THE DIAGNOSIS OF MALIGNANT OVARIAN TUMOURS AND MALIGNANT PERITONITIS.

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ON February 3rd, 1875, I read a paper before the Medico-Chirurgical Society of Edinburgh, on the Structure of the Ovary in relation to certain Forms of Disease of the Organ. After giving a short account of my observations on the development of the ova and the structure of the ovary, and contrasting them with the recently published views of Waldeyer, I proceeded to give the complete histories of two cases of malignant disease of the ovary which were under my observation during the months of September, October, November, and December 1874. During these months, I made careful drawings of certain cell-groups, which I had discovered in the ascitic fluid surrounding the malignant tumours in both cases; and these drawings were handed round to the gentlemen who were present at the reading of my paper, in order that they might form an idea of the appearances of the cell-groups while I read the description of them.

The fluid obtained by tapping the abdomen of the patients was allowed to stand for some hours, and the deposit was carefully examined with the microscope. "It contained a number of red blood-corpuscles, and numerous large round cells with bright sharply defined oval nuclei with nucleoli. On placing a drop of the thicker part of the sediment on a glass slip for examination, I saw with my naked eye many small white bodies, varying in size from a pin's head to mere specks; these, under a power of four hundred diameters, were found to consist of groups of cells in all stages of development. Each little body was a mass of cells proliferating in an extraordinary manner. At the margin of each mass, large cells with bright nuclei were seen projecting, and were exactly similar to the large free cells which I had noticed first in the sediment. From a minute solid nucleus invested with protoplasm up to the large free nucleated cells, all stages of cell-development could be seen in each mass. Once seen, such an appearance could not easily be forgotten." I concluded the histories of these two cases with the following remarks.

"I have given these two cases somewhat in detail, because I wish to direct attention to these little masses of proliferating epithelium in ascitic fluid as a means of diagnosing malignant peritonitis and malignant ovarian disease."

Dr. Matthews Duncan, the President of the Medico-Chirurgical Society, was present at the reading of the above paper, and, among other things, said as follows. "In the pathological aspect of the question, a most important point in the paper was the morbid condition of the connective tissue corpuscles in relation to the peculiar epithelial masses found in the ascitic fluid, which were evidently the product of ruptured cysts. The diagnosis of malignant ovarian cystoma by finding in the fluid, not only of the cysts, but in the ascitic fluid, those beautiful proliferating masses had been well shown. These masses were new to Dr. Duncan, and they could not easily be confused with any other structure. Dr. Foulis's observations were altogether on a different footing from those of most of his predecessors. He had begun the inquiry in the right and only way; viz., by first studying the development of the ovary and ovum."

A short abstract of this paper appeared in the BRITISH MEDICAL JOURNAL of February 27th, 1875, and a long and complete abstract of it was published in the *Edinburgh Medical Journal*, March 1st, 1875; and the paper itself in full was published in the BRITISH MEDICAL JOURNAL for June 26th, 1875.

Now, up to the time when I first described them, neither Mr. Spencer Wells nor Mr. Thornton, nor anyone as far as I can find, had said a single word about these cell-groups in cystic and ascitic fluid, or their importance as a means of diagnosing malignant peritonitis, etc. Still working at the subject, on July 7th, 1875, I read a second paper before the Medico-Chirurgical Society of Edinburgh, entitled Contributions to the Pathology of the Ovary. A long abstract of this paper appeared in the *Edinburgh Medical Journal* for August 1875. I then gave the histories of four cases of malignant disease of the ovary in which I diagnosed the malignant condition of the tumour and peritoneum by finding in the ascitic fluid the cell-groups which I had previously described, and in each case I had been able to verify my diagnosis by an examination of the bodies after death. For the second time, drawings of the cell-groups were shown to the members of the Society who were present.

On April 20th, 1876, i.e., thirteen months after my first paper and nine months after my second paper was published, during which time he became acquainted with the results of my work, Mr. Thornton

published his observations on "these most remarkable and characteristic cells and cell-groups"; and I shall now quote, from his paper read before the Harveian Society of London, the words used by him in his description of the cell-groups "to which he attaches the most importance as indicating malignant disease".

