TABLE ILLUSTRATING SOME OF THE DIAGNOSTIC AND THERAPEUTIC PROBLEMS THAT CAN BE RESOLVED BY RECOURSE TO THE AUTO INOCULATION TEST AND BY CONSIDERATION OF ITS EVENT—(*Continued*).

No.	Clinical features of case.	Diagnostic or therapeutic problem.	Procedure resorted to with a view to the induction of an auto-inoculation.	Particulars of opsonic readings.	Conclusion arrived at and remarks.
27	Large mass of glands in groin, followed by development of extensive nodular masses in abdomen.	Are the glands tuberculous or malignant?	Glands vigorously massaged.	*Tuberculo-opsonic indices.* Before massage ... ... 0·96 Immediately after ... 1·45 6 hours after ... ... 0·95 24 ,, ,, ... 1·70 *Neo-opsonic indices.* Before massage ... ... 1·02 Immediately after ... 1·02 6 hours after ... ... 0·95 24 ,, ,, ... 1·67	Patient is suffering from tuberculous glands and malignant disease. Patient died some weeks later and at the necropsy it was found that the pelvic peritoneum was infiltrated with lymph-adenomatous masses. The retro-peritoneal and mesenteric glands were all enlarged and in some definitely caseated tuberculous deposits were found.
28	Suspected tuberculous laryngitis. Patient sent up from out-patient department for diagnosis.	Is laryngitis tuberculous?	Talked vigorously for one hour.	*Tuberculo opsonic indices.* 24 hours before ... ... 0·94 18 ,, ,, ... 0·98 Immediately before ... 0·87 ,, after ... 1·00 ½ hour after... ... ... 1·12 3½ hours ,, ... 1·24 6¾ ,, ,, ... 0·83 8¼ ,, ,, ... 1·00 12 ,, ,, ... 0·88 20 ,, ,, ... 1·03 30 ,, ,, ... 1·00 2 days ,, ... 0·75 3 ,, ,, ... 0·75	Laryngitis is probably tuberculous.
29	Osteomyelitis of femur with sinus resulting. Sinus has persisted for seven years.	Is there here persistent staphylococcic infection?	Bier's bandage applied for one hour.	*Staphylo-opsonic indices.* Before bandaging ... ... 0·53 During ,, ... 0·81 Immediately after ... 0·72 ½ hour after ... ... 0·84 1½ hours ,, ... 0·93 2½ ,, ,, ... 1·10 36 ,, ,, ... 1·81 72 ,, ,, ... 0·62	There is here persistent staphylococcic infection.—The sinus completely healed under the influence of staphylococcic inoculation.
30	Affection of eye diagnosed as probably tuberculous; suspected tuberculous disease of lung.	Is pulmonary tuberculosis present?	Vigorous tennis playing.	24 hours before playing 0·65 Immediately before ... 0·75 ,, after ... 0·75 5 hours after ... ... 0·99 24 ,, ,, ... 1·00	Pulmonary tubercle is probably present.

In concluding this paper we desire to express to the Medical and Surgical Staff of St. Mary's Hospital our gratitude for generous assistance unstintingly afforded to us in the prosecution of these studies.

THE GROWTH OF MALIGNANT DISEASE IN MAN AND THE LOWER ANIMALS,

WITH SPECIAL REFERENCE TO THE VASCULAR SYSTEM.[1]

BY PROFESSOR E. GOLDMANN

OF FREIBURG.

ON two previous occasions I have had the honour of addressing meetings in London in connexion with work referring to the relation of cancer to the vascular system. In coming before you to-day I do not wish to travel over ground already known to you. It is my main intention to give you a short *résumé* of the whole extent of my work and at the same time to draw your attention to methods of investigation which I am sure will prove beneficial to all willing to coöperate with me in the solution of a problem so intimately associated with the biology of malignant growths. My work has been conducted on human and animal material. I owe a debt of gratitude to Professor Ehrlich of Frankfort and to Dr. E. F. Bashford of London for valuable material from the mouse, such as carcinoma in its various forms, sarcoma, mixed tumours, and chondroma. In the short time at my disposal I can only mention my general results. A detailed account of, and an exhaustive reference to, the literature of the subject will be found in a treatise forthcoming. The points of view from which I have approached my subject are the following: (1) How far is the vascular system responsible for the dissemination of malignant growths? (2) What are the general conditions of circulation in these growths? and (3) What purpose does the multiplication of blood-vessels in malignant growths serve—merely that of nutrition or also that of defence?

