the lymphatics of the musculature of the uterus of a woman, as seen in thin section, one section being through the anterior part of the wall at right angles to the uterine cavity, the other being perpendicular through the musculature of the neck, and parallel to the cavity. These preparations were obtained by a natural process that has often been utilised, and deserves more recognition and employment. It was obtained from a patient who died of cancer, which had appeared secondarily in the womb, and had there first shown itself in the glands of the mucosa, and afterwards infected the glands.

In an article published in the Archives de Physiologie for 1881, we have shown the course followed after infection of the lymphatics of the skin by cancer, and we have found that the same description applies equally well to the lymphatics of the uterus. According to that process we find that when the lymphatic vessels become infected in the immediate neighbourhood of the cancer, the effect becomes at once manifest in the nearest lymphatic gland, which bars further passage to the lymph-cells passing down the lymph stream, and these become aggregated within the lymphatics, filling them with a solid and tenacious plug of cells, which extends not merely between the gland and

These are the bundles which form the apparent fibres and ganglions which have been dissected out upon the gravid uterus of woman by Tiedemann, Robert Lee, and Snow Beck, and described by them to be the hypertrophied nerves of the uterus. These researches gave rise to much acrimonious dispute at the time between the latter two gentlemen, and obtained for the last named the gold medal and fellowship of the Royal Society. As the error committed by them seems never to have been explained, we venture to give this explanation, with the remark, however, that apart from the great error of describing such muscular structures as nerves, the beautiful dissections of Dr Beck, which he has often personally shown and explained to us, will always remain valuable as an artistic dissection of the subserous muscular arrangement of the human uterus when hypertrophied by pregnancy. The loops formed by the lymphatics which intertwine with these muscular bundles and with innumerable dilated blood-vessels, lie with their long axis transversely upon the organ, and only in the particular locality referred to. It is now too late to attempt to introduce drawings of these lymphatics into the present article, but these and others may subsequently be formed into a supplementary research for future publication.

the original seat of the cancer, but also beyond the latter structure, until the whole lymphatic system of the part is in a manner naturally injected with cells which rapidly become cancerous. In this condition they imbibe deeper staining than the surrounding tissues, so that when sections are made after preliminary injection of blood-vessels we have a complete and perfectly uninjured plan of the lymphatic system of the part. From such a plan figs. 17 and 18 have been drawn. Of course it is necessary to select a case where the uterus is unchanged in shape or dimensions, and where the disease has neither stopped short of, nor gone beyond, the mere filling of the lymphatics, and then nothing can be more satisfactory or correct than such preparations. In the drawing in question the lymphatics have been left blank, as being better than drawing the mere cast of cells within them.¹

The lesson taught by such preparations is that, in the musculature of the human uterus, the lymphatics, like the muscular bundles amid which they lie, are extremely irregular in course and distribution. They bear no special relation either to the blood-vessels or to the muscular bundles, and their size and shape vary very little in the whole musculature intervening between serosa and mucosa, except where, near the attachment of the broad ligaments, they join to form the great efferent trunks passing from the organ.

In fig. 8 of Leopold it is perfectly evident (even by comparison with his own fig. 7 of the lymphatics of the musculature of the sheep) that he has formed an interstitial injection of the part, so as to separate the different parallel muscle bundles

This complete injection or plugging of the lymphatics by even normal lymph-cells is in our opinion a by no means uncommon, although we believe hitherto unrecognised, general feature. Indeed, whenever either from tubercle, scrofula, or any infective process the lymphatic glands become swollen, that condition seems generally to be accompanied by more or less filling of the lymphatics leading to the swollen glands; in other words, where the lymphatic passage becomes barred at the glands, the wandering cells coming down the lymphstream gradually collect first in the gland, and afterwards upwards from it, until the whole of the lymphatics leading to the gland or glands become plugged with cells. A short time ago Professor Sappey showed us such specimens of cell-filled lymphatics in the human intestine, which he considered to be a normal condition, and connected with a theory he will shortly publish. To us they simply betokened a swollen condition of the mesenteric glands, in fact "tabes mesenterica."