"Various forms will be seen depicted faithfully in the drawings, some looking like mere clusters of lymph-corpuscles (like bunches of grapes), others like more or less flattened endothelial plates arranged in layers, and others presenting every variety of size and shape and every stage of growth. It is these latter to which I attach the most importance as indicating malignant disease, and under this term I include both the rapidly growing sarcomata and carcinomata and certain peculiar ovarian papillomata."

I have italicised Mr. Thornton's description of the cell-groups, which, he says, indicate malignancy; and, on comparing my description with this, there can be little doubt that we both are referring to the same objects. Indeed, the similarity of our descriptions is most remarkable. I think it right, however, to repeat that my description was given at least thirteen months before Mr. Thornton said a single word about "these most characteristic cells and cell-groups". At this date (four years after I first described these cell-groups), I have nothing to add to or take from my description of them; for it is sufficiently accurate to serve me and others who will follow it closely in the diagnosis of malignant ovarian and other abdominal tumours.

As the discovery of these cell-groups is a valuable one, and of great importance as a means of diagnosis, it is right that we should finally settle the question who first discovered them and drew attention to them. That it was not Mr. Knowsley Thornton, may be seen by the following statement made by him in his paper of April 20th, 1876.

"My friend Dr. Foulis of Edinburgh claims to have been the first to describe some of these cell-groups, which he considers to afford certain evidence of the malignant nature of the tumour, if it be ovarian. I will not dispute with him the satisfaction of being the first to draw attention to this important subject." On Sept. 7th, 1878, in the BRITISH MEDICAL JOURNAL, he confesses that "he had not published any paper at the time when Dr. Foulis published his first observations in the *Edinburgh Medical Journal*, March 1875", and says: "The only marvel to him is that, among so many workers in this field, no one had sooner called attention to these cell-groups, as they are so very remarkable and different from anything else found in the sediments of cystic and ascitic fluid."

I have no doubt that, at the end of the year 1874, Mr. Thornton had seen the cell-groups, as he states, and so had my friend Dr. Thomas Keith of Edinburgh; but I say, without fear of contradiction, that, had Mr. Thornton known their real value as a means of diagnosis, and their connection with the ovary, he would have lost no time in drawing attention to the subject. With such an enormous supply of material at his command, he ought long ago to have discovered the cell-groups, and to have directed attention to them; but he failed to do so until thirteen months after my first paper was published.

It was in August 1872 that Professor Turner of Edinburgh suggested as a subject of investigation the structure of the ovary and the development of the ova. As the result of two years' work, I was able to demonstrate that at no stage of its existence has the ovary any tubular structure; and that the eggs and follicular epithelial cells have a different origin. I pointed out that the cells of the membrana granulosa are derived from the connective tissue corpuscles of the stroma, and I may here state that recent investigations have convinced me of the correctness of this view. Now, this important observation—viz., the origin and growth of the cells of the membrana granulosa from the connective tissue corpuscles—has been of the greatest value to me as an anatomical basis on which to build the pathology of the ovary. It must be apparent to anyone that it is impossible to arrive at a correct pathology of the ovary or any other organ without having first gained sound knowledge of the development and structure of the organ; and I distinctly state that it was my knowledge of the development of the follicular epithelial cells from the connective tissue corpuscles of the stroma that enabled me to detect at once the connection between the cell-groups in the cystic and ascitic fluids and the diseased ovary and peritoneum.

Great, indeed, was my disappointment and surprise when I found that Mr. Spencer Wells, in his second lecture on the Diagnosis and Surgical Treatment of Abdominal Tumours, delivered before the Royal College of Surgeons of England on June 12th, 1878, gave to Mr. Thornton the entire credit of the discovery of the cell-groups, and omitted even to mention my name in connection with the subject; and I was much annoyed to find that Mr. Thornton, after having publicly admitted my claim to priority in the discovery, and that I was the first to direct attention to the cell-groups "which afford certain evidence

of the malignancy of the tumour, if it be ovarian", should permit Mr. Spencer Wells to give him the entire credit and to do me such an injustice. I must, therefore, vindicate my position, which I shall again clearly point out, and it is this. I claim to have been the first to direct attention to the subject of peritoneal infection from malignant ovarian cysts, and the first to describe the characteristic cell-groups found in cystic and ascitic fluid; and I say that Mr. Thornton has added little or nothing to our knowledge in connection with this matter beyond what was published in my papers of February 3rd and July 7th, 1875.