As to the dissemination of tumours along the vascular system, I may refer to a treatise of mine published several years ago in which I proved by means of an elective stain for elastic tissue that both in the early stages of sarcoma as well as carcinoma an extensive invasion of tumour cells into the coats of blood-vessels occurs. It is a striking fact that this happens far more frequently in veins than in arteries and again that the results of this invasion can only be traced locally, rarely exceeding the area of round cell infiltration. Exactly similar results have been obtained

[1] An address delivered before a meeting convened by the Surgical Section of the Royal Society of Medicine on Oct. 23rd, 1907.

in the case of carcinoma and sarcoma of the mouse. In examining mouse tumours we must always bear in mind that we are dealing with vessels of comparatively small dimensions, whose elastic coat is hardly comparable with that of man. And yet careful investigation reveals in tumours of mice all the various stages of vascular degeneration common to man. I place great stress on these conditions, as my extensive study of benignant growths, even of such verging upon the boundary of malignancy, for instance goitre, has proved to me that tumour cell infiltration into the walls of channels bounded by elastic tissue is a characteristic feature of malignant tumours only. I may add that in those cases in which carcinoma of the mouse invades the lymphatic glands the pathological condition of these glands is a counterpart to that found in man. The cells enter the marginal sinus and penetrate from here along the lymphatics into the medullary substance of the gland. It seemed to me a subject of great interest to inquire into the conditions under which the tumour cells enter into the vascular coats. At a first glance it appeared most probable that they travel along the lymphatics. Yet all anatomists concur in declaring that the vascular coats contain no lymphatics, a statement confirmed by evidence gained from pathological experience, especially in cases of retrograde transportation of tumour cells along the lymphatic channels. In these cases the cells are almost exclusively confined to the perivascular spaces and hardly ever penetrate the vascular walls. Hence we are bound to assume that the dissemination of tumour cells into the vascular coats is effected by blood-vessels. This seems all the more likely when we consider how different are the appearances of arterial and venous cancer and how the distribution of tumour cells in arteries and veins coincides with that of the vasa vasorum. In arteries the tumour cells rarely proceed farther than the outer coat, whereas in veins they are generally found beneath the intima. Thus arterial cancer appears as a form of periarteritis, veinous cancer as one of endophlebitis carcinomatosa. Now it is accepted on all sides that the vasa vasorum in arteries remain within the limit of the outer coat, rarely branching into the superficial layer of the middle one, whereas in veins they extend beyond the middle coat into the region of the intima. It is a remarkable fact that this question, which is of such vast importance in the pathology of the vascular system, has met with such scanty attention in recent years.

In order to gain experience of my own I made use of a series of injections performed on fœtuses, bodies of newly-born children, and on amputated limbs removed from individuals of various ages and for various reasons such as injuries, tuberculous joint or bone disease, and senile gangrene. I applied a method which furnishes us with ideal preparations and found that in fœtuses and newly-born children there is no material difference between arteries and veins as regards their nutrient vessels. The distinction previously mentioned sets in in the first year after birth and prevails as long as the vessels remain intact. Hence the artery performs its important function I should say with a minimum supply of nutrient vessels. This explains the fact that we may dissect out an artery completely from its surroundings without affecting its nutrition, and again, that the artery retains its marvellous powers of healing, although cut off from its original base. The blood-supply of the arterial wall explains another and almost more important fact and that is, as Virchow puts it, the arteries act as isolators of pathological processes. All this changes as soon as pathological conditions arise in the artery, from within or without. Then the connective tissue and above all the vasa vasorum begin to proliferate and finally we find vein and artery alike permeated throughout their whole breadth by numerous vascular channels. Such conditions are most common in vessels within the area of malignant growth and it stands to reason that such vessels are more likely to harbour the tumour cells than healthy ones.

