Chapter 15

The Good Doctor

"What we've got here is a message for anyone who is interested in the cause of cancer."

The whole of this remarkable woman's work, since the Oxford Survey turned up its revolutionary discovery about fetal x-rays and childhood cancer, has been a search for the cause of cancer. "This is the mystery, and it's kept me busy my entire life. To me the whole thing has been an effort to tease the story out, to understand the etiology of childhood cancer."

From the start she felt that their discovery about fetal x-rays had put them on to something momentous. "I regarded it as very important, a fixed point to steer by, like the polar star from which the science of navigation comes. I can remember saying to myself, if a mariner had set out without knowing where to go and what to do but was fortunate enough to discover the North Star, one fixed point in the firmament, he could fill in the other geographical components—if he could only hang on. We'd found our fixed point, our polar star, the sure thing we could navigate by.

"I think that's what kept me going on a subject nobody else seemed to be interested in. I'm quite certain that's what we're doing—from this one finding we're gradually building up all sorts of things."

Early on, she and George found a strong correlation between cancer and infection sensitivity. During the time the child is incubating cancer, he or she becomes increasingly sensitive to infections. By the end of the silent phase of immune-system cancers—cancers of the reticulo-endothelial system (RES)—he's more than three hundred times more infection prone than a normal child.[1] This correlation alerted Alice and George to relations between cancer and the immune system that were developed in subsequent theories about Sudden Infant Death Syndrome (SIDS), Burkitt's lymphoma, and cancer and inoculations.

Alice wishes this part of their research were better known: "I would

like to be remembered as someone trying to puzzle out the causes of childhood cancer, rather than a radiation expert, which I'm not. The x-ray story has attracted so much attention that people haven't heard about the rest of it—though it's all there in the literature."

It may be there in the literature, but it is tucked away so obscurely that it is in danger of being lost.

Unmaskings

One of the ironies of Alice's story is that although she is best known for discovering the link between fetal x-rays and childhood cancer, hers is not really a radiation-focused theory.

"I can remember the moment I realized this, working on the Oxford Survey—I suddenly realized, *supposing there had been no antibiotics?* I woke up in the middle of the night with one of those brain waves my mother used to get, knowing—it came to me in a flash—*of course* this is why we're seeing leukemia, it was on account of the antibiotics! The advent of antibiotics, by reducing the chance of death by infectious diseases, had allowed us to see the true incidence of leukemia. It's as if the tide had gone out and you could now see what the bottom of the ocean looked like. The true state of affairs was revealed for the first time.

"When you are developing a cancer of the immune system, you lose immunological competence: you have no resistance, you react badly to minor infections, minor infections become major infections. This means that before antibiotics and other drugs were introduced, even a common cold might be sufficient to remove a leukemia death from the official record. In the old days, the leukemia was there all right, it just didn't get a chance to show: infections, measles, mumps, pneumonia, whooping cough, other respiratory diseases, would kill the child first. The odds against surviving long enough to see the disease were so great that childhood leukemia was a rarity.

"Then along come antibiotics and up goes the leukemia figure two and a half times. They kept the child alive long enough for the leukemia to show.[2]

"I can remember my father saying, you rarely see a case of leukemia in a child, and when you do, you always notice that it takes the child who's never been ill. And this was a curious thing we found in the early days of the Oxford Survey—so many of the mothers claimed that the child who died had seemed to be the healthiest of their children. You can

see why: if he'd ever met with a serious infection in the days before antibiotics, he'd have died."

When she and her co-workers began looking at the rise of leukemia, David Hewitt's review of official statistics turned up an increase in leukemia mortality that had kept pace with a drop in general mortality.[3] A later study by George Kneale confirmed that during the years when pneumonia deaths of children are up, there is a drop in leukemia, though leukemia incidence rises again in the following nonepidemic years.[4] In the year 1918, the year the Spanish influenza swept the world, there was a massive disappearance of leukemia across the world: "never was the leukemia death rate so low as it was in 1918. Why? because no one incubating leukemia would have survived the influenza."

