CLINICAL ASPECTS OF THE CANCER PROBLEM

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It is not my purpose at this time to discuss the laboratory studies of cancer nor to make any references to the enormous literature on different phases of this vast subject, but rather to draw certain conclusions from the experience of my associates and myself in the treatment of 7,005 cases of cancer.

It is obvious that no one general rule of treatment, whether by surgery, irradiation or both can apply equally to malignant tumors of the different organs and tissues. Two general rules may, however, be stated and should be emphasized: (1) when possible every precancerous lesion should be removed; and (2) an established cancer should be removed radically if it is operable; if inoperable then palliative surgery or radiation or both should be applied.

From the mass of investigations into the cause and treatment of cancer no other safe method of dealing with a cancer has as yet evolved. From all of these studies which have included the incidence of cancer in relation to race, climate, age and the bodily tissues, method of growth, the effects of various physical and chemical agents, we have learned one sure fact, namely, that cancer, whether of the external and visible parts or of the internal, invisible organs, obeys one general law of growth, and the old dictum based entirely upon clinical experience is established more uniformly than ever — namely, that the one and only cure for cancer is its early and complete removal. It is probable that with extending knowledge of the operation of physical laws in biological processes, new light may be thrown upon the causation of malignant growths, and that from this knowledge new methods of cure may be evolved. Already, investigations have shown that the electric capacity and conductivity of cancer of any part far exceeds the capacity and conductivity of the normal tissue, while the potential in cancer is opposite to that in normal tissue. The histologic appearance of a cancer offers a static picture of the cells. The capacity and potential measurements present the dynamic status of the cells, and it is with the dynamic status of the cells that we are primarily concerned in interpreting the status of any malignant or pre-malignant condition.

Whatever these and other investigations may disclose in the future it is true that at present we must be guided by clinical experience and it is in order that these personal experiences of my

associates and myself may be evaluated with those of other reporters that this paper is offered.

Before proceeding to a discussion of cancer of the different organs and tissues, a statement regarding precancerous lesions should be included here. To my knowledge no cancer of the skin has ever grown upon a normal uninjured surface. Cancers of the skin are always located where there have been tumors, scars, moles, warts, keratoses or some form of irritation. The precancer stage may be a long one — a story of little scales picked off as often as they appeared; of a wart frequently irritated; of a neglected ulcer; of occupational irritation, etc.

Rarely, if ever, does cancer of the mouth occur in a perfectly sanitary mouth with normal teeth. There is always present an irritation from a ragged tooth, from leukoplakia, a fissure or a wart.

So, too, we know of few cancers of the gall-bladder without gallstone irritation; few or no cancers of the kidneys without stone irritation. In the intestinal tract cancer selects irritated areas such as the esophagus, the pylorus, the splenic flexure, the rectum.

We may conclude, therefore, that, in general, a precancer stage usually if not always exists and that in most instances the precancerous condition is remediable. Yet in spite of this fact, even in the visible precancerous conditions, how frequently do the physician and the patient supinely and irresolutely wait for disaster.

If every chronic irritation were removed; every chronic ulcer, wherever located, healed or excised; if every wart and mole were removed and every keratosis cured; if the mouth were kept wholesome and the teeth smooth; if unhealthy scar tissue were always removed and if needed the surface covered by skin grafting, then the problem of cancer of the skin and the mouth could be measurably, if not completely, solved.

The precancer conditions in the internal organs are in many instances no less amenable to treatment; the syphilitic ulcer or the papilloma which induces cancer of the larynx; the chronic ulcer of the stomach; the irritating stones and chronic inflammations of the gallbladder; the ulcers and chronic irritations of the large intestine and the rectum; the stones in the pelvis of the kidney; the benign tumor or inflammation of the breast; and so on through the long list of sources of irritation.

In view of this potency of the precancerous lesion the dictum that every precancerous lesion should be removed when removal is possible is secure.

The Skin: Radium appears to be the most efficient method for the treatment of cancer of the skin and subcutaneous tissues according to our experience with 597 cases with one exception — a pigmented mole should always be excised.