We must next consider as to whether these degenerative conditions in the vascular system are the causes of secondary growth. I believe that our views as to metastasis have been much modified by recent experience, which goes to prove that both in man and animals tumour cells pass into the circulation already at an early stage of the malignant growth. Lubarsch, Borst and others are therefore surely right in declaring that we must clearly distinguish between embolism and metastasis in malignant growths as so many of the tumour cells are destroyed within the circulation before they establish secondary tumours. The conditions under which these arise are most complicated and probably depend upon a number of factors, partly of a chemical nature hitherto quite unknown. The question which has given rise to much discussion is as to how these cells get into the vascular system. There can be no doubt that vascular degeneration, such as I have described, is a predisposing factor, and yet Martin Schmidt has proved almost to a certainty that in his remarkable cases of abdominal cancer in which diffuse embolism of the pulmonary arteries took place, without the appearance of secondary lung tumours, the cells entered the blood-vessel through the thoracic duct. I am inclined to believe that we gain a more definite conception of the whole question of metastases only by paying due consideration to recent research work bearing on acute wound infection. Besides other I have above all Nötzel's work in mind; he has proved in a series of experiments conducted on rabbits that after injection of bacteria into the knee-joints these bacteria appear within a few minutes in the regional lymphatic glands and in the general circulation as well. The fact that these experiments were performed on healthy joints without any damage to them and also without undue pressure of the injected material allows of one conclusion only, that the absorption of the injected bacteria was effected by the lymphatic system. The rapid dissemination of the germs in these experiments appears to clash with the current theory of lymphatic circulation, inasmuch as the interposition of lymphatic glands has always been regarded as a retarding factor. Nötzel justly reminds us that even in the lymphatic glands anastomoses exist between afferent and efferent vessels and that according to the extensive investigations of Druner such anastomoses are a most common occurrence among the larger lymphatic ducts. This, again, concurs with our surgical experience, which has shown that transverse ligature even of the thoracic duct, has no evil effect upon the lymphatic circulation. On this basis we fully understand how germs travelling along the lymphatics enter the vascular system both rapidly and without necessarily passing the lymphatic glands. We must therefore cease to regard the lymphatic glands as local centres of defence or as filters. All these facts have, to my belief, a most important bearing upon the problem of tumour metastasis.

As regards the relations between the lymphatic and vascular system I am inclined to assume that they are far more intimate than we have hitherto believed. It has struck me that on injecting veins, such as the jugular, which are encompassed by lymphatic glands, the injected fluid passes with greatest ease into the glands, from which I infer that the vascular system of gland and vein are closely associated. But there must even be relations of a more direct nature between the two systems.

I will not dwell upon the subject of hæmolymph glands which are said to occur in man also. I only wish to draw your attention to recent embryological research. Serbin of the Johns Hopkins University has shown that in man and mammalia of a higher order the whole of the lymphatic system is a derivative of the veins not only of the jugular but of the iliac veins as well. Numerous instances have been recorded by anatomists of the older school in which great lymphatic trunks have been found to enter into other than the jugular veins, such as the iliac, azygos, and others. Unfortunately Henle's repudiation of such observations has debarred others from following up more closely the question whether such connexions actually exist, or whether they are to be regarded as exceptional. Not until all these dubious points are perfectly cleared up can we hope to understand the question of metastasis in general and of tumour metastasis in particular.

I have arrived at my second point: What are the general conditions of circulation in malignant growths? For information on this score we are obliged to go far back into the history of medical science, back to the writings of John Hunter, Schroeder, van der Kolk, Broca, and others. In recent years Ribbert has been the only one who has dealt with this question in a short paper, in which he endeavours to prove that the deficiency of blood-vessels in carcinoma is the cause of cell necrosis. In order to elucidate this point more precisely I have applied different methods for the human individual and the mouse. In cases of human cancer I exposed the femoral artery and injected an emulsion of bismuthum and oil into the blood-vessels. After tying the afferent and efferent vessels of the cancerous organ I dissected them most carefully from their surroundings and exposed them to the x rays. Such injection specimens are incomplete from an anatomical point of view, yet they give us a general idea of the state of vascularisation in cancer. I mean to show you a serious of plates demonstrating cancer in the liver, stomach, bowel, bladder, and lung.