The most important factor in the rise of childhood leukemia, Alice insists—more important than the use of medical x-rays—is antibiotics. "The effects of man-made radiation on increased leukemia rates cannot be known until the story is seen in this context, of the control of infectious diseases. Thanks mainly to above-ground weapons testing, we've doubled background radiation worldwide; at the same time, childhood cancer has more than doubled. But how these two phenomena are related is difficult to determine. Radiation has its effect, of course, but how much the rise of leukemia is caused by the new sources of radiation and how much by the unmasking effect, is hard to say. It's impossible to measure precisely, since there's been this other enormous change, the eliminating of major competing causes of death."

Cancer, Infection, the Immune System

Alice believes that most childhood cancers originate from *in utero* exposure to background radiation or medical x-rays because hardly anything else gets through the placental barrier. "The uterus is the best protected organ in the human body. And it's got to be well protected to allow nine months for getting everything to do with normal development not only right, but in the right sequence. Fetal development requires tremendous protection against outside interference, and you can be pretty certain that in normal circumstances, nothing harmful gets through the barrier except the one thing that human beings can't protect against—and that is radiation. Chemical carcinogens play a part, of course, but as promoters—secondary, not primary, causes of cancer."

Alice sees *in utero* mutations as the cause not only of childhood cancers, but also as unrecognized causes of miscarriages, stillbirths, and

deaths in the early years. "You notice that there is a high death rate in the early stages of life—these are the children with congenital weaknesses or defects. Somehow nature says, you won't be strong enough to survive, so you're bumped off early. After that you're presumably programmed for a certain life span, a span which is partly determined by the strength of the material. Eventually the material wears out, like metal fatigue in an airplane—we die of heart failure or the failure of some other crucial organ. Natural selection is interested only in life to the point of reproduction. We're not meant to live forever and it would be a disaster to do so—though of course human beings may have other ideas.

"But what can kill you off in the interval between the congenital weaknesses and the final wearing out—what determines whether you survive—is whether you can recognize self from non-self in a situation where every moment, with every breath and every bite you take, you're taking in foreign matter and using it to replace your own tissues. So here you are, with this job of taking in non-self which has got to become a part of self. You've got this surveillance mechanism that's got to recognize self from non-self, and it must on no account destroy normal cells. And you can see that there are two great enemies—infections and cancer. Vulnerability to both increases with age: it's as though in the process of the wearing out, you become less able to muster the forces to defend against foreign invasions.

"It's the immune system that performs this function of recognizing self from non-self at the cellular level. It's a surveillance system geared to recognize foreign proteins—recognize and destroy them. Much is known about the way it works: cells chase around gobbling up foreign proteins, other cells come along and absorb what the first phalanx misses, and so on. One theory of cancer is that in order for a mutation to survive to become a cancer, to form a clone of cancer cells, there must be something wrong with the surveillance system.

"In infections and cancer you've got two very similar processes, though they seem to be so different. An infection is caused by a living organism with protein foreign from you, getting inside your body by some trick and multiplying. Now these organisms may get inside you but not multiply. We probably—many of us—have within us tubercular bacillus; perhaps we've had a slight attack of influenza when the tubercular bacillus was struggling to take over; perhaps we even have a scar on our lungs or little lesions. Disease happens when the foreign organism gets the upper hand and succeeds in multiplying.

"How does the immune system work to repel foreign invaders?

"We know that though you're born with a certain natural immuno-

logical competence, you've got to acquire a lot more during your lifetime, and you do this by constant contacts with infections that you learn to overcome. The system has to learn to detect and destroy foreign proteins, so it must be a very delicate mechanism: it's got to be able to recognize the difference between you and foreign molecular elements that are not part of your cells and stay away from the ones that are you. You have to be very careful not to kill yourself.