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from each other, and to fill up the interstices with the injection mass of gelatine. In the preparation thus formed, where the muscle bundles are, as it were, embedded in a matrix of coloured gelatine, a section across the axis of the bundles shows them, as it were, separated from each other by lymphatic spaces, a condition naturally non-existent, incorrect, and misleading. In his fig. 7, the only other drawing of the musculature given by Leopold, it is equally plain that although the lower half of the drawing corresponding to the lymphatics of the circular layer is probably quite correct, the upper half, corresponding to the lymphatics of the longitudinal coat, is certainly not so, but is an excellent example of extravasation in the interstices of the muscular bundles, showing apparently vessels which are certainly not lymphatics. Indeed, we fail to recognise that figure as representing the lymphatic arrangements in the uterus of the sheep, as far as similarity with either our own preparations or the drawings of Mierzejewski goes. The appearances due to extravasation appear to have also caused Leopold to use descriptive terms which the general similarity throughout the lymphatics of the musculature scarcely calls for. Independently of the terms signifying lymph-vessels, collecting tubes, efferent channels, main trunks, &c., he introduces such terms as Lymphspalten (lymph-clefts), Lymphröhren (lymph-tubes), which in the way he applies them are evidently only forms of extravasation.

While in the smaller mammals the principal and largest lymphatics lie between the two muscular layers, and next to these in development are the branches passing off from them to the peritoneal surface, the branches passing towards the mucosa surface being almost nil, these conditions become very much altered as we pass to the larger mammals. In these, owing to the great development of lymphatics in the mucosa, the lymphatics on that surface of the musculature arrive at the greatest degree of development, while the branches passing towards the peritoneal surface remain either unchanged in their comparative amount or become even less. It is, moreover, in the main lymphatic trunks of the intermuscular layer, and those which in the larger mammals lie on the mucosa surface of the circular muscles that we see an obvious provision for the changes

which take place in pregnancy. The series of shapeless and compressed valvular dilatations, seen in fig. 14, from the pig, is evidently so designed that, when distended by pregnancy, regular intervals of uniform straight tubes or vessels shall intervene between the different valvular dilatations, as is indeed showing itself in fig. 15 from the same locality in the pregnant uterus of the sheep. In both these drawings the portion of lymphatic represented has nothing exceptional about it, but resembles in form and size numerous other lymphatic streams lying parallel to each other in their respective preparations. Of course there is an immense increase in length and calibre at the same time by the addition of endothelial cells interposed between the original endothelium forming their walls in the normal uterus; and in order to make this increase more evident we have drawn fig. 14 from the normal uterus of the pig, under the same magnifying power as fig. 15 from the pregnant uterus of the sheep (the fœtus being half-grown), and shown in fig. 16, so that figs. 15 and 16, from similarly sized animals, may be compared, to show the change in size which has taken place at only half the distension of full pregnancy.

In the case of the mare, we have already compared the lymphatics lying upon the mucosa surface of the musculature to strings of eggs lying parallel to each other, and so closely packed together as to form a kind of mosaic of great oval valvular sinuses covering completely the surface of the muscle. These valvular sinuses were relatively similar both in size and shape to each other, and thus presented a different appearance from the distorted and irregular valvular sinuses, seen in the case of the pig in fig. 14. The long axes of these oval valvular sinuses were parallel to the fibres of the circular muscles upon which they lay, but their peculiar oval shape, as well as the short and dilated condition of the valvular sinuses of the cactuslike arborisations of the lymphatics on the deep surface of the mucosa, as seen in figs. 1 and 8, are evidently well fitted to become elongated into shapely lymphatics without any addition to the number of their valves when the distension of pregnancy supervenes.

Although figs. 14 and 15 are drawn from opposite surfaces of the circular layer of muscle, they represent the same kind of lymphatics, which in these animals lie rather between and parallel to the bundles of muscle in the circular, than between the circular and longitudinal layers. At the top of fig. 14 is also seen the cut lymphatic, where the vessel became continuous with the long parallel channels which characterise the deep lymphatics of the mucosa of the pig. In the case of the mare, where a special layer of lymphatics, as formerly described, covers the whole inner or mucosa surface of the musculature, the branches pass upon the deep surface of the mucosa, at various points in the circumference of the uterine tube, in order to form the plexus seen in fig. 1; but there is nothing abnormal, in any case, in the manner in which the lymphatics of the musculature join those of the mucosa. We should not even have referred to this point, had it not been that Leopold, misled by the non-success of his injections of the lymphatics of the mucosa, brings up misconceptions about funnel-shaped cavities, whose small ends or orifices join at this point with the lymphatics of the muscularis. Thus he states, at page 48: "At the boundary of the muscularis the lymph-spaces (of the mucosa) enter for a short distance (in human uteri farther than in those of animals) into the funnel-shaped cavity between two muscle bundles, and there gradually become narrow vessels to join the intermuscular lymph-vessels and sinuses." As, except by a hypothetical opinion of the cause of the failure of the injection method, there is no foundation for stating that funnel-shaped lymph-cavities exist in the mucosa with their narrow portions joining the lymphvessels and sinuses in the muscularis, it is curious to be told that such hypothetical narrow ends pass deeper, in the case of the human uterus, into the musculature before joining the lymphatics of the musculature.