On examining these various plates, the first point that strikes us is, that the regular distribution of blood-vessels is disturbed by the invading growth. We know from the splendid work which Mall and his pupils have done that the distribution of blood-vessels in the various organs is absolutely characteristic of them, and chiefly dependent upon their embryological development. As soon as a tumour develops in the liver, stomach, or any other organ, you see that this regularity gives room to chaotic irregularity. Then again we find that in the growing tumour extensive new formation of blood-vessels happens. This is most apparent in the zone of proliferation, which in infiltrating tumours corresponds to their periphery. As the cancerous growth increases in volume its centre gives way to necrosis and the newly formed blood-vessels merely occupy its capsule. Ultimately the blood-vessels seem to disappear altogether, so that in this stage cancer is far from rich in blood-vessels, but rather denuded of them. The mass of newly formed vessels is of small calibre and their branching is irregular to such an extent that big vessels split up into the smallest of their kind without intermediary types.

In order to amplify the results obtained in man I have injected spontaneous and experimental growths occurring in mice by means of the following method. After exposing the heart of the anæsthetised animal I punctured the heart and injected Indian ink, avoiding excessive pressure. Indian ink, as the Johns Hopkins School of Anatomy has shown, is a medium which flows easily into the blood-vessels and mixes freely with the blood. By manometrical regulation of pressure we are enabled to modify the result of the injection according to the desired effect. After injection the specimens were fixed and hardened in alcohol. For microscopical purposes transverse, and in some cases serial, sections of the whole animal were made which enabled us to gain an exact estimate of the relations existing between the transplanted growth and the surrounding organs. Such specimens likewise provide us with the power of judging of the origin of the newly formed blood-vessels, of their number, form, and width, as compared with adjacent tissues or organs.

Another set of specimens was cleared after the Schultze method by placing them first in alcohol to which a few drops of potassium hydroxide solution were added, then removing them into glycinerated alcohol, and, finally, into pure glycerine. Marked differences in the whole arrangement and number of blood-vessels were discovered in the various malignant tumours examined. One common feature was observable in all of them. As soon as infiltrative growth of the transplanted cells sets in a great commotion is produced in the system of surrounding blood-vessels. The degree of commotion is dependent upon the wealth of pre-existing vessels, hence in strongly vascularised tissue, such as the mammary gland or the muscle, the vascular irritation is far more pronounced than in the subcutaneous tissue poor in vessels. This irritation presents itself most distinctly in the vessels facing the growing tumour and can easily be traced in regions to which the tumour has not yet advanced. The most striking feature of this irritation is the dilation of the affected vessel. It curls itself up into spiral coils and sends forth numerous capillary offshoots towards the invading growths. In carcinoma the newly formed vessels arrange themselves almost entirely in the peripheral area. In relation to its increasing volume the number of vessels found in carcinoma decreases and eventually they disappear altogether, most especially in cases where complete necrosis happens.

In sarcoma, again, the numerous vessels of new formation are evenly distributed throughout the whole growth, presenting themselves as a delicate closely woven network even in the interior of the tumour. Nowhere are the differences as to vascular supply between carcinoma and sarcoma more apparent than in mixed experimental growths of the carcinoma sarcomatous type. Even in cleared specimens it is easy to single out the cancerous and sarcomatous spaces by the varied degree of vascular injection.

Wholly different are the appearances in chondroma of the mouse. As Ehrlich has shown, this extraordinary growth presents a blood-red surface on dissection, from which he infers that its cells have distinctly angioblastic properties. I found that its capsule is rich in vessels and likewise the derivatives of the capsules, the wide bands of connective tissue, which separate the islands of cartilage. A large number of these vessels penetrate into the cartilaginous masses and open out into the large vascular spaces, apparently losing all the characteristics of blood-vessels. These vascular spaces disintegrate the cartilage tissue. Numbers of cartilage cells are thus destroyed.

Since these various tumours are produced in the same species of animals by units of implanted cells the results obtained bring two points into clear prominence. One that has been recently demonstrated by Bashford and others is that the stroma of experimental tumours owes its origin to the inoculated animal and is not derived from the grafted cells. Another point of greater importance is the fact that the structural qualities of the stroma are determined by the tumour cell.

From what I have said regarding the vascular condition of carcinoma and sarcoma it might appear that there is a fundamental difference between them inasmuch as the new formation of blood-vessels in sarcoma is so much richer than in carcinoma. This view has been advanced by many of our leading pathologists who maintain that carcinoma and sarcoma, owing to their genetic affinity to the epithelial and connective-tissue cells, react respectively upon the lymphatic and vascular system. Unfortunately we know next to nothing as to what changes carcinoma induces in the number of lymphatic vessels. All we know is, that a reproduction of lymphatic glands sets in, in a manner first described by Bayer and recently confirmed by Ritter, who goes the length of proclaiming that the swelling and new formation of lymphatic glands is a typical and early response on the part of the body to the invading cancer cell.