"If your resistance is working, your body finds ways of localizing infection—you may get a boil or a carbuncle instead of a generalized disease, and that shows that your body has managed to contain it, to bring it down to size. Localized forms of infection are less dangerous than diffuse forms, just as localized forms of cancer, or tumors, are less dangerous than leukemia or lymphomas. Even if infection really takes over and becomes acute and you have high fever and infection everywhere, the body usually finds a way of settling the problem relatively quickly.

"But cancer presents different problems. Cancers are like infections in that something foreign is trying to get the upper hand, but in the early days the cancer cell may be only very marginally foreign. Something which is half you is different from a foreign organism. It's developed an apparatus it shouldn't have, to circumvent the body's defense mechanisms.

"I always say it's rather like having a delinquent child in the house—you can't treat him the way you'd treat a burglar. It's partly yours, a part of you—partly self, partly non-self—and very destructive: it can do a great deal more damage. The process is slow and subtle.

"Now what is cancer? Cancer starts with a mutation and develops when the mutant cells gain the upper hand. When radiation passes through matter it alters the molecules through which it passes, knocking away their electrons and creating chemically unstable particles. Radiation is a mutagen, that is, it creates a mutation. Not every mutation develops into a cancer—the body has extraordinary resistance. Ninety-nine times out of a hundred or 999 times out of a thousand, nothing happens. You can have lots of mutant cells without being harmed. Perhaps you've even been hit by radiation and had a mutation while we've been sitting here talking. (You realize, we only seem to be sitting quietly here, we're actually whirling through space and being bombarded with background radiation.) But most organs contain more than enough cells to spare and maintain normal function—you can afford to lose lots of cells and nothing happens. Obviously, a hit is more likely to cause damage when you're the size of a tadpole, consisting of a few clusters of cells, each of which is going to develop into a part of your body. If you should happen to be hit by

radiation when you're this size, there will almost certainly be a trail of trouble.

"There are three ways radiation can affect cells. One possibility is that cells may be killed outright, end of story—unless many cells are killed or a crucial cell in a developing embryo is affected, in which case you die. The second possibility is that cells may be damaged, but in a way that is harmless: a few malfunctioning cells will not affect an organ where most cells are behaving normally. But in the third case, cells may have their DNA damaged and yet survive and go on to spawn defective daughter cells.

"It looks as though the mutagen has to strike the cell at the moment when it's dividing for this kind of damage to occur. It's at the moment of cell division that the risk of DNA damage is greatest. When the cell divides, the nucleus unfolds to form a spindle with chromosomes on either side, each one of which contains duplicate sets of controlling genes in a particular sequence which it is important not to alter. The genes at this moment are not locked back in the nucleus where they're usually tucked away; they're out there and vulnerable. If a hit occurs while this delicate process is occurring, it's going to be difficult to get each part of the intricate system to reassemble properly.

"Provided that the DNA damage is limited to one of the helix crossbars, there will usually be full repair; if there is destruction of both members of a pair there will be attempted repair, but probably at the cost of permanent gene damage. You have to have a double hit that doesn't repair and doesn't kill the cell for a mutation to occur.

"The slightly damaged cell may succeed in reproducing itself, in setting up a little clone. The mutation gets by the body's surveillance mechanism by being sufficiently like the normal cells to pass without bringing the immune system down on it. The cell loses control of its own growth processes and stops obeying the instructions of the body as a whole; it becomes liberated from the usual checks on replication and proliferation and becomes a cancer."

Alice's main quarrel with the nuclear establishment is this: "they say that below a certain dose—which they call a threshold—you get chromosomal repair or radiation damage. They say repair reduces risk. I say it might *increase* risk. I use the example of a cracked plate: you can repair the plate, but you'll still have traces of damage, and all you need for cancer is a small trace. Every time it is stressed, it becomes more liable to break. It will not react to disease or physical injury as well as an undamaged cell, and when it reproduces, it will pass on its defect."

