INTRODUCTION

Letters illustrating clinical aspects of cancer

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Some may read this book because they or a loved one has cancer, students of science may read it because they are about to make career decisions, and students of cancer may read it because of a desire to be acquainted with aspects of cancer other than those with which they work. Although most students of cancer have never seen a malignancy in a human, they are nevertheless expert in one or more of the many fascinating and important aspects of the disease. They contribute to the understanding of DNA and its replication, control of gene expression, receptors and growth factors, developmental aspects, immunology, prevention, and treatment of cancer and a myriad of other important parts of the cancer problem. We are all impressed by the recent compounding of knowledge, but even more so by our lack of knowledge and understanding of how important facts generated in one aspect of investigation bear on another. Students, unaware of the clinical aspects of the disease, lack the information to make the correlations and see the important problems that result. In addition, they may be driven in their endeavors only by the intellectualism of their part of the problem. This book is designed to provide insight and understanding into the human aspects of cancer.

It is not our purpose here to present all-encompassing details of the clinical behavior of patients with cancer that are necessary for diagnosis, medical practice, and patient management. Neither is it our objective to detail clinical aspects that could be misunderstood or inappropriately applied. Rather, we present a flavor of the clinical aspects. The clinical problems are illustrated, and areas of ignorance and points of attack identified.

Cancer is a dreaded disease, and the impact of death and suffering are often lost when its research aspects are considered in isolation. Many believe research should be driven only by the intellectualism of the problem and not by practical concerns. But recall that the control of diabetes with insulin was driven by an

emotionally charged clinical problem. It is often satisfying to be driven in research by not only an intellectual charge but also a practical goal, providing perspective is maintained.

It was decided to begin this book with a series of letters written by patients, their relatives, clinicians, and friends. The events described in these letters are real, but of course the names of individuals and particular circumstances have been changed. They illustrate the diversity of clinical conditions caused by cancer, stress the commonalities of the conditions, and the points of research attack.

Colon cancer: Appendix, Section A.3; Chapters 1, 2, 9, and 10

Dear Uncle Harvey,

I am writing to tell you about Dad. I know you would have come to see him if you could have. I will bring you up to date about what has happened. You remember our feeling of fear and panic when his bowels became obstructed two and half years ago. It did not seem reasonable – a man only fifty-five years old, a tough old rancher. Yet, they said he would die within a week if the obstruction of his colon was not "relieved" surgically. They removed part of his colon and anus, because the tumor had spread into the anus. Then they did a colostomy on his belly (it is like an artificial anus). The surgeon said the tumor had not spread to the liver or lymph nodes, and Dad felt pretty good, even though he hated that new opening with a passion.

About a year after surgery, he began to lose weight, but we didn't pay too much attention to it, because he could stand to lose a few pounds anyway. Then, he began to feel run-down and had some pain in his stomach, most on the right side up high. They did some tests and the doctor told us the tumor had spread after all, and the liver was enlarged with it. That was causing the pain. They gave him chemotherapy and he was pretty miserable. Actually, it made him mad because what hair he had left all fell out. Why would a man's hair fall out? So then he wore his old baseball cap from high school. Anyway, he got much better, but then when symptoms recurred, they treated him with chemotherapy again, but it didn't seem to do anything at all. They said his tumor was resistant. He was thin and sickly and had a good deal of pain. We couldn't get him to eat to get his strength up. The doctor was pretty good and gave him pain relievers. After that, it was just one thing after another – he got pneumonia that was cured with antibiotics, then Mom heard about a man, somewhere in Georgia, who had a new cancer cure. It was a secret cure, because he was afraid the American Medical Association would take it away from him. She wanted Dad to try the cure.

I went to the American Cancer Society and they said this man was a quack and all quacks have a secret. I explained this to Mom, but she said it was worth it, and besides, she had saved up $3,750 and they would use that. To make a long story

short, the quack did not help, but Mom doesn't regret doing it even though she lost all her money.

Dad wanted to see all of my brothers and sisters. We talked and joked, but he was so frail and weak he could not spend much time with us. Would you believe he had lost seventy-five pounds? It broke our hearts. This was the guy who worked all day, partied all night, and wrestled the five of us to a standstill the next day.