Cancer of the Buccal Surfaces: A study of 4500 reported autopsies performed in patients who had died from cancer of the head and neck made for me some years ago by Dr. L. W. Hitchings showed that in less than one per cent were secondary cancer foci found in distant organs and tissues. This localization of the cancer is due to the protection afforded by the collar of lymphatics of the neck, every portion of which is readily accessible. As far as metastatic dissemination is concerned cancer of the head and neck presents a far more favorable outlook than does cancer of the breast, the lymph channels from which lead to thoracic and abdominal metastases, or cancer of the stomach or intestines with its inaccessible retroperitoneal and liver metastases.

Above this lymphatic barrier metastases may take place rapidly, although cancer of each part of the head seems to follow a law of its own. Thus, cancers of the skin, of the mucous membrane of the cheeks, of the mucous membrane of the edge of the jaw, usually do not metastasize; cancers of the lip almost uniformly metastasize to the lymphatic glands under the jaw; cancer of the floor of the mouth usually metastasizes in the glands of the same side. Paired organs or distinctly one-sided foci usually metastasize regularly; while unpaired organs, as the tongue, or mesial tissue, such as the middle of the lip, metastasize irregularly and widely. For example: a marginal cancer of one side of the tongue may metastasize to the glands of the opposite side, usually low down toward the clavicle, although the metastasis may occur at any site, high or low, on the right or the left side.

Early cancers of the buccal surfaces are usually treated by radium but once they've advanced to the stage where lymphatic invasion is possible not only should the primary focus be removed but a block dissection of the regional lymphatics should be done also. The local excision of the primary focus alone is as illogical as the excision of a cancer of the breast without the removal of the regional glands. Next in importance to the block regional excision is the minimum handling of the carcinomatous tissue to avoid the possibility of the implantation of cancer cells in the operative field. In certain cases cauterization is the method of choice for the removal of the primary focus. Thus cancer within the mouth may be destroyed completely and more easily by the cautery than by surgical operation. In the choice of method, however, it should be borne in mind that surgery

produces the best scars, and when the cancer is in the cheek or well back in the jaw the cautery may produce a badly contracting scar and a plastic operation in a postoperative cancer field is to be avoided. Moreover, the cautery does not provide for the removal of a "platter" of underlying bone as is advisable in cases of cancer of the buccal mucous membranes.

It should be emphasized that while radiation of the local lesion may be indicated, radiation of the involved lymphatic glands of the neck should not be done, as this treatment cannot be depended upon. If the glands of the neck have been irradiated and the patient has recovered, we must conclude that the glands of the neck probably were not involved. After operation on any part of this field, postoperative treatment with deep, accurately measured x-ray or radium radiation is of advantage.

Our series includes 564 cases of cancer of the buccal surfaces among which there were 259 cases of cancer of the lip, and 128 cases of cancer of the tongue.

The Antrum: In the treatment of cancer of the antrum, of which our series includes 30 cases, any method which destroys the tumor is of value as it is enclosed in a bony box. Treatment with radium is, therefore, eminently successful although the application of diathermy and the electrocautery may be followed by good results. Whatever method for the removal of the tumor itself is employed a wide open surface wound is necessary, a point which has been emphasized by Dr. T. E. Jones, as this makes it possible to see and treat any recurrences as soon as they develop.

The Larynx: In view of the strategic position and importance of the larynx in its relation to the respiratory tract, it is not surprising that the encroachment upon or within it of a malignant growth should be viewed by the layman with peculiar and almost hopeless dread, or that the successful removal of the larynx should be one of the later achievements of surgery. Yet the complete extirpation of an intrinsic cancer of the larynx is one of the most successful operations for cancer as far as the ultimate cure of the cancer is concerned, and the comparative safety of the laryngectomy itself is attested by the fact that in my own series of cases the mortality rate compares favorably with that of excisions of the tongue or of the rectum for cancer.

The ultimate cure of a given case of cancer of the larynx depends principally upon whether it is primary or secondary; and if primary, whether it is intrinsic or extrinsic. If secondary, the cancer is an extension through the lymph channels from the tongue, throat or

some other part of the head or neck, and it is obvious that, in such a case, the removal of the larynx would almost inevitably be futile.

