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Non-Hodgkin's Lymphoma™ UPDATE

Patient Education Series

Bridging the Gap between Research and Patient Care

EDITOR

Neil Love, MD

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2 Audio CDs
Program Transcript

FACULTY

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CME Certified

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for more information or to download MP3 files of this audio program.

EDITOR'S NOTE

Grand rounds

From the very first day of medical school, the doctors of tomorrow learn that the most effective way to master clinical medicine is to "make rounds" with great teaching physicians. This process continues into residency and fellowship, as these neophytes follow and observe their experienced mentors at the bedside and take part in extensive case discussions of the patients they observe. Of particular importance during rounds is the review of the most recent clinical research findings and how these might affect the patient's care.

For over 20 years, the "rounds" approach has been a key feature of the audio education programs our group in Miami has produced for physicians and nurses who treat cancer patients. The enclosed patient education audio program was developed with the same concept in mind. For this issue, we visited the practice of community-based oncologist Dr Lowell Hart in Naples, Florida. Dr Hart arranged for us to meet three of his patients with lymphoma, and we invited MD Anderson Cancer Center's Dr Fredrick Hagemeister, an internationally recognized clinical research leader in lymphoma, to serve as our expert "attending" physician.

On this program, you will hear the perspectives of these three patients on lymphoma and its treatment, Dr Hart's presentation of these cases with the management course he recommended and Dr Hagemeister's commentary on the latest research data that should be considered during decision-making in these three situations. The transcript of these conversations is included on the first audio CD and is posted at **www.NHLUpdate.com/Patients** along with a downloadable MP3 file of the audio program. As with our prior pilot program, we are grateful for any feedback and suggestions.

— Neil Love, MD
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AUDIO PROGRAM GUIDE

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Transcript of the Audio Program

Neil Love, MD
Editor, *Non-Hodgkin's Lymphoma Update*
Miami, Florida

Welcome to *Non-Hodgkin's Lymphoma Update* and our second special patient education edition. This is medical oncologist Doctor Neil Love. For 18 years, our cancer education group in Miami has produced audio programs for doctors and nurses, and more recently we began producing programs for patients. This audio program is also available for easy downloading from the internet at **www.NHLUpdate.com/Patients**. And now for our program. The traditional way that doctors in training learn about medicine is by making rounds with their professors and after meeting patients, to listen and question the experts about issues raised by different cases. For this issue of our series, we took a similar approach and visited the community based oncology practice of Doctor Lowell Hart in Fort Myers on the west coast of Florida. Doctor Hart arranged for me to meet and interview three patients with lymphoma from his practice, and I then interviewed both Doctor Hart and clinical researcher Doctor Rick Hagemeister from MD Anderson Cancer Center in Houston to comment on the cases. We begin with Doctor Hart, who presents the first case.

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CD 1

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Please note that for clarity, Zevalin® and Bexxar® will be referred to by their trade names throughout the text of this monograph.

Case 1: Mr S

A 77-year-old man with gastric lymphoma who was treated successfully with chemotherapy, rituximab and radiation therapy

DR HART: He's a gentleman in his mid-seventies who's been in previously pretty good health. I actually knew him slightly, because he attends the same church as I go to. And he was referred to me by his gastroenterologist, having been just diagnosed with what was felt to be a gastric lymphoma.

DR LOVE: And that's lymphoma in the stomach?

DR HART: That's correct. This is an area where non-Hodgkin's lymphoma can certainly show up. It can be seen in almost any part of the body. And in the intestinal track, that's one of the more common places to have it show up.

DR LOVE: And he told me he had some symptoms, I guess — indigestion or GI symptoms that caused him to see the gastroenterologist.

DR HART: That's generally what happens. People have what they think are heartburn or gastric reflux symptoms or those sort of things. So that's why, in the commercials, they often say, "If you have persistent heartburn, see your physician."

DR LOVE: What did the — the gastroenterologist — see in the stomach?

DR HART: He saw what appeared to be something similar to an ulcer. So a lot of times these tumors can present with an ulcer-like appearance.

DR LOVE: And then he took a biopsy?

DR HART: Yes, he took a biopsy through the endoscope, which is the flexible scope that they insert down into the stomach. And that showed that this was a B-cell type non-Hodgkin's lymphoma. It was a type called a diffuse large-cell lymphoma, which is probably the most common type to be seen in the stomach.