Then he got really sick with a high fever and pneumonia, and they took him to the hospital. He died three days later. He had some kind of infection of the blood they couldn't treat. It was called septicemia. He had been in great pain, but there wasn't much we could do.

Mom is fine, but she feels guilty about Dad's death. I don't see what she could have done differently. I feel bad about some of his so-called friends who never came to see him, and I am angry about what happened to him. To see a strong, husky, independent man become bedridden and frail and have to be looked after hand and foot just didn't seem right.

Yours sincerely,

George

Author's note

This letter reveals much of what happens with people who have cancer of the colon (see Appendix A.3). At the onset, changes in bowel habits, passage of blood in the stools, or some nonspecific and vague pains in the abdomen may occur. It is not uncommon for the individual to present ("present" is medical jargon for appearance before a clinician for examination or treatment) with an obstruction, and it depends on the location whether the tumor can be removed and the bowel anastomosed (reconnected) end to end or whether a colostomy has to be made. As in this case, some patients find it extremely difficult to adapt to a colostomy, but fortunately organizations that can help patients deal with this or other cancer-related problems are available (in the United States, call the American Cancer Society at 1-800-ACS-2345 or the National Cancer Institute's Cancer Information Service at 1-800-4-CANCER). At the time of surgery the tumor had spread, but it took time for the metastases (Color Plate 11; Chapter 2) to grow and become clinically evident. Metastasis, wasting, and the death of the patient due to infection (in this case septicemia) are commonalities of the malignant phenotype. The loss of hair and diarrhea result from the killing of fast-growing normal cells of hair follicles and intestinal epithelium by the cytotoxic chemicals used in attempts to kill tumor cells (Chapters 1, 9, and 10). These chemicals lack specificity for cancer cells.

Note the strength of will and determination of human beings and their loyalties and lack of loyalties. Friends are often embarrassed and afraid to visit people with cancer, and as a result the patients are lonely.

Breast cancer

Dear Ed,

Well, it is the big C again. We thought we had it licked, but it is back. I am writing to you for some of your free legal advice.

You will remember that Joyce had that "thickening" in the breast. Her doctor told her it was nothing and not to worry about it. She went for her annual checkup ten months later and the doctor again said not to worry about it, that it was okay. Then, it began to enlarge, so she went to the doctor again, but he was away. His partner said she had a tumor and at her age it was probably cancer and should be operated on immediately.

When they removed the tumor, they also removed the fat from her armpit because this cancer usually spreads to the lymph nodes in the armpit first. They found it had spread to twelve of fifteen lymph nodes examined by the pathologist. The doctors said this was a very bad sign. She had X-ray treatments and chemo. She didn't like the chemo treatments and was glad to be done with them. They nauseated her and gave her diarrhea.

She was well for fourteen months, and then about six months ago she felt lousy and began to lose weight. We thought it was flu or something like that. Then she stepped off our back stoop and her hip broke. It turned out the cancer had spread and was quietly growing in her bones, of all places. It ate away the top of her leg bone, causing the fracture. Now she has pain in her back because the tumor has spread to her spine. She is losing weight and clearly cannot live much longer. I hate to say it, but this will be a blessing because of the suffering.

I am angry. I don't think that doctor knew what he was doing when he told her not to worry, that the lump was nothing. He let it grow and spread. I know that suing him won't help Joyce, but I don't think a man like that should be practicing medicine. If I sue him, I can say that publicly and maybe the warning will help other people. What should I do? Joyce doesn't want me to sue him, but if I don't I'll probably beat him up. I am desperate and angry, and I don't know what I am going to do. When you have been married to somebody for thirty-five years, it is difficult to reconcile what has happened. I will appreciate your advice.

Yours sincerely,

Ted

Author's note

As you will learn in this book, early tumors tend to behave less aggressively than later ones. The transition from less to more malignant is termed progression (Chapter 1). Usually the earlier the tumor is diagnosed and treated, the better the prognosis (outlook or predicted disease outcome) for the patient because the tumor has not progressed to the stage of invasion and metastasis. Delay in therapy can result from patient fears or, as in this case, misjudgment or ignorance on the part of the physician.