In the BRITISH MEDICAL JOURNAL for July 20th, 1878, I protested against Mr. Spencer Wells giving Mr. Thornton the credit of a discovery, the right to which the latter had previously disclaimed. Mr. Thornton questions the correctness of certain statements I then made in connection with the diagnosis of malignant ovarian tumours and malignant peritonitis; and I shall now proceed to take up the points of dispute, in order that I may state, once and for all, what are the conclusions at which I have arrived as the result of four years' work; and thus a comparison may be made between Mr. Thornton's views and my own.

1. Mr. Thornton says:—"Dr. Foulis still thinks that simple prolonged irritation, as from an innocent ovarian tumour, may cause these sarcomatous growths from the peritoneum, and compares them with the well known drawings of Klein. I, on the contrary, am quite certain that these growths produced by this mere irritation, as apart from cell-infection, are of a different nature, and can be distinguished by microscopic examination."

In reply to this, I must first say that my words were as follow:—"Masses of sprouting cells may grow from the peritoneum directly as the result of chronic irritation, caused by a growing ovarian tumour or by fluids that have escaped from ovarian cysts, and even the pleural membrane may become involved in the irritation." I compared these outgrowths with the drawings of Klein, and stated that the masses of cells which grow from the pleuro-peritoneal membrane as the result of chronic irritation resemble the masses of sprouting cells found in ascitic fluid surrounding sarcomatous tumours of the ovary. They resemble them inasmuch as they are masses of sprouting cells; but I have nowhere said, and I certainly do not think, that the simple masses of sprouting cells cannot be distinguished by careful microscopic examination from the malignant cell-groups. On the contrary, I say distinctly that the microscope is able to place on the one side the cell-groups that are of a malignant nature, and on the other side those that are not; viz., those produced by chronic irritation. Klein's outgrowths, as may be seen in his drawings, are remarkable for the sameness of size and form, and the non-malignant character of the component cells; but the truly malignant cell-groups, such as I first described, are remarkable for the variety in size and shape and polynucleated condition of the cells in each group. I agree with Mr. Thornton that mistakes have been made, and are likely to be made, by careless observers, if they do not sufficiently distinguish between the simple inflammatory and the truly malignant cell-groups.

The following extracts are from my paper of July 7th, 1875. "Dr. Foulis again showed drawings of the little masses of sprouting cells, which he had discovered in ascitic fluid surrounding ovarian tumours, and by the presence of which he had diagnosed malignant ovarian tumour and peritonitis in the cases whose histories he had already given to the Medico-Chirurgical Society; and he now gave short notes of three additional cases, in which he had discovered the same little masses of sprouting cells in ascitic fluids, and in two of these cases a *post mortem* examination verified the diagnosis made during life—viz., malignant ovarian tumour and peritonitis."

"The third case is that of a woman still alive, and in the ascitic fluid present an enormous quantity of the little masses of sprouting cells were found. It remains for future observation to settle the question whether these little masses of sprouting cells are ever found in ascitic fluids surrounding other malignant tumours, say of the omentum, peritoneum, etc., structures in which fibrous connective tissue exist in quantity; and I take this opportunity of asking medical gentlemen to examine ascitic fluids with the microscope, in all cases, both of men and women, with a view to settle the question."

Now, the third case, to which I have just referred, came under Dr. Thomas Keith's care in the end of June 1875. I had never seen the lady; but bloody fluid from the peritoneal and pleural cavities were sent to me for microscopic examination. The case was supposed to be one of ovarian tumour. In both fluids I found a great number of masses of sprouting cells of a most malignant character. The diagnosis I returned to Dr. Keith was as follows: "The tumour is malignant, and the peritoneal and pleural membranes are affected by malignant disease."