Another analogy Alice finds useful is that of the aftermath of a train wreck: "you may reassemble the parts and get the train back on the track and get it to its destination all right, but some of the passengers happen to be dead. Think of the carriage as the chromosomes containing the genes. Because the chromosomes manage to reassemble themselves, this doesn't mean you haven't done some damage to the DNA within."

Alice's guess is that even after the damaged cells manage to clone themselves, a lot of these mutations get to this stage and no further: in fact, all the forces of the body are working to contain them. She sees evidence for this in the fact that precancerous conditions of the cervix often reverse themselves even when women fail to come in for follow-up, though in theory they should develop into cancer; but she also points out that such reversals occur only in women under fifty, and the younger the woman, the better her chances. "Our Hanford studies show that the odds against the mutation developing into a cancer are very high when you're about twenty, but that they decrease with age and the weakening of the immune system—the age effect again."

Mutations may produce tumors, on the one hand, or birth defects, on the other hand. If it's a germ cell that's been damaged—a cell in the ovaries or testes—and that germ cell later forms a child, the child will suffer from an inherited abnormality. "Or the damage may skip a generation before you see anything—and not only one, but two or three generations. If the defective gene is recessive, it has to wait to meet up with the same damage in another parent before it manifests the damage;[5] it may take generations to manifest—but it will be there. Once you've fed defective seeds into the gene pool, they lurk as potential trouble for the future."

Theory of Childhood Cancer

Alice sees childhood cancers as *delayed congenital defects,* or late effects of *in utero* mutations. She believes that the *in utero* initiation of these cancers accounts for the tissues they affect and the forms they take, producing developmental effects different from those leading to adult cancers.

Early in development, an embryo consists of a mass of primitive, undifferentiated cells called *blast* cells, each of which is a stem cell undergoing rapid division. Because its cells are rapidly dividing, embryonic tissue is vulnerable to mutagens. "When you're the shape and size of a tadpole, you're going to be especially vulnerable to mutagenic hits. If a hit occurs in a tissue that's going to form an essential component of

the body such as the lungs or intestine, you won't survive. This is why children do not get cancers in these organs—these children don't get born. But an embryo has tissues that are not needed later, that are necessary to its development but have no future; some of these remain even as new systems develop. It can survive a mutation in a vestigial tissue."

Childhood cancers develop from three groupings of cell systems in the embryo: the autonomic nervous system, which is involuntary and will soon become subservient to the central nervous system; the reticulo-endothelial system (RES), the blood-forming and bone marrow tissues, which are the basis of the immune system; and the Wolffian ridge, a large, semi-circular structure attached to the back. The Wolffian ridge shrinks down to become the kidney, and from it come the genito-urinary system, lungs, intestines, and limbs. Cancers of the Wolffian ridge become Wilms' tumors; cancers of the autonomic nervous system become neuroblastomas and cerebellar tumors; and cancers of the RES are leukemia and lymphoma.

Virtually all children's cancers develop from these types of tissue: vestigial, the immune system, or the brain. About 50 percent of children's cancers are either leukemias or lymphomas—RES neoplasms—whereas only 5 percent of adult cancers are. Half of the remainder are brain or neural tumors (neuroblastomas); half the remainder of these are Wilms' tumors; and the rest, about 10 percent, are other types of cancers.

If the Wolffian ridge undergoes a mutation, the mutation will, as the embryo develops, take the form of a tumor surrounding the kidney, Wilms' tumor. The tumor develops on the outer rim of the kidney and sits on top of it, leaving it still able to function. If it's the brain tissue that's affected, the mutation may become a brain tumor. It is significant that 99 percent of the brain tumors of children are in the hindbrain, the cerebellum, which develops earlier than the forebrain and is larger in the embryo and therefore more likely to receive radiation hits. (The brain tumors of adults are mostly in the forebrain, the cerebrum.)