DR LOVE: And when you did your initial evaluation of him, what were some of the things that you were looking for in terms of the history that you got from him and your physical examination?

DR HART: Well, certainly, we always want to ask the patient how they're feeling, if they've lost weight, if they're having fevers, if they're having sweats at night. Those sorts of symptoms can be symptoms that the lymphoma is not as localized as you might have expected. So, he did not have any of those symptoms.

He then had some scans performed to see whether there was any evidence of any lymphoma anywhere else. It's very important in staging the lymphoma, to know if it is showing up anywhere else.

DR LOVE: So staging is looking to see where else in the body the lymphoma might be present?

DR HART: That's correct, because the stage differentiates between lymphomas that are in one lymph node group, two lymph node groups, outside of a lymph node group or if it's disseminated throughout the body. And they all have a slightly different prognosis.

DR LOVE: And what were the diagnostic staging tests that you did on him?

DR HART: Well, we did CAT scans on him at the time. At that time, we were not routinely doing what are called PET scans, which are called positron emission scans that are now commonly done. So we've done some on him since that time. But those two scans are the mainstay, really, of the staging of lymphomas.

DR LOVE: What about a bone marrow biopsy?

DR HART: Yes. He did have a bone

marrow biopsy at the time of diagnosis, which is also done most of the time in lymphomas, because, obviously, these cancers start from lymphoid cells. And those cells usually originate in the bone marrow. So it is common in some types of lymphoma to have involvement of the bone marrow. It's not as common in the type that he had. And there are ways now to look at the bone marrow very closely with techniques like a flow cytometry, which is putting some of the cells through a machine so you can pick out one or two cancer cells out of many normal cells.

DR LOVE: And so when you did all those tests, did you find anything outside of his stomach?

DR HART: We didn't find anything outside of the stomach.

DR LOVE: And what were you thinking at that point in terms of treatment?

DR HART: Well, I was thinking that he was clearly going to need treatment with chemotherapy. And usually now, for these B-cell lymphomas, we add the antibody treatment rituximab. And that's clearly been shown to improve the response and is used almost universally now.

I told him that since his tumor appeared for the most part to be localized — although I could certainly not say 100 percent — that I thought he had a reasonable prognosis from this with some treatment, that I would be planning on giving him some chemotherapy and perhaps consolidating the treatment with some radiation just to the involved region of the stomach at the completion of the chemotherapy.

DR LOVE: Can you talk a little bit about, in terms of gastric lymphoma, the connection between that and infection?

DR HART: Right. It has been found, especially in the lower-grade types of gastric lymphoma. Sometimes you can see it in the more aggressive ones, like my patient, too. But there's a lower-grade type that's called a mucosa-associated lymphoid tumor. And that's the malt-type lymphoma, which is not only seen in the stomach, but it is described often in the stomach. And that is a very low-level type of malignancy. It seems like it sort of comes about as almost a reaction to inflammation or an infection that's kind of gotten a little bit out of control. And most lymphomas, we don't really understand exactly what the cause is. But I think when we understand more, it may be that infection or some reaction to an infection may be behind a lot of lymphomas. It's just not all worked out yet. But I think, certainly in these low-level gastric lymphomas, they are very frequently associated with Helicobacter, which also seems to cause quite a bit of the peptic ulcer disease that's around.

And interestingly, the first treatment that's generally used now is to try to eradicate this Helicobacter with the use of antibiotics. So, there's sort of a triple antibiotic package that the gastroenterologists use. And that's, generally speaking, the first treatment that's done. And sometimes, if you eradicate the infection, the lymphoma goes away; not always, but usually the first treatment now — unless it's very extensive or very deeply involved — if it's the usual type that we see, would be to treat the patient with antibiotics and then have them get their endoscopy, with a flexible scope, repeated, and a repeat biopsy done. And if everything's gone, then they're done. If it's not, then you can go on to other treatments, occasionally. It's also very sensitive to radiation therapy. So radiation can be used and, occasionally, I've sometimes given some rituximab. Not everyone does, but I've sometimes given some rituximab along with the radiation for that.

DR LOVE: And what kind of chemotherapy did you recommend?