Extrinsic cancer of the larynx, as the term implies, has its origin in some part or parts outside the larynx proper, such as the epiglottis or the arytenoids. Because of the abundance of lymphatic connections, this form of laryngeal cancer extends rapidly and is quickly fatal, and operation for its relief is at best but a desperate palliative remedy.

Intrinsic laryngeal cancer, on the other hand, starts within the larynx itself, in the vocal cords, the ventricular bands or the parts below. Since the walls of the larynx consist of hyaline cartilage, and cancer can rarely penetrate cartilage, intrinsic cancer of the larynx is contained as it were in a safety deposit box. Its only avenues of egress are through the thyro-hyoidean membrane, through mucous membrane invasion upward, and to a very limited extent through the sparsely supplied lymphatics. Because of the early involvement of the vocal cords, the presence of the cancer is early made known by every spoken word and there is a persistent hoarseness which promptly leads the patient to seek relief. Not every instance of chronic hoarseness, however, is due to cancer.

In extrinsic cancer of the larynx the only hope lies in the local removal of the growth and a block dissection of the gland-bearing area. In inoperable cases in which only tracheotomy can be attempted radium is of value as a palliative measure.

For intrinsic cancer of the larynx, laryngectomy is indicated. If the cancer is entirely intrinsic, laryngectomy offers a practical certainty of cure. Radium, therefore, is not indicated but the postoperative application of the x-ray may be of value as it may check any extension of the growth for there may be some undiscovered extrinsic focus or some cancer cells may become imbedded in the course of the operation.

Our series includes 159 cases of cancer of the larynx, in 74 of which laryngectomy was performed. Among the patients regarding whom we have later data, seven have survived for more than five years; of these seven patients, one has lived 17 years and one 31 years.

The Thyroid Gland: In our total series of 16,770 thyroidectomies there has been a malignant tumor in 265 cases. In about 90 per cent of these cases malignancy was due to the degeneration of an adenoma. For this reason I believe that all adenomata should be removed. Treatment of malignant tumors of the thyroid gland is thus mainly a problem of prevention. Once malignant changes have taken place in the gland, it should be removed surgically if

possible; otherwise, it should be treated with x-rays. If the malignant process has developed to the inoperable stage, a decompression operation will give temporary relief from obstruction and the resultant partial asphyxiation, and this operation should be followed by radiation.

It has been estimated that in the average case of inoperable carcinoma of the thyroid the patient will live without radiation for approximately a year. There is, at present, no basis upon which to found a judgment as to the average length of life when such a case is treated with radiation. In all cases of malignant disease of the thyroid, however treated, the possibility that myxedema may develop should be borne in mind. This condition, however, is readily corrected by the administration of thyroid extract.

Sometimes, as the result of radiation, the carcinoma will disappear; in other cases radiation seems to be of no avail. What the end-result of decompression and radiation may be in any given case cannot be foretold, but the patient is certain to have a period of relief. It must be borne in mind that involvement of the neighboring tissues is almost sure to be present, and that if the cancer involves the trachea there is practically no hope of cure.

The Breast: The one important point to bear in mind in the consideration of any tumor of the breast is that it may be the starting point of a malignant growth. This is true whatever etiological factors may seem to have been involved in the formation of the tumor; whatever its site, whatever the age of the patient, whatever the family history may disclose. There are certain lesions of the breast, however, which may safely be omitted from this generalization; simple cysts, lipomata, traumatic fat necrosis, hypertrophy, acute mastitis, mastitis neonatorum, mastitis adolescentium, echinococcus cyst, and syphilis.

Chronic mastitis deserves special consideration because of the diversity of opinion as to its cancerous potentialities. In general it is acknowledged that a lesion of this type may become malignant, especially if the lesion is unilateral. If the condition is present in both breasts malignant changes almost never develop.