Leopold devotes fourteen closely printed pages to his description of the lymphatics of the musculature, but the whole being hypothetical, and founded in great part on injection extravasations into the tissue, we may be excused quoting it to show the wonderful exactness introduced by Leopold into his description of non-existent lymph-spaces. In his conclusion, he, however, states (p. 48) of the lymph-vessels and lymph-spaces in the musculature: "The walls of both are formed of the intermuscular connective tissue. The former are lined by a fine endo-

thelial lamella which possesses openings and holes here and there. The latter are lined with thick cell-plates."

In respect to these opinions, we may state that the walls of the lymphatics throughout the whole organ, like the lymphatic walls throughout all the organs in the body (this does not refer to the great efferent systemic lymphatics), are formed or lined by the same crenated-edged endothelium, and that, except in the increased number of these cells, pregnancy itself makes no difference or addition to these lymphatic walls, while as to the openings, holes, or stomata, to which Leopold gives such importance in his research, and over which Dr Lucas Championnière rejoices, as a fulfilment of his prophecy, there are none whatever, except where they have been made in the preparation by the preparer himself, or are simulated by small deposits of albuminate of silver. In the hundreds of specimens we have made and examined of the lymphatics of this organ (or of any other organ) in different mammals, we have never seen anything corresponding to a stoma or natural opening. We cannot even understand for a moment what function it would subserve which is not already exercised by the lymphatics; while, as far as any stomata exist in mammals connecting the peritoneal cavity with the lymphatics on the peritoneal surface of the musculature, the idea is as hypothetical and mythical here as when applied to other serous surfaces throughout the body.

We almost feel ashamed to have so often to recapitulate our disbelief, or rather our denial of the existence of stomata in connection with the lymphatics; but it is almost impossible to take up any German research on the lymphatic system without meeting some kind of assertion as to their presence or existence. Like Sappey (loc. cit. p. 794), we "long to see those stomata which will, after having shone with an ephemeral brightness, go modestly to join their ancestors, the absorbing mouths, which William Hunter thought he saw upon the villi, which Haase thought he had discovered on the surface of the skin, and which Mascagni believed to exist on the convex surface of the liver, those open mouths, always disproved, and yet always reappearing in some other form in the history of our errors, and which still remain as examples of the unfortunate tendency of many otherwise eminent minds to be led astray by

illusions and vain theories when under the influence of some preconceived idea."

Before summarising our conclusions we wish specially to record our indebtedness to the kindness of Mr Bartlett, the well-known and able superintendent of the Zoological Gardens of London, who has taken a great deal of trouble to provide us with most of the material upon which the present and previous researches published in this Journal have been made.

CONCLUSIONS.

- 1. In the uterus, the lymphatics are found principally as layers connected with each other, and corresponding to the distinct layers of tissue in the uteri of the lower animals.
- 2. In monkeys and in mankind, the complex arrangement of the muscular bundles leads to a corresponding irregularity in the arrangement of the lymphatics of the musculature, but even there the principle of layers, corresponding to the bundles of muscle, can be clearly recognised.
- 3. The complexity and amount of the lymphatics increases as a rule very distinctly as the size of the class of animals increases.
- 4. In rats, mice, and similar small mammals, there is only one main plexus lying between the circular and longitudinal muscles. From this plexus small twigs pass around the outer or longitudinal muscular layer, but return again to the plexus. These have been erroneously spoken of as the lymphatics of the subserosa. Few or no lymphatics pierce through, or appear on, the mucosa surface of the circular layer of muscles. Their mucosa possesses few or no lymphatics.
- 5. In medium-sized animals, like the sheep or goat, the lymphatic twigs passing to the subserosa retain their comparative amount and size, but the circular muscle is now pierced by large lymphatics which ramify in the mucosa. The larger portion of the lymphatics of the mucosa ramify like a cactusplant on its deep surface, and send loops towards the free surface, from which, however, they are generally separated by a certain thickness of tissue, and a very regular and complete blood-capillary plexus.
- 6. In large mammals, like the mare, no lymphatics appear on

the peritoneal side of the musculature, but a great development of lymphatics takes place on the mucosa surface and within the mucosa itself. The lymphatic plexus on the deep surface of the mucosa is formed by immense valved vessels, which send off branches both as loops and villous processes, that pass right up to the epithelium of the inner surface of the uterus. Under that epithelium the villous processes end, but the loops often ramify as sinuous channels between the openings of the uterine glands.