As against the theory of diminished vascular activity in cancer, it may be stated that various forms of cancer vary in their wealth of blood-vessels. Bashford has acquainted us with the interesting fact that in his long series of experimental cancer he has observed complete and distinctive differences in his strains. A tumour which was poor in vessels and widely necrosed was transformed into one of exactly opposite qualities. In this connexion I may refer to Ehrlich's interesting observation on the transformation of carcinoma into sarcoma in the mouse. As you know, Schmorl was the first to record a similar case in man affecting the thyroid gland. But recently I was obliged to deal with a case of mammary cancer in which complete removal of the breast and the axillary glands on both sides failed to have the desired effect. Numerous secondary growths formed in the front chest wall. After the patient had recovered from a bad attack of pneumonia and extensive suppuration spreading over the front chest wall, the metastatic tumours in the skin broke down and formed polypous, extremely vascular, growths which ultimately led to the patient's decease. On examining these tumours of the skin in their later stages it was found that all traces of cancer had disappeared and that fusiform-celled sarcoma had taken its place. On the strength of all this evidence I do not hesitate to declare that the difference in the vascular activity of carcinoma and sarcoma is a quantitative and not a qualitative one. A difference merely exists as far as the destructive powers of the carcinoma and sarcoma cells are concerned, since destruction of blood-vessels is so very much more apparent in cancer than in sarcoma.

I mentioned that the impetus which gives rise to the proliferation of blood-vessels emanates from the invading cell. On the other hand, the study of experimental tumours has proved that the new formation of blood-vessels itself is dependent upon the general powers of the individual to react, as well as upon the physiological condition of blood-supply in the invaded tissues. It seems more than probable to me that in a system weakened by age or pre existent disease the vascular reaction induced by the malignant growth remains below the mark or fails to take place, thus giving rise to a condition first described by Thiersch as premature senescence of the connective tissue in cancer.

In any case, I regard vascular neoformation as a standard by which we may test the body's power of reacting against malignant tumours. On the other hand, we can measure the virulence (*sit venia verbo*) of the tumour cell by the extent of necrosis found in the growth. I suppose most pathologists of the day are agreed that necrosis is not caused by accidental reasons, such as pressure, malnutrition, and others. Borst has rightly pointed out that in growths highly vascularised necrosis is a common occurrence. I may refer you to the case of chondroma in the mouse, a growth essentially vascular and yet permeated by cell necrosis.

Necrosis, as Ritter has put it, is bound up with the primary cause of the disease, in the same sense that it is in tuberculosis or other infectious diseases. I differ from Ritter in one essential point. He looks upon the border of healthy cancer cells surrounding the necrotic area as a reactive cell proliferation on the part of the body and the area of necrosis as the tumour *sensu striotiori*. These cells on the necrotic border, I rather believe, are the militant survivors of the invading brood, whereas the body's reaction is marked, as I have tried to show, by the newly formed blood-vessels and connective tissue. The area of necrosis is, in my opinion, the battlefield on which assailant as well as the defender perish, for it is not only the tumour cell that is destroyed but the stroma as well.