The question I had raised on July 7th, 1875, as to whether little masses of sprouting cells, diagnostic of malignant growths, are ever found in ascitic fluids surrounding malignant tumours of the omentum, peritoneum, etc., was, a few days later, once and for all, settled. The lady died, and I performed a careful *post mortem* examination. A large quantity of bloody fluid was found in the peritoneal and pleural cavities, and in these fluids was found a great number of cell-groups of a most malignant character, the drawings of which I possess. A large flat pancake cancerous tumour of the omentum was discovered, and several fungating growths were seen on the peritoneal surface. The ovaries were not diseased, as far as the naked eye could tell; in both pleural cavities, on the surface of the diaphragm, and elsewhere, were many cancerous nodules, some of them fungating.

Be it recollected that, up to this time, I had found the malignant cell-groups in ascitic fluids surrounding four different ovarian tumours, and a *post mortem* examination in each case had verified the diagnosis made during life; and I now was able to say that the malignant cell-groups are found in ascitic fluid surrounding malignant tumours other than ovarian.

The point I wish to bring forward clearly is this: The malignant cell-groups found in ascitic fluids are not diagnostic of any one form of tumour, but of the malignant condition of the tumour in question, and of the peritoneal membrane and its appendages; and, if found in fluid in the pleural cavities, all one can be sure of is that they are diagnostic of the malignant condition of the pleural membrane.

At the time I wrote my first description of these malignant cell-groups, I had found them only in the cysts and in ascitic fluid in connection with malignant ovarian tumours; but, so certain was I of their value, that I stated at once: "I considered them to afford certain evidence of the malignant nature of the tumour, if it were ovarian."

In conclusion, if these cell-groups, such as I have described, be found in the cysts of an ovarian tumour, the cysts, and probably the whole tumour, are malignant. If they be found in the cysts of an ovarian tumour and in the ascitic fluid surrounding the tumour, the peritoneal membrane and the tumour are affected with malignant disease; and if they be found in fluid in the pleural cavities, malignant growths exist in these cavities. If they be found in the ascitic fluid surrounding any abdominal tumour, the peritoneum and the tumour are malignant. The malignant growths in the pleura may be secondary; the primary malignant growth being either ovarian or other abdominal tumour.

I think it right to state that, as far as I know, attention has not been hitherto directed to the cell-groups found in pleural fluids as a means of diagnosis.

As ovariologists and ovarian pathologists, we have to deal with abdominal tumours of women, which are, as a rule, ovarian. Physical examination can, in most cases, determine the seat of the tumour in question; but physical examination alone is not sufficient to tell us if the tumour be malignant or not. The microscope is our best friend in such cases: hence the necessity for a careful microscopic examination of the fluids, both within (if such exist) and surrounding the doubtful tumour. Although the cell-groups which I have described are not diagnostic of any one kind of tumour, but of the malignant condition of the tumour, in the case of an ovarian tumour, we frequently find mixed up with the malignant cell-groups, in the ascitic fluid, fragments of tissue and structural elements, which we know from past experience to be of ovarian origin; and from finding these, we are able to say that the tumour is not only malignant, but ovarian. As an additional means of diagnosis, puncturing or tapping the tumour after the ascitic fluid has been removed, by means of an aspirator, will generally afford us valuable information as to whether the tumour is ovarian or not.

2. Mr. Thornton says: "I still maintain that the finding of the cell-groups in the cyst-fluid is the all-important point, as, by prompt operation and care in performing it, we may hope to prevent infection of adhesions or peritoneum."

In reply to this, I must mention the fact that, in three out of the four cases whose histories I gave on July 7th, the malignant tumours were either solid or semi-solid, and no cysts were present sufficiently large to admit of tapping; and, in all four cases, such a large quantity of ascitic fluid was present that it was necessary to withdraw this before one could get at the tumour. In one case, the abdominal cavity was first tapped and emptied of the peritoneal fluid, and then the cysts of the malignant tumour were tapped. Similar cell-groups were found in both fluids, but all the information I required was obtained by an examination of the deposit in the ascitic fluid in each case. "Solid ovarian tumours are usually malignant", so Mr. Thornton says; but he might have also said malignant ovarian tumours are usually solid or semi-solid, and rarely present cysts sufficiently large for tapping in the ordinary way. It must be Mr. Thornton's experience, as it is mine, that an examina-

tion of the ascitic fluid alone, surrounding doubtful tumours, is generally sufficient in itself to tell us if the peritoneum and the tumour in question are affected by malignant disease; and Mr. Thornton must know that, in the great majority of cases, malignant ovarian and other abdominal tumours are surrounded by ascitic fluid, often in such quantity that it is extremely difficult to say if any tumour exist, and the seat of it, until this peritoneal fluid has been removed. In opposition to Mr. Thornton's statement, I still maintain that the finding the cell-groups in ascitic fluids is the all-important point.