"You can survive the early effects of brain tumors—in fact, hardly any of the nervous system matters much until you are born—so the cancer can go unnoticed. And you can survive the early effects of leukemia because the immune system is not needed until a month after birth—your mother's is doing the work for you until then, longer if you're being breast-fed, in which case you receive immunity from your mother for six to nine months. You don't need your immune system until you go off hers, but then you need it very quickly."

Which tissue is affected determines the age at which the cancer appears. Since the cancer partakes of the characteristics of the tissue and reflects its growth rate, each kind of cancer has a time when it typically manifests. Leukemia has its peak instance before the age of five, but slow-growing tissue makes for slow-growing cancers: bone cancer has a peak in young adult life. Hodgkin's lymphoma peaks at around fourteen to twenty years of age—this is the slowest growing of the RES neoplasms.

"The cancers that peak latest, I'm going to guess, are testicular and early breast tumors. Nobody has ever looked at them this way, but I think that early breast and testicular cancer may be delayed congenital effects, manifesting later because of the late unfolding of the sex organs."

Sudden Infant Death Syndrome: An Untested Theory

When, in the early days of the Oxford Survey, Alice began looking into childhood leukemia, David Hewitt's study turned up this odd and unusual peak age of two to four years. Alice had long been wondering, why these peak ages? And why did children get only lymphatic leukemia and rarely myeloid leukemia?

She then noticed another curious thing—that twice as many children who died of leukemia under six months were born in the first half of the calendar year. There seemed to be no discernible pattern in children who died when they were older than six months, but Oxford Survey data revealed that children who died from leukemia under six months of age were *twice* as likely to be born between January and June than in the second half of the year, between July and December.

"Why? There is no seasonal difference between the first and second half of the year—they're both half winter and half summer. In Britain, the population regularly records more deaths between October and March than between April and September. But the number of deaths between January and June is not different from the number between July and December. So how to account for this difference?"

She soon worked out that the difference was whether a child who had survived to one month of age was moving into warmer or colder months. "You can see that all one-month-old infants who are born in the first half of the year will experience more warm weather before six months of age than during the next six months, whereas all one-month-old infants who are born in the second half are moving into the cold. The children born in the first half of the year, January to June, are moving into the warmest months, whereas those born from July onwards are moving

into winter, where they have more exposure to danger from infection. Since those babies moving into summer are less likely to meet with an infection at the most crucial times, they have a better chance of surviving six months—to die of leukemia. So it looks like children born in the first half of the year get more leukemia.

"And exactly the opposite is happening on the other side of the calendar. If you're born in the second half of the year in Britain, you have three times as much exposure to the colder months by the time you're six months of age than if you are born in the first half of the year. So just before you're coming up to die of leukemia, you get nipped in the bud with an infection. It looks like it's good to be born in the second half of the year because you're less likely to die of leukemia, but it isn't really: it just means you've died of something else before leukemia has a chance to show."

But what could that something else be? "So I said, let me see if I can't find a cause of childhood death that is commoner in the winter than in the summer (and so affects babies born in the second half of the year), something which has not been affected by the advent of antibiotics and which is concentrated in the first six months of age. In other words, I was looking for the obverse or mirror image of the leukemia deaths." Alice is not called Alice for nothing, as she's fond of saying: "I see everything through the looking glass."

And there it was, a cause of death that hadn't decreased with antibiotics: in fact, it had become more prominent—Sudden Infant Death Syndrome (SIDS), known as "crib death" in the United States, "cot death" in England. It kills between 6,000 and 7,000 babies a year in the United States alone, between 2 and 3 cases per 1,000 live births, or one in every 350 babies.[6] Nobody knows what SIDS is, nor why it's on the rise. What is known is that it occurs more often in winter than summer and that it occurs mainly between four and six months of age.

Alice believes that these sudden infant deaths are masking myeloid leukemia. "My theory is this: the reason we aren't finding myeloid leukemia in children is that the child with myeloid leukemia is dying of a sudden unexplained death, if he hasn't already died of anoxia during the second stage of labor. Most SIDS deaths occur within one and six months of age, which is just when the child is losing its mother's immunity and achieving its own. While the normal child is gradually acquiring his own immunity, the child with leukemia is gradually losing immune competence. Since you get from your mother defenses against infection in the form of passive immunity for one month or more, the weakness in the

system doesn't get put to the test until you go off your mother's immune system."