I have reached my last point in considering what purpose the new formation of blood-vessels serves. It seems to militate against all our modern views concerning the functions of the blood if we assume that only nutrient and not also defensive material is borne along the newly created blood channels. How can we account for the difference of vascularisation in the healthy and diseased blood-vessel on the basis of a nutritive theory. A healthy artery performing vital functions has a minimum of nutritive vessels confined to its outer coat. As soon as disturbance of any kind sets in blood-vessels spring up and ramify throughout the whole breadth of the vessel's wall. Is it at all probable that the body would produce such a mass of vessels in order merely to feed a circumscribed thickening of the inner coat, frequently the only anatomical lesion definable? Does it not seem far more likely that the newly formed vessels serve an intensified circulation in the arterial coat, thus guarding it against change from within or without? Here, again, as in the case of Ehrlich's side chains, is an instance of an arrangement in the body originally destined to safeguard one of its organs but eventually developing into a cause of harm. In this connexion I may recall to your mind observations of my own recently confirmed by Schmidt, Lubarsch, and others. Tumour cells constituting a thrombus or embolism may multiply within a blood-vessel and spread along its branches without forming adhesion to the vessel's coat. In case such adhesions form—i.e., as soon as infiltrative growth occurs—the mass of cells is organised in the fashion of the ordinary blood clot. In such cases it is quite the rule to observe that the cells degenerate frequently to such an extent that the cancerous nature of the thrombus or embolism is completely obliterated. Only by means of serial sections may we determine the true genesis of the organised thrombus. I am certain from my experience that similar conditions frequently prevail in lymphatic glands, apparently the seat of secondary cancer. Clinically all the symptoms of regional metastasis are evident, and yet histological sections of the gland merely reveal inflammatory hypertrophy. This accounts for the great difference of opinion amongst gynæcologists as to the advisability of removing lymphatic glands in cancer of the womb. I do not hesitate to declare that, as in the case of cancerous embolism, careful examination of the glands in serial sections would show that they contain isolated cancer cells but that the bulk of these cells has undergone degeneration. All these facts prove that the body commands powers of combating cancer and healing it. An overwhelming amount of evidence on this score has been recently brought to light by Lomer. He refers to upwards of 200 cases of cancer in which the clinical diagnosis was almost invariably confirmed by histological examination and in which recovery set in, partly without surgical interference, partly after incomplete removal of the growth. In his first series of cases the cure was preceded by constitutional alterations of the blood induced by febrile infections of general nature, by severe hæmorrhage, by extensive burns, and by blood poisoning. In the second series the cut surface of the incompletely removed growth was cauterised by heat or by chemical agents.

Are we justified in doubting the potential efficacy of the x rays and radium in cancer in the face of all that has been recorded in man and animal? If we analyse the anatomical basis of all those cases of cancer in which complete recovery or retarded growth has been achieved spontaneously or by means of mechanical, physical, and chemical agents, we always discover the same reaction on the part of the body—namely, the formation of stroma. It is of great interest, perhaps also of fundamental importance, that extensive local hæmorrhage serves as the precursor of this cell proliferation.

From these remarks it might appear that I regard the blood-vessels themselves as agents of defence. On the contrary, I staunchly uphold Virchow's doctrine, so ably confirmed by Ehrlich's famous researches on the varied powers of oxidation in the body, that the cells are not fed by the blood-vessels but that the cells fed themselves. Therefore I regard the network of newly-formed vessels merely as the useful means of more active blood circulation. Intensified circulation itself, if I may so call it, is the effect of all those healing powers which I have just referred to, inclusive of inflammatory agents, such as have recently been recommended for the treatment of cancer by Bier and others. The efficacy of this intensified circulation is naturally dependent upon the presence of defensive factors in the blood. It will remain a subject for future research to discover what these defensive substances are and, above all, where they are manufactured. It seems to me that our present clinical and pathological knowledge already enables us to infer that the body's first line of defence is established on the boundary of the invading growth. From this point of view we understand cases like the following, which I believe have come within the notice of every surgeon. Patients suffering from cancer of slow growth and long duration are advised to have it removed instantaneously. The operation is successfully performed and the healing process is normal. Yet the patient returns within a short time suffering from a recurrence which has grown rapidly and has assumed features of an alarming nature. It appears to me that in such cases the surgeon's knife has done harm. In removing the growth he has destroyed the barrier of defence which the body has carefully raised up during the long period of the tumour's existence. I know full well that many of my surgical colleagues will disagree with me. And yet I feel that the time has come for us to consider whether stereotyped surgical interference is the only remedy of the future for malignant growths. Should we not rather begin to individualise as we do in every other disease which is brought to us for treatment. But how can we individualise if we pay no attention to the individual characters of the case we treat, if above all things we pay no heed to the efforts of the body to ward off the threatening danger? Can we wonder that such contradictory views still exist as to the rational and radical treatment of cancer? All of you know too well what a marked contrast there is concerning the operative treatment and its ultimate results in mammary or uterine cancer as advocated by Bryant, Halsted, by Wertheimer, Olshausen, and others. Nothing is more harmful to the progress of our science than doctrinary stagnation. We should not pause before the spectre of apparent retrogression. In our attempts to force the stronghold of cancer we fare no better than the engineer whose railroad winds round and round the height he means to pass. And yet how comforting the knowledge that whenever we complete a circuit we have ascended to a higher level of truth.