In regard to the so-called benign tumors, Deaver has stated, "Tumors of certain types having certain structure are constantly harmless; those of other types, having another structure, are persistently invasive, destructive and constantly fatal. Unfortunately these are the extremes of a series between which lie many tumors that may or may not be harmful, or whose structures may fail to give a clue to their true disposition." I am far from recommending the radical operation in every case of tumor of the breast, but I do

wish to emphasize the importance of frequent examination of the breast after the local excision of what appears to be a benign tumor, so that the radical operation may be performed immediately if the lesion shows any suspicion of malignancy. A biopsy should never be performed, for if the growth should prove to be malignant there is danger of its dissemination, and whatever its character, in any case it should be removed entirely and then sectioned.

Since the potentially precancerous lesion may be treated by simple excision, while once malignancy has been established the regional glands must be removed also, the problem for the surgeon is the accurate differentiation between benign and malignant tumors. Frank cancer is easily diagnosed, but the diagnosis of border-line cases is by no means a simple problem. Bloodgood at one time submitted specimens from over sixty border-line cases to a number of pathologists. These pathologists were divided into two groups, one of which favored a diagnosis of cancer, the other believed the growth to be a benign lesion. "In not a single case has there been a uniform agreement as to whether the lesion was benign or malignant."

Ewing states that "the great majority of mammary cancers are rather easily recognizable by inspection and palpation." In cases in which the clinical symptoms and the frozen section cannot give absolute proof of the character of the tumor, the utmost safety of the patient demands the complete excision of the breast and of the regional lymphatics, for unlike cancer of the head and neck or the imprisoned, intrinsic cancer of the larynx, the abundant, lymphatic channels from the breast may readily and easily produce thoracic and abdominal metastases.

There has been a great deal of discussion during recent years regarding the relative values of radium combined with deep x-ray therapy and of radical operation in the treatment of breast carcinoma. These discussions have centered about three phases of the problem: (1) the value of preoperative radiation; (2) the value of postoperative radiation; (3) radiation in preference to surgery.

From a study of the end-results in our own series, Portmann draws the following conclusions:

"1. Intensive x-ray therapy, especially by the cross-fire method, is not the preferred procedure for the postoperative treatment of carcinoma of the breast.

"2. Postoperative x-ray therapy by moderate repeated dosage decreases the number of recurrences and metastases, and prolongs the lives of many patients suffering from carcinoma of the breast."

We, therefore, give radiation therapy as soon as possible after operation, not waiting until the wound is healed. Only if a case is

entirely inoperable is radiation employed as a palliative measure instead of surgery.

Our series includes 1522 cases of cancer of the breast.

Esophagus: Cancer of the esophagus, of which we have seen 147 cases, is one of the most hopeless among malignant conditions, as the disease is usually well developed when diagnosed and the progress of the disease is always exceedingly rapid. Thus, in a study of 31 of our cases of carcinoma of the esophagus, the duration of symptoms had been less than 10 months in all but 5 cases, less than 6 months in 18, less than 3 months in 11, less than 1 month in 6, and yet in many of these cases emaciation and exhaustion as a result of dysphagia were already marked.

Cancer of the esophagus is one of the hopeless types of malignancy as the disease is usually well developed when diagnosed. The surgical removal of the tumor is an exceedingly formidable operation and is hardly justified, the best treatment being the application of radium through an esophagostomy, and this does little good. Deep x-ray therapy is not applicable to these cases, as radiation may produce fibrosis of the lung.

Stomach: As in the case of cancer of the esophagus, a cancer of the stomach is characterized by a rapidity of growth, and an extent of lymphatic involvement so that the "dead line" of inoperability is reached very early in its progress. A period of a few weeks may be sufficient to carry the patient from an operable to a completely inoperable condition and consequently in the majority of cases the patient comes to operation too late for possible cure. A study of the records of our 713 cases of cancer of the stomach shows that the history is commonly a history of vague initial symptoms of indigestion or ulcer; that ulcer of the stomach has a moderate potentiality as a precancerous condition; that the history and the x-ray findings coupled with the effects of ulcer management on the size of the mass as revealed by repeated x-ray examinations are the most valuable means of diagnosis; that a differential diagnosis between an old ulcer and early cancer cannot be made with certainty; that when the probability of cancer is suspected an exploration should be made at once. In late cases, as in late cases of cancer elsewhere, even though the operation is survived and the local lesion removed, there is great danger of metastases, especially in the liver or retroperitoneal glands.