By the time definitive treatment was started in this patient, spread of the cancer to so many regional lymph nodes and distant organs had occurred that the patient's prognosis was hopeless. Note that some tumors often metastasize to particular sites (Chapter 2). In this case, breast cancer (Appendix A.1) has a predilection to spread to bone. Note the commonalities: growth leading to a rapidly enlarging mass, spread of cells (metastasis), and weight loss (cachexia).

Patients are fearful of cancer and cancer surgery, but all of these fears must be put aside because the only hope for the patient is early diagnosis and adequate initial therapy prior to progression of the disease. Chemotherapy and endocrine therapy for the patient with metastasis is palliative.

Acute leukemia: Appendix A.13; Chapters 9 and 10

Dear Aunt Molly,

I am sure you have heard that Jamie, our three-year-old son, was diagnosed with leukemia. I didn't write at the time the diagnosis was made because we were overwhelmed by what happened subsequently. He was such a lovely child – so pleasant, so full of energy, and we miss him so. Jamie developed an acute fever, and overnight became seriously ill, with bleeding from his gums and nose. He also had large bruises, but we knew he had not been hurt. The doctor suspected leukemia and said the illness resulted from "displacement of normal white blood cells from the bone marrow by the malignant leukemia cells." As a result Jamie could not fight infection. The leukemia cells also displaced the cells that stop bleeding. The doctors said it was very serious, but most children with acute lymphatic leukemia are saved with new types of treatment. They took a sample of blood and bone marrow, but although he did have acute lymphatic leukemia, he was not one of the lucky ones. He was a little better after chemotherapy and X-ray, and then he developed septicemia, was bleeding, and was so lethargic. Last night Jamie died. It is hard to believe. He had been sick only nine weeks but it seemed like ages. I hate to say it, but I feel relieved. He suffered so and he was so good. Now he doesn't have to suffer anymore. Please come and stay with me – I need your help.

Your loving niece,

Mary

Author's note

This letter speaks for itself. Malignant disease often has a bimodal incidence and occurs most commonly in the young and the elderly. Acute lymphatic leukemia (Appendix A.13) is a disease of the young, and its treatment is one of the triumphs of modern chemotherapy. The disease, which before modern treatment caused death in a matter of weeks, now allows cure in 50 percent or more of patients. However,

in this case, the malignancy failed to respond to treatment (Chapters 9 and 10). There is no way of knowing which patients will respond to chemotherapy. Note commonalities of rapid growth of malignant cells that invade and displace normal tissue and interfere with its function, in this case replacement of normal marrow with malignant cells. This loss of white and red blood cells and platelet-forming cells makes the patient prone to opportunistic infections, anemia, and bleeding, respectively.

Lung cancer: Appendix A.7; Chapters 2, 7, and 8

Dear Cousin Janet,

We have bad news to report. You will recall that my dad had that nasty chronic cough. Well, it got worse and he developed pneumonia. The doctor took X-rays and treated him with one of the new antibiotics. He got better, but then six weeks later he developed pneumonia again in exactly the same spot. It made the doctor suspect lung cancer, because Dad was fifty-five and had smoked two packs a day for the last thirty years. They made him cough up sputum and found malignant cells in it. These were "small cell lung cancer cells," which are the worst kind. They are so malignant that the doctors refused to operate because by the time these tumors are discovered, they have already spread all over. They gave Dad radiation treatments and chemotherapy, but they did not help much. He became disoriented and then had some convulsions. The doctor said the tumor had spread to the brain. They suggested irradiating the brain, but my brother and I decided it was no use. We were not surprised that the doctors and nurses agreed with us. Dad died in his sleep just a month ago today. Mom is doing really quite well.

Sincerely,
Dorothy

Author's note

This individual was in the cancer age group with a smoking history (Chapters 7 and 8) that placed him at great risk for developing cancer of the lung (Color Plates 5 through 10; Appendix A.7). This case also illustrates the propensity of lung cancer to metastasize (Chapter 2) to the brain. This occurs so commonly that if a person presents with signs and symptoms of a brain tumor, the clinician must always rule out the possibility of metastasis to the brain from a primary lung cancer.

Note an additional commonality: the cancer diagnosed as a small cell lung cancer lacks tissuelike, or "epithelial" or "glandular" differentiation as viewed in the light microscope. Lack of differentiation correlates with rapid growth and a poor prognosis.