DR HART: Since he was an older gentleman, I gave him a modification of the standard CHOP chemotherapy, which has cyclophosphamide, doxorubicin — the "H" is for doxorubicin, from the chemical name for it — vincristine and prednisone, which is a cortisone-like drug, plus the rituximab antibody.

And in his case, because he was an older gentleman and had, I thought, some risk factors for cardiac disease, I substituted another drug, called mitoxantrone, which is in the same general class as doxorubicin, but is kind of a kinder and gentler form. It does not damage the veins. It does not cause the hair loss or as many of the side effects. It may be, in some studies, slightly less efficacious. So, if he had shown evidence of having a very widespread, very aggressive lymphoma, I probably would have given him the CHOP anyway. But I made a judgment in his case that he could still have a reasonable chance of being cured with a slightly less aggressive treatment.

DR LOVE: And when you're talking about the heart, I guess the concern is that, specifically, the doxorubicin can, in some, I guess, very unusual situations —

DR HART: Right.

DR LOVE: — damage the heart.

DR HART: That's correct. You don't want to be using doxorubicin in someone who has preexisting heart failure or has a very weak heart to start with. As far as we know, it does not usually cause heart attacks or those sort of anginal symptoms, but it can weaken the heart if it's been given for many doses. Usually, the short course that we would use in lymphoma treatment at the start is usually not enough to do that.

DR LOVE: So what was the schedule of how often he got the chemotherapy and the rituximab?

DR HART: He got the chemotherapy once every three weeks and got his rituximab once every three weeks, also. He got a total of four cycles of the chemotherapy and, after that, I referred him to the radiation oncologist. He had looked to be in good

condition at that point, and my feeling was, since this appeared to be, for the most part, a localized process that I would feel comfortable with then moving away from the chemotherapy and letting him have radiation to the involved part of the stomach, which he indeed tolerated very well. He got about 4,000 rad, or centigrade. That's just a dosage term for radiation therapy. And that would kind of be a consolidation dose for lymphomas. Lymphomas are very sensitive, in general, to radiation therapy.

DR LOVE: So I know, in general, with cancer treatment, you give a treatment and then you try to figure out whether it's helped. And I guess in his situation, the main thing you had to judge was doing the endoscopy, where the gastroenterologist looks down into the stomach to actually see this. Did he have that repeated?

DR HART: Yes. He had that repeated and that has remained clear since that time. So, he had the endoscopy repeated.

DR LOVE: And at that point, there was no evidence of the tumor?

DR HART: That's correct. There was no evidence of the tumor.

DR LOVE: How did he tolerate the chemotherapy? How did he tolerate the rituximab and how did he tolerate the radiation therapy?

DR HART: He tolerated everything quite well overall. He did complain of some fatigue, just a general sense of tiredness. And he'd been a very active gentleman, sings in the choir at church and is very active with his wife, and they go out to do lots of senior activities and go out to eat frequently. So, he curtailed quite a bit of that during his treatment, but he has since then snapped back to pretty much of his normal self. He tolerated the radiation therapy quite well. They did give him a bit of some anti-nausea medication. Radiation will not cause nausea unless you're radiating the stomach. And since he was getting his stomach radiated, he had a bit of nausea from that. But it just responded to the usual anti-nausea medication.

DR LOVE: How did you observe him and his wife cope with this emotionally, as this moved forward?

DR HART: It was a stress on them, but they're a very close couple. And I think they sort of went through it together. And his wife tends to be even a little bit more — she worries a lot for him, because he's a very stoic sort of a Midwesterner type — not a complainer, and just sort of goes with the punches and is – one of the doctor's favorite type patients, who just says, "Do the best you can for me, Doc. I know I have something serious, and try your best."

His wife got a little bit more anxious than he did, I think, over how he was going to do with the treatments.

He's an inspiring patient, especially since he is a gentleman who got this when he was in his mid-seventies. And it's proof that no matter what age you are, if you have a reasonable quality of life, it's worthwhile preserving that. And hopefully, he'll have many more years of being able to contribute to the community.

He just has a wonderful inner strength. He is, as I said, a person of faith. And perhaps that has something to do with it. But he just a positive person. He does have a lot more strength, I think, and I don't even have a clue, if I was in the same position as he was put into all of a sudden, if I would deal with it as well as he did.

DR LOVE: It must be rewarding for you, as a physician, to see him come back with his wife and see him in church and see them out, active and doing well.