Myeloid leukemia is more acute than lymphatic leukemia. It has a shorter latency, manifesting between one and three years of age rather than two to four years, and it involves the red blood cells as well as the white. Children who are incubating myeloid leukemia are—like all preleukemics—more infection sensitive than normal children. But they are also born with a defect in their hemoglobin: they have something wrong with their red cells as well as their white cells.

"While in the womb," Alice explains, "the fetus produces fetal hemoglobin, which is geared to receiving oxygen through the placenta; but soon after birth this is replaced by adult hemoglobin, geared to receiving oxygen through breathing. At birth you have both kinds of hemoglobin present, enabling you to breathe both through the placenta and through the new apparatus of the lungs; then you gradually get rid of the fetal hemoglobin. But children who are incubating this kind of leukemia don't make the changeover from fetal to adult hemoglobin and are left with too much fetal hemoglobin. This hemoglobin fails to take up oxygen from the lungs, so that when they go into a deep sleep, or have the first effects of a respiratory infection, the oxygen level falls to a fatal level and they're liable to go into anoxia—shortage of oxygen.

"There have been studies showing that children who die of SIDS have an exceptionally high ratio of fetal to adult hemoglobin, something like sixty-five to fifteen—though this is difficult to measure after death, and it's not something all hematologists accept."[7]

Alice's theory is that SIDS children have difficulty replacing passive immunity with active, and fetal hemoglobin with adult, and the two effects combined might be sufficient to cause a sudden death. SIDS children die when they're sleeping, and the mechanism of death seems to be respiratory obstruction—purple bruises are sometimes present, tiny bleeding points called "petechiae," perhaps resulting from the infant's attempts to take deep breaths against some obstruction in the airway.[8] Since the child is so sensitive to low air pressure situations, it may take only the shallow breathing of deep sleep or the slight respiratory blockage of a cold to cause death.

"SIDS deaths are more common in winter than summer, which is when the immune-compromised child is more likely to succumb to infection. They often occur in a family situation where an older child brings an infection home, or where everyone in the family has a cold and the child goes to bed with sniffles and doesn't wake up. You have no defense of

your own, so you meet with an infection and go out like a light. This also fits our findings on the Survey that the firstborn get more leukemia—because the firstborn doesn't meet with infections brought home by an older sibling and so has a greater likelihood of living long enough to manifest leukemia.

"It is also known that SIDS children have an easy delivery with a short second stage of labor. The second stage of labor is when the baby becomes dependent on its own hemoglobin for breathing and when any defect in its system could be fatal. This fits my theory—these babies would *have* to have got into the world fairly easily because if they'd had a difficult labor, they'd have died. It also fits with something else found by the Oxford Survey: that leukemia is uncommon in the second twin. Second twins have difficult second stages of labor—they have the longest time before they breathe—and a defect in the system would kill them."

Alice believes that these missing myeloid leukemias may account also for many miscarriages and stillbirths. She notes that 5 percent of stillbirths are totally unexplained and occur—during the second stage of labor—to apparently healthy babies.

Alice's theory of SIDS has been there in the literature since 1975, but nobody's picked it up.[9] This is the more remarkable, since it could so easily be tested. "There's a blood test done on all children shortly after birth—the same test should be used to look at the proportion of fetal to adult hemoglobin. Then when the mother gets a follow-up exam at four weeks, do a second test for proportion of fetal to adult hemoglobin—then monitor the population for all causes of death in the next eleven months.

"According to me, you'd expect children who died of SIDS to have shown a high proportion of fetal hemoglobin at one month of age. You can't test for this after death, since the blood count can only be diagnosed by flowing blood, but you could monitor children while alive—and you could easily establish whether SIDS children have a disproportionate amount of fetal hemoglobin.