When operable, as in the case of cancer elsewhere, resection with the widest possible excision of the growth is the indicated procedure. Blood transfusion, saline infusions, nitrous oxide analgesia, the application of hot packs and divided operation may

suffice, however, to carry through many patients in whom the prognosis appears to be hopeless, but in whom the anatomical possibilities of operations have not been passed.

Radiation cannot be applied in these cases because it is impossible to deliver sufficient radiation to the stomach to destroy a malignant process without harming the adrenals, liver, pancreas, etc.

Gallbladder: Carcinoma of the gallbladder is usually associated with cholecystitis and consequently in most cases the disease has extended into the liver and adjacent deep structures before the malignant condition is recognized, and it is then too late for any operation to be of avail. For this reason the prognosis is extremely unfavorable even after a radical operation. However, if the presence of the malignant condition is recognized before extension to the liver has occurred an immediate cholecystectomy is indicated.

Our records include 67 cases of cancer of the gall-bladder and bile ducts.

Intestines and Rectum: The diagnosis of carcinoma of the small intestine is made from the history and clinical signs and the x-ray picture. If the presence of a cancer is indicated then an exploratory operation should be performed to determine operability, with immediate removal of the growth if possible. As in the case of carcinoma of the stomach, every available method for the conservation and restoration of the patient should be employed. Our records include 25 cases of carcinoma of the small intestine.

As for cancer of the large intestine and rectum of which we have seen 819 cases, the following points summarize the present status of opinion regarding its treatment: carcinoma of the large intestine tends to remain local; wide excision of the cancer should be made — the excision including the related lymphatic glands; the cancer tissue should be handled lightly; in cases of acute obstruction a colostomy should be performed first and the resection deferred; postoperative radiation probably contributes to cure; the treatment of cancer of the cecum and of the ascending colon is more successful than that of cancer in any other portion of the large intestine.

It should never be forgotten that cancer of the large intestine, like cancer anywhere else, may spread by three routes: (a) by direct extension through tissue, (b) through the venous system, (c) through the lymphatic system. In cases of carcinoma of the large intestine and rectum, a colostomy should be performed, followed by radical operation, x-ray radiation being employed after the operation. In cases in which the growth is so low in the rectum

as to be readily accessible, the implantation of radium needles and the application of radium packs may be sufficient. In inoperable cases a colostomy should be done, followed by radiation. There should be a period of about ten days between the colostomy and the final operation, or rather, between colostomy and the decision as to the method of treatment, as a period of that length of time is necessary to allow the inflammatory reactions of the disease to subside sufficiently to make it possible to determine what operation shall be performed. This decision depends, of course, upon the findings of an exploratory operation. The entire picture may change during this period.

While the application of deep x-ray radiation is beneficial after operation or after radium treatment, it is of little, if any, value in the treatment of recurrences.

A statistical study of our cases made recently by Dr. T. E. Jones shows that after resection and radiation 20.6 per cent of the patients survived for more than five years, while this survival period was reached in only 7.2 and 7.4 per cent respectively of the cases in which resection alone or radiation alone was employed. These figures show, however, as Jones has reported, that although operation by the abdominoperineal route, combined with radiation, yields the best end-results with a primary mortality of 10 per cent, if operation is refused or if the condition is inoperable, there is sufficient evidence that a cure can be obtained in certain cases and marked palliation in others by the use of radium and roentgen ray.

Genito-urinary organs: In general, reliance must still be placed upon surgery for the treatment of carcinoma of the genito-urinary organs. In some cases carcinoma of the kidneys in children will be reduced by deep x-ray therapy, but the radiation must be followed later by surgery. In the case of deep-seated bladder tumors, radium has seemed to prevail in certain cases, but here also the results are still too uncertain for radiation to be used routinely. Postoperative radiation is employed in many cases, but more because it is hoped that it may be of avail than because of any definite results. For malignant tumors of the kidneys in adults the indicated treatment is surgery with radiation both before and after operation. In many cases radiation will so reduce the size of the tumor that cases which have seemed to be inoperable become operable. Tumors of the kidney should be irradiated no matter how hopeless their outlook. In the case of deep-seated bladder tumors, radium has seemed to prevail in certain cases, but the results are too uncertain for radiation to be used routinely. Postoperative radiation is employed in many cases, but principally because of the hope that it

may be of avail rather than because of any definite results that have been secured up to the present time.