7. The changes caused by pregnancy are best marked in the intermuscular layer of lymphatics, which increase greatly in size, but not appreciably in number. The changes are marked to a much less extent, both in the lymphatics of the mucosa and of the longitudinal muscular coat.

8. The uterine glands have no connection with the lymphatics, either in the pregnant or non-pregnant uterus, and their function seems entirely suspended during pregnancy.

In the subserosa of all animals, there are no lymphatics having their commencement there, as a collecting plexus. The small twigs found there come from the deeper lymphatics of the intermuscular plexus, and after a very short course return thither, so that there is no ground for speaking of these twigs as belonging to a separate category of subserous lymphatics.

DESCRIPTION OF PLATES I. AND II.

LYMPHATICS OF THE UTERINE MUCOSA.

(Drawings made by the aid of the Camera Lucida.)

Fig. 1. Sheet or plexus of huge valved efferent lymphatics lying

upon the deep surface of the uterine mucosa in the mare, 12.

Fig. 2. Terminal sinuous twigs of superficial and valveless collecting lymphatics, appearing immediately underneath the lining epithelium of the uterine mucosa in the mare. These twigs are the ultimate radicles of the plexus seen in fig. 1, both figures having been drawn under the same magnifying power, and representing the opposite surface of the same mucosa, $\frac{1}{12}$.

Fig. 3. View under high magnifying power of the extreme point of one of the villus or cul-de-sac terminations of the lymphatics on

the free surface of the uterine mucosa, immediately underneath its covering epithelium, showing specially its relations to the openings of the uterine glands in the mare, $\frac{1}{130}$.

Fig. 4. Magnified view of a portion of one of the terminal twigs of the sinuous variety seen in fig. 2, in order to show its relations with the glands, blood-vessels, and branched cells of the locality, \(\frac{1}{60} \).

Fig. 5. Summit of the arch-like bend of one of the superficial lymphatics of the uterine mucosa in the pig, where the lymphatic approaches nearest to the surface but still lies underneath the regular superficial blood capillary network characteristic of this and of the bovine animals, but which does not exist in the mare. In this animal also the gland openings are so far apart that none of them appear in the same field with the lymphatic, and only the larger branches of the blood capillary plexus have not been removed by the scalpel, \frac{1}{60}.

Fig. 6. Superficial portion of the lymphatics of the uterine mucosa in the sheep, forming loops or arches dilated at their centres. These loops do not come so near to the lining epithelium as on the mare, but lie between the branching uterine glands and the surface epithelium, \(\frac{1}{6.0} \).

Fig. 7. View under a low power of the terminal loops in the

sheep, of which fig. 6 is a portion highly magnified, $\frac{1}{12}$.

Fig. 8. Highly magnified view of a portion of the plexus, of efferent lymphatics lying on the deep surface of the uterine mucosa in the goat. This plexus corresponds to that seen in fig. 1 from the mare, and it is intended as a companion to fig. 6, in continuation of the superficial lymphatics of the mucosa in the sheep, the character of the uterine structure being similar in the two animals, $\frac{1}{6.0}$.

The following letters apply equally to all the above figures:—l, lymphatics; g, uterine glands; c, branched cells; v, blood-vessels.

LYMPHATICS OF THE UTERINE MUSCULARIS.

Fig. 9. View under very low power of the lymphatic twigs appearing on the outer or subperitoneal surface of the longitudinal muscular layer of the non-pregnant uterus of the mouse, showing that these belong to the muscle and not to the subserosa, $\frac{1}{12}$.

Fig. 10. Highly magnified view of one of the twigs seen in fig. 9, in order to show comparatively the changes effected in the size of the endothelium and calibre by pregnancy, by comparison with fig. 11, $\frac{1}{60}$.

Fig. 11. From the same locality and under the same magnifying power as fig. 10. From the pregnant uterus at term in the mouse, ¹/₆₀. Fig. 12. View under low power of the lymphatic twigs on the subperitoneal surface of the longitudinal muscular layer of the non-preg-

nant uterus of the goat, for comparison with fig. 13, $\frac{1}{10}$.

Fig. 13. View under the same power as fig. 12 of the same description of lymphatics dilated by pregnancy in the sheep, the fœtus

Fig. 14. View under high power of the lymphatics belonging to, and lying parallel with, the circular layer of muscle of the non-pregnant uterus of the pig. This figure is drawn from the mucosa side of the

muscular layer, although it really lies in the same plane with that

layer.

Fig. 15. View under very low power of the lymphatics or lymphatic of the circular muscular layer in the pregnant uterus of the sheep, from which fig. 13 was drawn, in order to show the dilatation caused by pregnancy in two similarly sized animals like the sheep and the pig. Fig. 14 has been reproduced in fig. 16, under the same magnifying power as fig. 15, for comparison with the latter, $\frac{1}{10}$.