3. Mr. Thornton says: "Dr. Foulis still attaches importance to the bloody or port-wine colour of the ascitic fluid. I have for some time ceased to do so."

On April 20th, 1876, Mr. Thornton said as follows: "The colouring of the ascitic fluid with blood, along with these cell-groups, I believe is a certain indication of malignancy."

It is difficult to understand how Mr. Thornton can so contradict himself as he does in these two sentences.

I have nowhere said anything about *port-wine colour*. What I did say was this: "If we find the cell-groups in bloody ascitic fluid, we may then conclude there are vascular villous growths on the peritoneum." By bloody, I meant not the red colour, but the actual presence of blood, as may be ascertained by the microscope. I quite agree with Mr. Thornton that sometimes bloody ascitic fluid becomes clear or straw-colour; but it is my experience that this takes place only when the patient has had prolonged rest, as is the case after tapping, and the bloody colour is apt to return if the patient moves about much.

4. Mr. Thornton regards the following statement of mine as dangerous and misleading: "We must not pay too much attention to the presence of little masses of sprouting epithelium within the cysts; it is when they are found in ascitic fluids surrounding ovarian tumours that they become objects of the greatest importance."

In support of this statement, I have to say that, when the cell-groups are found in ascitic fluid surrounding an ovarian tumour, we may conclude that the peritoneum is affected by malignant disease, and the entire absence of them in ascitic fluid shows that the peritoneum is not seriously affected; and, if they be found in the cyst of an ovarian tumour, all we can be perfectly sure of is, that particular cyst is in a malignant condition, although we may suspect that the whole tumour is malignant. The finding of them in the cystic fluid, and their entire absence in ascitic fluid, points to the immediate necessity of attempting to remove the tumour, as, by prompt operation, we may hope to remove it before its connections have become affected by malignant disease. In three cases that have come under my notice, the lining membrane of one or more of the cysts in each tumour was in an extraordinary thickened and villous condition, certainly malignant; yet, in all the cases, the tumour was completely removed by operation, though with great difficulty. In each case, there was an entire absence of ascitic fluid. All three patients are in the enjoyment of good health at this date. There are some cases, however, in which there is an entire absence of ascitic fluid, and in which the tumours, as can be ascertained by physical examination, are bound down by most extensive adhesions. In some of the cysts of such tumours we may find the sprouting cell-groups; but, in such cases, the presence of extensive adhesions, especially in the pelvis, points to the almost impossibility of completely removing such tumours, without leaving behind some seeds of malignant disease.

5. In contradiction of my statement, Mr. Thornton says: "Cancerous or malignant tumours of the ovary are remarkably rare, and the cases of recurrence after operation still more so." "Under the term malignant" Mr. Thornton "includes both the rapidly growing sarcomata and carcinomata, and certain peculiar ovarian papillomata." Let us now turn to Mr. Spencer Wells's book on *Diseases of the Ovaries*, edition 1872, pages 464 to 468 inclusive. Here we shall find twenty-four cases recorded in which an exploratory incision was made, and twenty-eight cases in which ovariectomy was commenced but not completed, making fifty-two cases in all; and of these, eleven were cases of malignant disease, nine of which died within thirteen months after the incomplete operation. Looking at this list of fifty-two cases, one is struck by the number in which a large quantity of ascitic fluid was found surrounding the tumour. I do not hesitate to say that, had this ascitic fluid been carefully examined with the microscope, the great majority of these operations would have been avoided. It must not be forgotten that the cases of malignant disease here recorded were operated upon by Mr. Spencer Wells in ignorance at the time that they were cases of malignant disease. It would be interesting to know how many cases of malignant ovarian disease have come under Mr. Wells's notice since he began to operate—cases which he at once diagnosed as malignant. During the last five years, I have seen six cases of malignant disease of the ovary; and Dr. Thomas Keith tells me that, since he began to

operate, he has seen at least twenty cases of malignant ovarian disease; and in Mr. Thornton's paper in the *BRITISH MEDICAL JOURNAL*, October 19th, 1878, he records the brief notes of six cases of abdominal section, in four of which the ovaries were found to be the seat of malignant disease.