DR HART: It's very, very, very rewarding. I certainly would know it, if he was not doing well, because I see him almost every Sunday. But it is very nice to see him.

Mr S and his wife:
Adapting to life on chemo-therapy and rituximab

DR LOVE: I met with the patient and his wife to learn their perspective on the diagnostic and treatment process, and the patient began by commenting on the retirement lifestyle he has been leading for more than 15 years.

MR S: I'm a very active person. I go to the workout center three days a week. I work out. And I'm active — I play golf one day a week. And we were going to the beach. We do some volunteer work. We volunteer for the Ronald McDonald House soup kitchen. And I've always been in pretty good health. It started out one night — I woke up with a stomachache. It wasn't real bad, but it was a stomachache. The next morning, I didn't think nothing of it, so I mentioned it to my wife. And she says, "I want you to go and see our gastrologist."

So, she got me an appointment with him and he talked to me. And he says, "Well, it's probably nothing, but let's take a look down in your stomach." So he run a test and he called me a couple of days later and said it was lymphoma — cancer. So he asked me what cancer doctor I'd want, and Doctor Hart is a member of our church. We were real close. So, I told him I'd like to go see Doctor Hart.

DR LOVE: I'm curious what the reaction was for both of you, when you found out that this was a cancer.

MRS S: Oh, it was devastating.

MR S: She was upset more than me. What I told myself when they said I had cancer, I said, "I don't know anything about cancer, just what I've heard. I must leave my health to Dr Hart and to the good Lord."

And I prayed about it. And I just relaxed. I haven't thought any more of it. And I go for my treatments, and that's about all I can say.

MRS S: I worried enough for both of us.

MR S: Yeah. Mm-hmm.

MRS S: It made me very sick. I had to go to a psychiatrist, because I couldn't handle it. And I'm okay now.

MRS S: George never seemed to be concerned about it. And I always thought that maybe he was just trying to act like that, because he didn't want me to be concerned about it. But I was very concerned. I thought, "Well, what am I doing to do? What's going to happen to us? What if he dies? What am I going to do?"

DR LOVE: When you met with Dr Hart to sort of go through what was going on, what did he explain to you in terms of what type of tumor it was and sort of what the plan was going to be?

MR S: Well, he said it was in my stomach and it was a lymphoma? And he says, "I'm going to start you out with chemo, and you're going to take treatments in chemo. Then, after that, you can take some radiation, and we'll go from there."

And then he says, "Your health is good." He said, "You've got a good attitude."

My health is still pretty good. Like I say, I'm still working out and doing the things that I normally do. And he said, "I think you'll get through this okay."

MRS S: He was very optimistic, actually.

MR S: Yeah.

MRS S: He says that he really thinks that it's going to be curable.

DR LOVE: Was that a surprise to you?

MRS S: Yes.

MR S: Mm-hmm.

DR LOVE: What had you heard about cancer, or thought about cancer?

MRS S: Well, you always think about the bad things of cancer. Dying.

MR. S: Yeah. And that's really what I thought. I said, "Well, maybe there's nothing can be done." But after I talked to Dr Hart and I felt better, like I said, I just didn't worry about it. And I think not worrying has helped me more than anything, any medicine or anything else.

DR LOVE: What did he tell you to expect in terms of side effects or problems from the chemo?

MRS S: He told him that he might lose some of his hair, but he didn't think so.

MR S: No.

MRS S: But he might. And, actually, George got along very well. He did lose a little hair, but he got it back.

MR S: It grew back.

DR LOVE: And when you were receiving the chemotherapy, did you have any sickness to your stomach, nausea, vomiting?

MR S: Never. Huh-huh.

DR LOVE: Did you feel very tired during the chemotherapy?

MR S: No.

DR LOVE: Normal energy level?

MRS S: No.

MR S: I didn't work out at all during the chemo, did I?

MRS S: No.

DR LOVE: So, you stopped working out?

MR S: Yeah.

DR LOVE: But were you able to do your other sort of daily activities?

MR S: Yeah.

DR LOVE: Did he have as much energy — as normal?

MRS S: No, he did not.

DR LOVE: How difficult a problem was it? Was he in bed or —

MRS S: No, no, no. He was never in bed. But, I mean, he just didn't have the get-up-and-go that he had had.