If I have succeeded in proving to you that it is our duty not only to study the biological problem of the tumour cells but to gain a deeper insight into the defensive agencies of the body as well, the purpose of this lecture has been achieved.

As the practical result of my work I regard the following: A careful study of the vascular conditions prevailing in malignant growths affords an anatomical test of the reactive powers of the body. It will be necessary to collect more extensive evidence on these lines in order to bring it into closer relation with our clinical knowledge of the varied appearance and history displayed by the different forms of cancer affecting the same organ. In future, for example, in the case of the mamma it will not be sufficient for clinical and therapeutical purposes to distinguish between scirrhus, adenoma, &c., from a purely histological point of view as to the arrangement of the tumour cells, their different forms of degeneration, &c. It is equally important to discover their reactive powers on the body as tested by stroma formation. By this means we shall sooner realise my demand for treatment based upon a knowledge of the individual qualities of the growth.

On a future occasion I may be permitted to give you an account of my investigations into the causes of retarded metastases and into the peculiar vascular conditions prevailing in localities predisposed to malignant growths. Above all things, I hope to be able to report on a first attempt to penetrate into the darkness of physiological conditions existing in malignant growths. I am engaged in research on the varied powers of oxidation and reduction characteristic of the various tumour cells.

I have purposely refrained from comparisons of any kind between malignant growths and infectious diseases and yet it will hardly have escaped your notice that every point which I have discussed revealed most striking analogies between them. As far as syphilis and tuberculosis are concerned I have dwelt upon these analogies exhaustively in a paper read before the International Cancer Congress at Heidelberg.

A CASE OF RUPTURED BLADDER: OPERATION 42 HOURS AFTER THE ACCIDENT; RECOVERY.

BY P. H. LANG, M.B., CH.B. MELB.

THE patient, a man aged 49 years, working on a station in the district of Camperdown as men's cook, was thrown out of a buggy on the evening of May 26th owing to the wheel striking a stone. He was driving home after spending the Sunday afternoon at an adjoining station, and had taken several drinks but said that he had passed urine about an hour before the accident. Directly after the fall he felt severe pain in the abdomen, and this became worse during the night. On the morning of the 27th he had frequent desire to micturate but could pass nothing, and had passed no urine since the accident. By this time the pain was extremely severe, and the only position in which he could get any ease was standing in a crouching position hanging with his hands on to a rope tied above his head. This position he maintained for the next 28 hours. Owing to a groundless fear of getting their mate into trouble none of the other men said anything to the owner of the station in regard to the cook's condition, and the only treatment they adopted was occasionally to bathe the genitals with hot water in the hope of getting him to pass urine. Finally the patient's condition became so bad that some of the men informed "the boss," who, recognising that the case was urgent, sent him into Camperdown and lodged him at the private hospital. The distance is close on 20 miles, but was quickly covered by motor-car; the patient, being unable to sit down, stood in the tonneau of the car with his elbows resting on the back of the driving seat and a man sitting alongside held him from falling over during the journey. He was admitted on the morning of the 28th. On arrival at the hospital he was able to walk, with the body very much bent forward, but on lying down he had terrible pain, so bad as to make him scream out. He was quite unable to extend the legs, but they had to be held up with the knees bent to make the pain at all endurable while he was being examined. His temperature was 97·4° F. and his pulse was 120 and of very poor volume. The face was drawn, the expression was anxious, and the breathing was hurried. The abdomen was distended, dull in the flanks, and resonant elsewhere. No motion or flatus had been passed since the accident, and all the urine passed had been a few drops on the day following the accident. Vomiting was frequent, occurring every few minutes, a few ounces of dark-coloured fluid being brought up each time without apparent effort. This was very offensive in smell but was not fæcal. On passing a catheter a few ounces of deeply blood-stained urine were drawn off. As it was plain that the bladder was ruptured preparations were made for immediate operation. The patient had been given a hypodermic injection of morphine immediately the examination was completed and a diagnosis arrived at. Just before being placed on the operating table he was given a hypodermic injection of strychnine.