Now, as to the question of recurrence of malignancy after the operation of ovariectomy, I find, on looking at Mr. Spencer Wells's list of five hundred cases of completed ovariectomy, that in four hundred and thirty-three operations performed during the years 1858-71, thirteen of the patients died of cancer, scirrhus, carcinoma, malignant disease, as it is distinctly stated by Mr. Spencer Wells, in periods of time varying from a few days to seven years after the operation. His second and third hospital cases died of malignant disease seven years and ten months respectively after the operation. Among the five hundred cases of completed ovariectomy, there are several in which "no return" as to health is given, and several in which the cause of subsequent death is doubtful.

Dr. Thomas Keith (*Spencer Wells, Diseases of the Ovaries*, page 306,) thus states, in speaking of his own results: "Of 144 operations, since 1862, there have been 117 recoveries and 27 deaths." On page 307, he further states: "Nine cases have died since being operated on"; and 5 of these died of cancer.

To sum up, of Mr. Spencer Wells's 433 cases of completed ovariectomy, 13 died of cancer after the operation. Of Dr. Thomas Keith's 144 cases of completed ovariectomy, 5 died of cancer after the operation.

Enough has been said to show that malignant disease of the ovary is not uncommon; and the cases of recurrence after operation are by no means rare.

Mr. Thornton says he has long worked at the histology of the ovary, and has failed altogether to find the transition described by Dr. Foulis in his paper "On the Development of the Ova and the Structure of the Ovary". There are different ways of working at the histology of the ovary, and different results, as a consequence, are obtained; but if Mr. Thornton will spend two or three years in the systematic investigation of the development of the ovary, I feel sure he will, by the end of that time, have secured a firm foundation on which to build the pathology of the ovary. I am sorry Mr. Thornton has not been able to see what I have described; but I will undertake to demonstrate to any one the truth of my descriptions. When such men as Professor Turner and Professor Rutherford of Edinburgh, and Professor Allen Thomson, take the trouble to spend many hours in the examination of my preparations, and then tell me that my drawings and descriptions are in exact accordance with what they have seen in my preparations, I can well pass over Mr. Thornton's adverse criticisms. Mr. Thornton, as far as I can judge, has given no evidence whatever that he has carried out any original investigations on the development and structure of the ovary, and he has not told us upon what anatomical foundation he is laying his "bricks". After all that he has said and written; "after five years' work with ample material"; "he remains much in the same state of doubt". Mr. Thornton, I fear, will never do good pathological work until he has a sound anatomical basis on which to build.

As a result of a series of investigations, I have ascertained that the stroma of the ovary is derived from, and is directly continuous with, that structure which I call the stroma of the peritoneum. The stroma of peritoneum and of the whole pleuro-peritoneal membrane is remarkably rich in lymphatics, as Klein has shown, which are continuous with the lymphatics which pass along with the blood-vessels and nerves into the ovary at its hilus and ramify throughout its entire extent. Here, then, we have a wonderful connection between the ovary and the whole pleuro-peritoneal membrane and its appendages.

In my first paper on Cancer of the Ovary, I pointed out that the epithelium of the cysts, as well as the connective tissue corpuscles of the stroma, by excessive proliferation, may give rise to sarcomatous growths, which in the ovary must be classed as malignant forms of disease; and in the cases whose histories I recorded I showed how important a part is played both by the epithelium and the connective tissue corpuscles in the production of these forms of malignant disease. The ovary is remarkable for the number of epithelial and cellular elements in its structure, and it is an organ subjected to the most extraordinary variations of blood-supply and nerve-excitement. Is it to be wondered at, then, that the ovary, under certain conditions of excitement (the exact nature of which we do not at present understand), should pass from a physiological into a pathological condition? It does so very frequently; and when once the boundary-line of the physiological state is passed, disease may go on to an unlimited extent, and the whole organ may be converted into one mass of disease. Malignant disease thus produced is not confined to the ovary itself, but soon parts at a distance become affected. The cystic portions of such a