DR LOVE: So it sounds like while you were getting the chemotherapy, other than some tiredness, it really didn't have a big effect on you.

MR S: No.

MRS S: It didn't.

DR LOVE: Was that surprising to you?

MRS S: Was to me.

DR LOVE: You were expecting it to be a lot more difficult?

MRS S: Mm-hmm, because we read all the books and things —

MR S: Oh, yeah.

MRS S: — they gave us.

MRS S: And it indicated that it would be...but he was very fortunate.

MR S: Mm-hmm.

DR LOVE: Did you have any side effects when you got the rituximab?

MR S: No.

DR LOVE: Sometimes people, the first time they get rituximab, get kind of a reaction during the infusion. Did you have any problems during the infusion?

MR S: No.

DR LOVE: At all?

MR S: Uh-uh...

DR LOVE: No hair loss?

MR S: Very little hair loss.

DR LOVE: It didn't make you sick or anything like that?

MR S: No. My appetite was good. I lost about six pounds when I first started the treatments. Then I started gaining them back. And right now, my weight is the same it was two years ago.

DR LOVE: Now, when you getting just the rituximab alone, did you have normal activity and energy levels? Did it go back to normal?

MR S: Yeah. I think I did.

MRS S: Yeah. You're taking rituximab now, honey. That's what you've been on.

DR LOVE: You're still on the rituximab now. Do you feel the same as you walk around, same activities as you did before this whole thing started?

MR S: Yeah. Mm-hmm. Mm-hmm. Mm-hmm. Yeah.

DR LOVE: So, what's your take on this whole experience?

MR S: I'm excited about it.

DR LOVE: Are you surprised about what happened?

MR S: Well, I'm surprised that it happened that fast, but, like I say, I didn't worry about it. Because I figure, if I start worrying about it, that's the worst thing I could do. And I think anybody today that gets cancer, try not to worry about it and try to live a normal good life, if you can.

MRS S: And go see Doctor Hart.

MR S: Yeah. And go see Doctor Hart.

DR LOVE: Do you know much about rituximab?

MRS S: No.

MR S: Nothing.

MRS S: Isn't it about the same thing as chemo?

DR LOVE: Actually, it's different. It's actually considered an immune type of therapy, whereas chemotherapy is a very strong type of treatment that attacks —

MR S: Yeah.

DR LOVE: — rapidly dividing cells, kind of, in general. So it might attack, for example — people lose hair, because it can affect the cells in the scalp. It can cause nausea and vomiting in some people. So it has more general effects. Rituximab is much more specific, and it's actually an antibody-type of therapy.

MRS S: Yeah.

DR LOVE: It's an immune therapy. So it's kind of a newer type of treatment.

DR LOVE: It's — I guess it's been around for some years now, but it's thought to be more targeted, more precise in how it deals with the cancer.

And that's really part of a trend in cancer therapy in general, more and more treatments like that that are very specific to the cancer.

DR LOVE: What have your interactions been like with Doctor Hart?

MR S: I think he's great. He and his people, the nurses, are all just wonderful. They kept close check on me when I was taking the chemo and — well, a matter of fact, they just — every 15 minutes, they were checking each patient. And seemed like everybody in there was happy, oh, talking and everything. So, I — no, I never — actually, like I say, I didn't worry about it. And I had a lot of confidence in Doctor Hart.

DR LOVE: What was it like to go to his office and see people with all the different kinds of problems...

MRS S: It was an absolutely devastating thing. When you go into a place and you see rows of recliner chairs and people in every one of them with a needle in them who have cancer — it's really an eye-opener. It's almost unbelievable.

DR LOVE: In what way?

MRS S: Well, you just can't believe that that many people have cancer.

MR S: And we're not doing enough for cancer. That's my personal opinion. I don't think the government – I don't think anybody is doing enough

DR LOVE: If you were going to sit down with another couple who was exactly where you were, at the very beginning. You had your biopsy. You're going to your doctor. Your doctor said, "I think you should get chemotherapy, radiation therapy."

MR S: Mm-hmm.

DR LOVE: What would you say to them? Any advice you would give them?

MR S: Well, the first thing I'd say is, don't worry about it, because worry is going to put you in the grave faster. And try to live as much normal life as you can. And then you listen to the doctors. If they say do something, you should do it, because they know more about cancer than you do.