Malignant tumors of the testes are treated by surgery with radiation both before and after operation.

Whether or not prostatectomy or radiation is the preferred treatment for carcinoma of the prostate remains to be decided. According to the belief of Dr. Lower prostatectomy is to be preferred in uncomplicated cases, but in cases in which a high blood urea cannot be reduced, radiation may provide the only possible method of treatment, or it may tide the patient over until prostatectomy can be performed. Dr. Lower's series includes 316 cases of cancer of the prostate, 379 cases of cancer of the urinary bladder, and 39 cases of cancer of the kidney and ureter.

Uterus: The preferred treatment of carcinoma of the fundus still seems to be *sub judice* both as to whether surgery or radiation is the treatment of choice, and as to the type of operation to be performed. The end-results of surgery and of radiation are approximately the same. It would seem, however, that since surgery in combination with the postoperative employment of radium and x-ray gives the assurance of saving a large majority of the patients who present themselves in the operative stage, and of palliating suffering and prolonging the life with a fair prospect of ultimate cure in doubtful cases, we should hesitate to abandon such certainties for the uncertainties still presented by the use of radium and the x-ray without surgery in cases of carcinoma of the fundus.

In inoperable cases of carcinoma of the fundus deep x-ray therapy is of value as a palliative agent and for the prolongation of life.

As to carcinoma of the cervix, on the other hand, the preeminent value of radiation appears to be established. At the Cleveland Clinic we now use radiation rather than surgery in the treatment of carcinoma of the cervix, reserving our final judgment until sufficient time has elapsed for a definite comparative study of the end-results.

As the presence of any but a frankly benign tumor of the breast demands the removal of that organ, especially in a patient past middle age, so when an intermittent or continuous uterine discharge occurs in a patient who has passed the menopause, we believe that a complete hysterectomy should be performed at once. Even if the character of the discharge does not appear to indicate the presence of a malignant growth, this operation should be performed without delay.

Our records include 885 cases of carcinoma of the uterus of which 659 have been cases of carcinoma of the cervix.

Ovary: Cancer of the ovary is rarely primary. When it is primary the removal of both ovaries is indicated. If the peritoneum is extensively involved deep x-ray therapy may retard the progress of the disease.

We have confined this discussion to carcinoma of the various organs and tissues. We shall, therefore, not discuss the treatment of malignant diseases of the bones. The relative merits of the treatment of these diseases by radiation or by surgery are still *sub judice* but may finally be decided by means of the data which is being accumulated by the Registry of Bone Sarcoma of the American College of Surgeons.

In conclusion it should be emphasized that whatever his present point of view regarding the method of choice in the treatment of a malignant tumor of any organ or tissue, the surgeon must hold himself in readiness to alter that view if accumulating experience indicates that other methods are to be preferred or are at least worthy of trial. It may be that as the result of the researches — clinical and experimental — which are in progress in many clinics and laboratories, some new and effective measure may be developed of which we should be ready to avail ourselves.

All the vast researches into the cause and cure of cancer have thus far yielded neither an adequate explanation of its primary cause, nor a specific cure. Until that specific cure is discovered, therefore, the one and only method of prevention is the removal of the precancerous condition.

The layman, laying aside morbid fears, must report to his physician any persistent abnormal visible growth or symptoms of abnormal interest; and the internist must instruct his patient that the early and complete removal of the affected parts offers the only hope of cure, and with the surgeon, must carry on in the clinic and laboratory researches for more definite methods of diagnosis and more efficient therapeutic agents. The surgeon, for his part, must develop his technic so that the cancerous growth may be completely removed with the least possible trauma, and must discover further means by which to conserve and increase the vital forces of his patients. As the cancer problem stands today, the disease is to be conquered only by the closest "team play" of these three — the layman, the internist, the surgeon.