Smoking has been shown to be the most important etiologic factor in cancer of the lung. Only fools play Russian roulette or smoke cigarettes.

Kidney cancer: Chapter 1

Dear Fred,

I need to talk to someone, and since you are my oldest friend and a urologist to boot, you have been selected. I began to pass blood in my urine so I went to the doctor. He told me that because of my age, he had to rule out bladder cancer. I was cystoscoped and the bladder was okay, but then he injected a dye in my blood and took X-rays. The dye was passed from the kidney into the urine, and there in the kidney was a tumor filling this pelvis-thing (the part that drains the urine out of the kidney). I had to wait a week because there were other tests that had to be done.

This was the worst week of my life because I had these horrible guilt feelings – I had never bought as much insurance as I should have because I wanted a nice home and things for the family. Now I am sure I have cancer and I am going to die. My wife is going to have trouble managing, and the kids won't be able to get an education. I really need some time, and I am angry besides. I didn't booze or smoke or play around, why should this happen to me? My doctor seems okay and I like him, but with something this important, I am not sure if I should let him do the surgery or go elsewhere. Please call and let me know.

Sincerely,
Charlie

Dear Charlie,

I was distressed to read your recent letter. I will be happy to come and help or do whatever is necessary. First, let me give you some advice. It sounds as though you may have a cancer of the pelvis of the kidney. This doesn't mean you will die tomorrow or the next day or at all as a result of this disease. But it does mean that unless this tumor is completely removed, it will in fact kill you someday. It may not, because about half of these tumors in the kidney pelvis, even though malignant, behave in a very benign manner, so possibly simple surgical removal of the kidney will cure you. In the event the tumor spreads, it will probably spread to the bladder. (It is a good sign that the bladder is not affected at this time.) That doesn't mean to say you are out of the woods, but it says the tumor cells have not become aggressive enough to spread through the urine to the bladder. If this spread occurs, very often it can be handled using the same type of procedure they used when you were cystoscoped. They can take out small tumors through a resectoscope inserted into the bladder through the penis. If the spread to the bladder recurs repeatedly and becomes extensive, you may lose your bladder, but this usually takes years. You'll have lots of living to do in the meantime, and it doesn't happen that often anyway. Finally, a few of these tumors spread via the

lymphatics and bloodstream and go to distant organs. That is the worst possibility because the tumors do not respond to chemotherapy or irradiation and nothing can be done about them. I have my fingers crossed for you.

Yours sincerely,

Fred

Dear Charlie,

This get well card is sent with a great deal of relief. Gloria told me on the phone last night that your tumor was a grade 1, stage 1 noninvasive tumor. If you have to have a cancer, this is the best one and we are all optimistic you have been cured by surgery. Since you and I have always leveled with each other, I feel I should tell you that there is still a chance the tumor may have spread, but it is remote and with any kind of luck you're home free. I'm going to be in the Rockies this September. Let's go trout fishing!

Fred

Author's note

Fred's second letter to Charlie says it all. The degree of differentiation of tumors is graded 1 to 4 with 1 the most differentiated and least aggressive. Grade of tumor plus stage (in this case noninvasive) sets the prognosis as excellent. The combination of stage and grade together gives a more accurate prognosis than either alone (tumor grades and stages are discussed in Chapter 1).

Squamous cell cancer: Chapters 1 and 2

Dear Eileen,

I am writing to tell you about Grandpa, who is having a terrible time. Ever since Gram died four years ago he has not been quite right, if you know what I mean. He had this sore on the inside of his gum and refused to have it looked after. He claimed it was caused by his dentures. So he whittled and sanded his dentures with his knife, but the sore did not go away. We coaxed him to go to the doctor, but he refused. After about a year of tinkering with his dentures, they finally broke. The dentist told him he had cancer of the gum – a squamous cell cancer. It's strange, but that's a skin cancer. Well, he'd figured out all along he probably had cancer, but he didn't want to know. He claimed Gram was okay until they told her she had cancer, and he was damned if he would let them do it to him.