Fig. 17. Transverse section through the musculature of the body of the human uterus, showing the lymphatics injected by cancer cells in section, and their relationship with the dilated blood-vessels, \frac{1}{10}.

Fig. 18. Antero-posterior section through the front wall of the same uterus as in fig. 17, in the mesial line of the neck, showing that even in the irregularly arranged musculature of the human uterus the lymphatics still appear to be in layers (diagonally across the drawing), $\frac{1}{12}$.

In the above the following letters apply throughout:—e, peritoneal

endothelium; l, lymphatic; m, muscle; v, blood-vessels.

Fig. 19. Comparative view of the size of various endothelial and epithelial cells, having special reference to c, the cells lining the great bursal cavities lying between the uterine mucosa and muscularis; a, lymphatic endothelium; b, lining epithelium of the uterine cavity; d, lining epithelium of the uterine glands; e, venous endothelium, $\frac{1}{100}$.

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Fig. I.

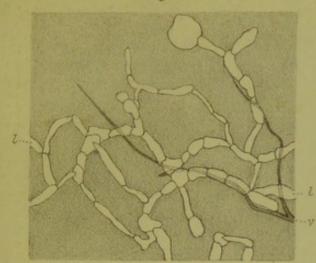


Fig. 2.



Fig. 6.



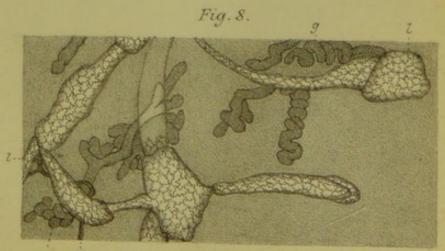




Fig. 4.

Fig. 7.





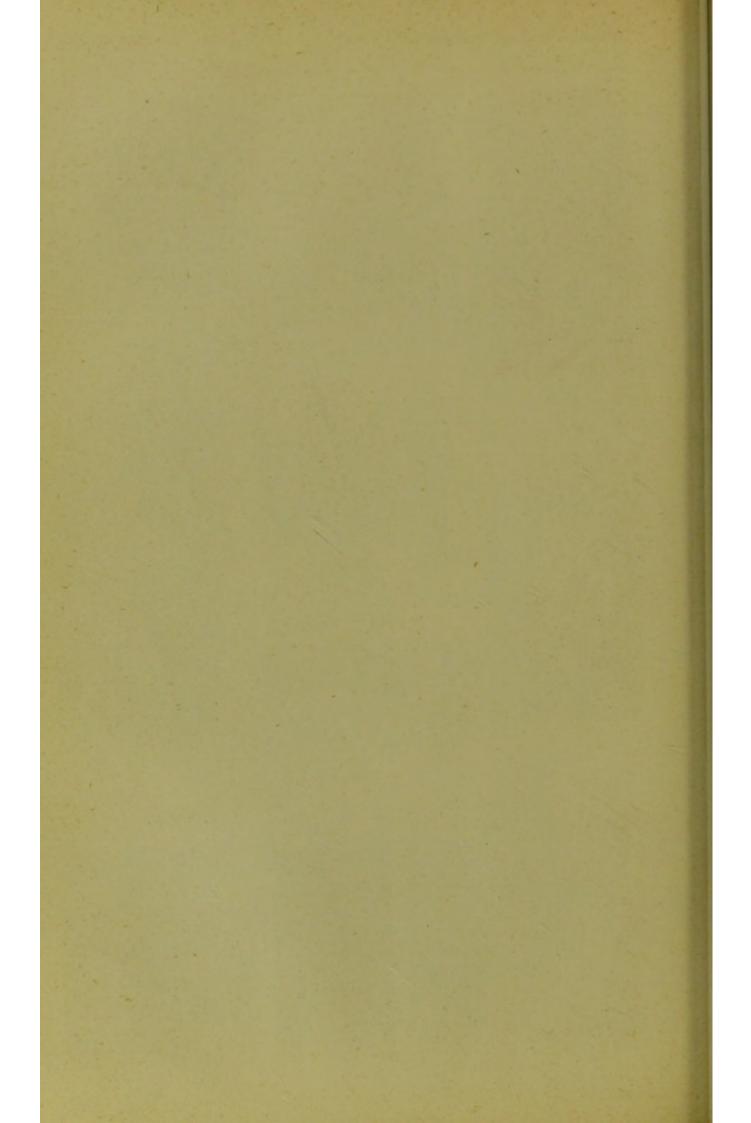


Fig. 9.

Fig. 13.