diseased ovary rapidly become choked up with malignant growths, and are very liable to burst, the result being the escape of fragments of malignant tissue into the peritoneal cavity; but, also, the more solid portions of the mass may crack and burst, and, as we often find, present large fungating surfaces, from which are shed cellular elements and fresh blood. It is seldom, indeed, that the disease proceeds thus far without affecting distant parts, and I have no doubt that sometimes seeds of the disease pass from the ovary along the lymphatics to all parts of the pleuroperitoneal surfaces, and secondary malignant growths form on all parts of that structure and its prolongations. In these two ways the diseased ovary affects distant parts: *a.* By shedding from its broken surfaces cellular elements, which settle down on the peritoneal membrane, and in many cases take root and grow; and *b.* By the passage of seeds from the malignant tumour along the lymphatics to all parts of the pleuro-peritoneal membrane. Directly the peritoneal membrane becomes irritated by the diseased ovary or other malignant growth, peritonitis results, and a quantity of fluid is poured out; and the same exudation may take place in the pleural cavities. The secondary nodules of cancer on the peritoneal and pleural surfaces may soon fungate, and shed cancer-cells and blood-corpuscles. In this way we have bloody ascitic fluid produced. A case has come under my notice where, some months after the removal of a doubtfully malignant ovarian tumour, the patient has returned to die of cancer of the peritoneal and pleural membranes; and after death, in each of these cavities, several fungating cancerous masses were found. The tumour had been removed, but its seeds were left behind, and time only was necessary to develop these into malignant fungating growths.

What I have said with regard to the infection of distant parts by a diseased ovary holds good in the case of other malignant abdominal growths, *i.e.*, of the omentum, uterus, etc. Just as we have the axillary, cervical, and thoracic glands affected secondarily by a carcinoma of the mamma, so we have the pleuroperitoneal surface affected throughout its entire extent from any diseased centre within the abdominal cavity.

It so happens, that in some cases it is impossible to say, from the patient's general condition, if she be the subject of malignant ovarian disease. She may have a large malignant ovarian tumour, and yet present no external signs of such disease. In one of Dr. Keith's cases, the patient looked so healthy that he operated for the removal of her ovarian tumour, although I strongly advised him to tap the abdomen and examine the ascitic fluid present before operating. This he did not do. On the first incision, bloody fluid poured out from the abdominal cavity, some of which I caught in a dish and examined microscopically. It contained an enormous quantity of the malignant cell-groups. Dr. Keith could not remove the large soft cancerous ovarian tumour exposed by the incision. The patient died very soon afterwards. Hence the great necessity for examining ascitic fluid in all cases.

In conclusion, a careful examination of the sprouting cell-groups affords us an excellent illustration of the growth of cells by the process of budding. From a minute solid-like nucleus invested with protoplasm up to the large free cells, all stages of cell-growth can be seen in each mass. In the ascitic fluid in which these cell-groups are observed, we have all the conditions necessary for cell-growth; *viz.*, a bland nutritious fluid derived from the blood and sustained at the temperature of the body. As to this process of cell-budding, I shall say little at present; but I wish to record the fact that in the cell-groups we may see the growth of young cells, which first appear as minute buds, projecting from the protoplasm surrounding the nuclei of older cells. In these minute buds no distinct nucleus can be detected, but the central portion of the bud appears more dense than its surrounding material. In slightly more advanced cell-buds we can observe the first appearance of a distinct central nucleus, which we recognise as differentiated from the perinuclear protoplasm; and, in still older cells, the nucleus gradually comes to present the appearance of a clear vesicular oval or round body with a nucleolus within it, and shows a sharply defined wall. Frequently we see a single bud projecting from the margin of a single parent-cell; and, in another case, this bud has grown almost to the size of the parent-cell; the double cell now looks as if it were a single large cell in the act of division, each half containing a well defined nucleus; but it is easy to see, from a series of such double cells, that the dumb-bell appearance of the cell is brought about by the younger cell attaining the size of the parent cell to which it is attached. The growth of cells by the process of budding resembles very closely what one sees in the case of the "Torula" or yeast plant. Not unfrequently one sees well grown young cells partly separated from the parent-cell, and projecting from it by a long neck; the younger cell thus presenting a balloon appearance.