The abdomen was opened by the usual median incision below the umbilicus. On incising the peritoneum a regular fountain of blood-stained urine shot out, having evidently been under considerable pressure. Several quarts of this urine were present in the peritoneal cavity. The coils of intestine which presented in the wound were very distended and a general peritonitis was present. There was a rent in the posterior surface of the bladder sufficiently large to admit three fingers. Even with the patient in the Trendelenburg position, with the distended intestines shut off with flat gauze pads, considerable difficulty was experienced in obtaining good access to the wound in the bladder owing to the thickness of the abdominal walls The rent in the bladder was sewn up as accurately as possible with catgut in iodine solution. Owing to the sodden and swollen state of the tissues it was difficult to make out accurately the demarcation between the bladder and peritoneum at the site of the rent, and one felt rather dubious as to whether the stitches would hold, since the tissues seemed very rotten. At this stage of the operation the patient's condition was extremely bad, so the peritoneal cavity was rapidly washed out with normal saline solution, the wound was sutured up in one layer with silkworm gut, and a large rubber drainage-tube was left in the lower angle of the wound to drain the pelvis, while a strip of gauze was passed down beside the tube to the site of the sutured wound in the bladder. A catheter was passed and tied into the bladder. The head of the patient's bed was raised and he was also propped up to some extent with pillows with the object of causing fluids to gravitate away from the more absorbent zone of peritoneum about the diaphragm into the pelvis. Hypodermic injections of strychnine were ordered every four hours, one-grain doses of calomel were given every hour for six doses, and the patient was infused to the amount of several pints in the next 24 hours. In addition to this large rectal injections of normal saline solution were given every four hours, with the object of reversing the current of the lymph stream—the idea being, according to an article by Mayo Robson in THE LANCET of Dec. 29th, 1906, that large rectal injections cause the mouths of the peritoneal lymphatics to pour out fluid which carries septic material into the pelvis instead of their absorbing this septic material as is usually the case. After the operation vomiting was frequent, dark-coloured fluid being brought up without apparent effort every ten minutes or so. This vomiting continued for four days with longer intervals gradually occurring between the vomiting, so that on the third day it only occurred every hour or so. For about two days the vomit consisted of a dark brownish-coloured, very offensive smelling fluid, which, however, was never distinctly fæcal in character. On the second day attacks of hiccough were frequent, but by the fourth day there was only an occasional short attack of hiccough, and it ultimately subsided.

Up to the fourth day the patient was kept going with nutrient enemata in addition to the rectal injections of normal saline solution, but by the fourth day he retained small drinks of iced brandy and water and peptonised milk. The patient's temperature was subnormal on the evening following the operation and the pulse ranged between 120 and 140. On the day following the operation the temperature was 98·4° and the pulse was between 120 and 140. On the succeeding day the temperature rose to 102° and the pulse-rate kept over 120. From this time both temperature and pulse came steadily down until by the fourth day the morning temperature was 98·4° and the pulse was 62. In spite of frequent enemata and aperients (none of the latter of which were retained, however, owing to the vomiting) no action of the bowels occurred until the third day and the abdomen remained very distended. On the third day there was a free action of the bowels, and after this for 24 hours the bowels were quite beyond the patient's control and were moved very frequently. The catheter was removed on the fourth day after operation and the patient after this passed urine himself. The wound drained well and there was no leakage of urine until the seventh day. A urinary fistula then developed and the greater part of the urine was passed through the wound. This fistula finally closed and six weeks after operation the patient was up out of bed with the wound quite sound.

The endurance of the man was remarkable. When the pain became so bad as to render it impossible for him to lie down he adopted the position of greatest ease—i.e., standing on the floor with the body crouched and supporting his weight by hanging on to a rope tied above his head. This position he maintained for 28 hours and though in terrible pain was anxious to continue in this way so as to avoid informing "the boss," as he said he thought "it would work off." He then had a long motor journey of close on 20 miles and was unable to sit down all this time, but stood in the tonneau of the car with his elbows resting on the back of the driving seat while a man sitting beside him held him from falling over. In all about 42 hours elapsed from the time the bladder was ruptured until he was operated on.

My thanks are due to Dr. J. G. Desailly for his skilful assistance and advice during the operation and to Dr. Haynes for the way in which he administered the anæsthetic.

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