"I tried to launch a study of SIDS in America through the Childhood Cancer Research Institute, but there wasn't enough funding, and nobody in England has shown the slightest interest. I simply can't understand why. No one knows anything about this mysterious syndrome—they're stuck—so why not test my theory. As long as SIDS remains a mystery, my theory is as good as any other."

She adds, "I think it would be a great comfort to the mothers of these children—the children often come out in bruises, so they look battered. It

would be a comfort to these mothers to know they didn't murder their children—they were victims of an inevitably fatal disease."

The sort of monitoring Alice recommends might also provide a way of detecting leukemia at one month, and "you might then invent something to stop it, something to boost the immune system—inoculations, for example." Alice and George found evidence in Oxford Survey data that inoculations act as cancer inhibitors. "In the Oxford Survey, you'll remember, we pitted a cancer case against a live control, and we discovered quite an extraordinary thing—that our controls had been inoculated more often than our cases. Perhaps they were alive *because* they'd been inoculated? George put the data through his tests and we found that 20 percent of children incubating cancer had been lucky enough to have inoculations at a moment when they seemed to arrest the cancer. The inoculation had to occur at just the right moment, and the critical moment seems to be late in latency—as though the child, about to develop leukemia, happens to get an inoculation and it nips the cancer in the bud.[10]

"Inoculations don't prevent you from getting cancer, but they may be a way of stopping it, by giving a boost to the immune system. They don't affect the initiation of the disease, but they may interrupt an otherwise ongoing process. This is consistent with the rest of what we know: if leukemia and other cancers weaken resistance to infection, you can imagine that by boosting the body's immune system, you might strengthen resistance to cancer and reverse the process. There is undoubtedly a tremendous amount to be gained just by boosting the immune system in every possible way you can think of. But you have to hit it at exactly the right time.

"We applied for funding to some drug companies to test this, but again—nothing. It looks as though this is another Stewart theory that's going to have to go untested. I seem to be constantly bumbling into situations where nobody thinks the way I do."

Burkitt's Lymphoma

Another of Alice's theories concerns Burkitt's lymphoma as a contained form of leukemia. Burkitt's lymphoma is the most common kind of children's cancer in parts of the world where there's widespread exposure to malaria. Alice suggests that it may be a form of lymphatic leukemia that gets contained by a highly developed immune competence.

"In tropical Africa and other places where there's lots of malaria, Burkitt's lymphoma accounts for about 90 percent of childhood cancers. It's a rather mild form of cancer, easy to treat, and the children don't suffer a lot. In England and America, Burkitt's lymphoma is very rare—it appears in areas of the world where children have lots of attacks of malaria. Everyone thinks it's a special viral infection, but I think it's the children showing exceptionally strong resistance to the mutations that cause leukemia because they've developed such high resistance to malaria.

"These are children who have not only had repeated attacks of malaria, but who are born of parents who've had repeated attacks, so that maternal levels of immunological competence are exceptionally high. The progress of the mutation, instead of running rapidly to a diffuse disease as it does in our part of the world, where it becomes either lymphatic or myeloid leukemia, turns to a localized form because abnormally high levels of immunological competence hold it in check. The child's resistance seems to allow for a containment of the cancer process: the children get enormous tumors, and they occur in places where you'd expect to see infections.[11]

"A further reason for seeing Burkitt's as a localized lymphatic leukemia is the appearance, in these parts of the world, of a localized form of myeloid leukemia, virtually unheard of anywhere else—chloromatous myeloid leukemia. Normally in children, the myeloid cells are so vigorous that they become diffuse throughout the body, but here they collect into localized tumors called chloroma, tumors on the scalp, greenish in color, consisting of myeloid cells." Alice recalls that in the first few years of data collection for the Oxford Survey, there were two cases of chloroma: "they were probably the last cases in England, left over from those days when children got multiple infections; they soon disappeared when the infection rates fell off."