My observations in connection with this subject I shall publish shortly.

SURGICAL MEMORANDA.

ON KERATOTOMY FOR HYPOPYON ULCER.

DR. HUDSON, in his interesting communication on Iridectomy *versus* Sämisch's Operation in Hypopyon Ulcer of Cornea, in the JOURNAL of September 28th, has expressed himself as anxious to learn the experience of others; and having myself practised keratotomy in many instances, I venture to offer a few remarks on the subject. In a town like Sheffield, with its varied branches of industry, injuries to the eye are of unusual frequency, and traumatic sloughy corneal ulcer of common occurrence, especially among grinders. Workmen of this class get pieces of metal or stone embedded in the cornea, and apply to a fellow-grinder for removal; and this, though generally skilfully performed, often results in an infiltrated condition of the cornea, with perhaps purulent deposit in the anterior chamber. For these cases, as well as the idiopathic class, I have in a large number of instances performed keratotomy. Relief of pain and a more healthy condition of cornea have generally been the almost immediate result. Sleep, which had in many cases been absent for nights, returned directly after the division of the cornea. The operation, whilst it seems to be quite as serviceable as iridectomy in staying the progress of the disease and promoting a return to a healthy condition, appears to me to be preferable to iridectomy, as it leaves one free to select the most favourable position for making a subsequent artificial pupil, if it be rendered necessary by resulting corneal opacity. But one case, which was little relieved by keratotomy, was at once benefited by an iridectomy. While, however, I am of opinion that keratotomy is of great value in these and other corneal affections, I have not recently performed it so frequently. In two instances, where the immediate results were all that could be desired, the cornea yielded at the incision, and became staphylomatous; one of the cases being particularly unfortunate, as it set up sympathetic inflammation in the fellow organ. Nor do I now think the operation so frequently necessary as I once did, but rely more upon atropine, constantly applied warm fomentations, opium, tonics, with rest in bed, and this I may say with very satisfactory results. I would add that eserine, which seems to be a decided reducer of tension is often of benefit in these affections.

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SAEMISCH'S OPERATION IN HYPOPYON KERATITIS.

In the JOURNAL of September 28th, two communications appear dealing with the treatment of hypopyon ulcer of the cornea, and in their conclusions differing widely. Dr. Hudson of Redruth advocates Sämisch's operation, while Mr. Hodges of Leicester prefers what I am bound to call an expectant treatment assisted by tonics, fresh air, etc. This last is exactly the treatment we followed here for many years, and with fairly good results; but still a large percentage of eyes were lost, and I was not satisfied with it. At the same time, I was reluctant to adopt the bold surgical treatment of Professor Sämisch. The very excellent results obtained by one of my colleagues, however, converted me, and, being unable longer to withstand the evidence of my senses, I finally adopted it with unexpected success.

I may say here that, among the many cases that occur in this large manufacturing centre treated by corneal section, I have never seen a single case of "weak cicatrix", and only one of staphyloma, which occurred in a debilitated drunkard, who had annually been under treatment for recurrent iritis. One solitary case ended in panophthalmitis, in a man who delayed too long before seeking proper advice, and who had employed himself in the interval by assiduously preparing his eye for destructive suppuration by the vigorous application of bread-poultices alternated with infusions of "golden ointment".

Iridectomy is best done afterwards, when the eye has quite recovered itself and is practically healthy. Iridectomy is much more easily practised at that stage than when attempted on an exquisitely painful eye, where the incision is made through a swollen and hazy cornea, too often to find a friable and rotten iris come away piecemeal. The cases which are most suitable for Sämisch's operation are those which owe their origin to traumatic causes. Operation is not indicated in the hypopyon of children; this form generally gets quite well if the pupil be kept dilated by atropia, a protective bandage applied, and sulphate of quinia administered internally.

We are here accustomed to make the section boldly through the long axis of the ulcer, commencing and terminating the wound in sound tissue. The corneal slough is removed by means of a very fine pair of straight iris-forceps, a protective bandage is then applied, and