The cancer has spread to lymph glands in his neck and to the floor of his mouth and jaw. They told Grandpa they were going to do radical surgery to take out part of his tongue, jawbone on the right side, and all of the lymph glands in his neck. "The hell you say," said Grandpa. "You can't cure me, and you aren't going to cut on me."

The doctors have really been working on me to get him to submit to surgery. They say, in the first place, if he had gone and had this looked after when the sore first developed, he could have been cured with very little effort. Now they say if they do radical surgery, they can spare him a lot of discomfort and even if they take out his jaw, they can rebuild another one.

He smells pretty bad because of the infection in the tumor. Some of it is decaying, and it would appear we are in for a bad time. Grandpa just looks me in the eye and says the medical profession is after his money and he would rather give it to his grandkids than to those lousy doctors. He says he knows it is going to get bad for him, and when it gets too bad he will just cash in his chips. I don't know what to do with him, but I think it might be a good idea if you came to visit while he is still able to do the things he enjoys.

Yours sincerely,

Nelly

Author's note

In this situation the patient delayed seeing a physician because he was afraid he might have cancer. Thus he will die of a disease that, under ordinary circumstances, is curable with modern therapy. Note his strength of will, characteristic of many elderly people who have been through the school of hard knocks. It would be interesting to know the events at the terminus. Did he lose his resolve and accept therapy? Many people say they will refuse therapy, but when they are faced with dying, they often opt for treatment even though they know it offers little chance for cure. Note the commonalities: growth, invasion, and destruction of tissues, and distant metastasis (Chapter 2). Weight loss will follow, then infection and death (Chapter 1).

Testicular cancer: Chapters 1, 2, 9, and 10

Dear Dennis,

This letter is to thank you for your advice and support during our trials and tribulations with my son's testicular teratocarcinoma. Do you remember in medical school how the professors teased us when they lectured about testicular cancer and how they made light of such a grim disease? Never did I think I would come face to face with the realities in my own family. Bill is twenty-six years old. We were at the lake and he told me he had a large testicle, but it didn't hurt, so he had not done anything about it. It proved to be a teratocarcinoma that had metastasized. We did a retroperitoneal lymph node dissection and then treated him intensively with chemotherapy. He has been disease-free for two years, which means he is almost surely cured.

He had some side effects of the chemotherapy: he lost his hair – about which he was embarrassed – and although he can have sexual relations, he has no ejaculate. Luckily, he and Marge had the baby before he got sick.

I look back over this nightmare and realize in a sense how fortunate we are. He was cured with modern chemotherapy, which did not exist ten years ago. I guess temporarily losing your hair and having "dry" ejaculations is not too heavy a price to pay for life.

Your help and counsel were much appreciated,

Sam

Author's note

This individual was in the typical age group for a teratocarcinoma (twenty to thirty-three years) of the testis. He was probably embarrassed to seek medical advice, which caused delay and the development of a large tumor. Because these tumors have a tendency to metastasize (Chapter 2) via the lymphatics along the aorta, the surgeons removed all of these lymph nodes and any tumor that might have spread into them. Then the patient was given massive doses of chemotherapy with the attendant side effects, which occur because the toxic chemicals lack specificity. Even so, such cures are among the marvels of modern chemotherapy (Chapters 9 and 10), and over 70 percent of such patients are cured. The cause(s) of the differential responses of tumors to chemotherapy has not been a high priority of the medical establishment.

These tumors are extremely rare, but research on them has clarified many problems in oncology (Chapter 1).

Stomach cancer

Dear Mom,

I am enjoying my first year of residency very much, and after all the stainless steel and scientific medicine we learned it is fun to see some of the old-timers practice.

An old Scot came into clinic the other day not feeling very well with some vague upper abdominal pains that sounded like dyspepsia. I was going to give him some medicine to tide him over the weekend when the attending physician came in. The doctor is an equally dour old Scot, and he learned that after eating porridge every morning for fifty years, this patient no longer had a taste for oatmeal. He winked at me and said we better work him up. Well, we worked him up exhaustively and found he had a tiny adenocarcinoma of his stomach. People with this disease may lose their taste for a favorite food, and this old doctor knew about it. Well, we operated on him. Apparently the tumor had not spread, and we think he is going to be one of those lucky people who beats stomach cancer. When you consider that