According to Alice's theory, if malaria were to disappear from an area, the ordinary form of leukemia would start appearing instead of the localized form. And sure enough, a study in the Suez area found that when the malaria rate came down, so did the incidence of Burkitt's lymphoma, and the usual form of leukemia appeared instead.[12]

"It's one of my two outrageous and outstanding theories, the other being SIDS. There's a brief account of both in 'Childhood Cancers and Competing Causes of Death,' a paper I wrote in a temper when I heard Doll was dismissing the whole of the Oxford Survey as having done nothing but turn up a doubtful x-ray effect."[13]

Free of Charge

As Klarissa Nienhuys suggests, "Alice and George were finding out things about the immune system that were quite ahead of their time, that may in the long run be more important than the radiation discoveries."

Alice's theories of childhood cancer, of SIDS as an effect of leukemia, of Burkitt's lymphoma as a contained leukemia, and of inoculations as cancer inhibitors, all came out of Oxford Survey data. "It shows how important it is just to go on monitoring the situation, to continue gathering data. The Oxford Survey should have continued. It wasn't costing much, it could have ticked quietly away. If you are interested in diagnostic problems, which I obviously am, then you want to get to the root of the thing—you don't want to leave it halfway. I feel we were within a few years of answering questions about SIDS and inoculations that might have solved the mystery of cancer.

"Ever since I woke up in the middle of the night realizing how important antibiotics were in the rise of leukemia, everything we've discovered has pointed to the centrality of the immune system to the prevention of cancer."

Other sorts of correlations were turning up. "Early in the Survey, we found an excess of Down's syndrome among the leukemic children—thirty times higher than normal—and this fits with the rest. Down's syndrome prevents the normal development of the blood-forming tissues; these children have deficient immune systems that make them extremely susceptible to infections—and to leukemia. Before antibiotics they rarely survived infancy. Other congenital diseases (ataxia-telangiectasis and Bloom's syndrome) have the same genetic defect that prevents normal development of the immune system, and these also have strong associations with infections and leukemia—though only after the advent of antibiotics did these children live long enough for these associations to be recognized."[14]

Another project Alice hoped to launch, which could have been tested had the Oxford Survey been allowed to continue, was on the effects of ultrasound. "Ultrasound came in 1975 and our data stopped after 1980, so it's necessarily left unsettled. Once the use of ultrasound becomes universal, it will be impossible to study, because once it's uniform, there will be no control group—as is the case with background radiation. We have data on some of these transitional years, it would have been nice to have gotten more—it would have been important to look closely at what happened as ultrasound came on the scene. I have no hunch about whether

there's a cancer effect. I wouldn't be all that surprised to find one, though I wouldn't be surprised not to. Non-ionizing radiation doesn't shatter the cell the way ionizing radiation does."

Even with the Oxford Survey's termination in the early 1980s, it continues to offer riches. There is Tom Sorahan's discovery about paternal smoking and childhood cancer, which Alice calls "of key research interest and very good news for the Oxford Survey. I've always known there were lots of uses to be made of the data. The records are there for new theories to be placed on them. I've always known that our discovery about fetal x-rays was like the mariner's North Star, the fixed point in the firmament."

It is poignant, hearing Alice toss out her cutting-edge theories to audiences of activists and students who are unlikely to do much with them. As she was expounding her theory of SIDS to an audience at Portland State University, she was asked, "Why aren't you doing a study of SIDS now?" "I'm too old," she replied; "I couldn't get a grant in my own name. Even if I were younger, it's not as if I had a big department and an honorary position anywhere and could gather a team of people around me. But you see, I've alerted your interest. I think there's a prize there for somebody."

Someone from the audience commented, "we get these ideas free of charge." Alice responded, "we give all our ideas free of charge. We put out these ideas on the table—for others to develop. The most I can do is throw the pebble into the pool and create circles and leave it to somebody else to get on with the work."