I think living a normal life is the number one thing that helped me with the cancer. And I think if I talked to anyone else, I would suggest to them that they should try to live as normal life as possible. As much as possible, enjoy their family and wife and —

MRS S: And their friends. We continue to go dancing and —

MR S: Yeah.

MRS S: We didn't dance quite as often as we did before, but we continued to do everything. We went out with our friends.

MR S: We were doing things that we like to do. We did them before I had cancer, and we decided — she plays her bridge and I play my golf on Monday or Tuesday and we go out on Thursday, dancing. We play our cards on Wednesday. And we didn't try to change our life. I just wasn't going to let the cancer beat me. That's the way I feel. And I would tell anybody else, oh, no. Don't let the cancer beat you." I'd say, you can beat it.

MRS S: Well, we can't always.

MR S: Well, no, you can't always. But you can sure try.

Dr Hagemeister:
Discussion of case 1
Management of lymphoma of the stomach; mechanisms of action of rituximab and chemotherapy

DR LOVE: I asked Doctor Hagemeister to comment on this case, and he began our conversation by providing an overview of lymphoma of the stomach. Large-cell lymphoma in the stomach is an interesting type of illness. It's one of those malignancies that we think — or at least, traditionally, has been thought of as being a disease that is a little different than other kinds of large-cell lymphomas. It may or may not be. But we do know that there are special sites of lymphoma, particular places where lymphoma shows up. I mean, why would you develop lymphoma in your stomach? There are no lymph nodes in the stomach. So why would malignant lymphocytes, or cancerous lymphocytes, end up in the stomach?

It is assumed, I suppose, that there are certain receptors or certain molecules that are on the surface of these cells, that tell them that they can grow in certain areas of the body quite well without relying on lymph nodes to grow in.

The stomach is one of those. The gastrointestinal tract is a favorite place for some lymphomas to grow.

DR LOVE: So just in general with lymphoma, we think of it as developing in lymph nodes, but then it can migrate to other parts of the body?

DR HAGEMEISTER: But we don't think that in this particular case. We already know that certain lymphomas, in particular, slow-growing lymphomas, that are known as marginal-zone lymphomas or malt lymphomas, actually start in the stomach. And they end up starting there because, theoretically, there is some irritation in the stomach, because of a particular bacterium called *Helicobacter pylori*. And that inflammation induces a response — a reaction, which attracts lymphocytes. And those lymphocytes, because of continued irritation, develop into malignant cells, because of the constant irritation that takes place.

DR LOVE: Now, Dr Hart actually told me that he did a *Helicobacter* test on this patient. Is that kind of routine? Everybody does that?

DR HAGEMEISTER: It would be in a gastric lymphoma, to do that on a regular basis. And it would be also routine to look for areas that show that there was a slow-growing lymphoma perhaps in the background, and maybe the large-cell lymphoma grew out of this slow-growing lymphoma. But there's nothing to say that there's not some other kind of, perhaps, primary irritant in some way. It doesn't have to be *Helicobacter pylori*. We are still very, very much in our infancy in oncology in understanding what causes lymphomas to grow in particular areas and why they happen to migrate there or grow there more easily.

For example, this patient very likely had those malignant cells seeding other places, but they didn't grow in those places, you see? That's why it only showed up in his stomach. Given enough time, those cells would eventually learn that they could grow elsewhere. And they would grow in nodes, perhaps, or spread to other areas in the body without obviously just spreading locally; in other words, growing and just spreading outside of the stomach, in the area of the stomach. But it might have spread to other sites.

DR LOVE: Now, this patient had a negative *Helicobacter* test. But have you had patients where you've given them antibiotics and the lymphoma goes away?

DR HAGEMEISTER: Oh. That happens with indolent lymphoma or marginal-zone lymphoma, or MALT, as it's otherwise known. That's mucosal-associ-

ated lymphoid tissue lymphoma. That happens very commonly that you can get a response, that patients will have their lymphoma disappear when they have a slow-growing lymphoma. But I'm not aware that treatment for *H-pylori*, in cases of large-cell lymphoma, induce remission from the lymphoma by being treated with antibiotics.

In fact, the Germans have done a study — probably the largest study that's been done giving antibiotics for patients with marginal-zone lymphoma involving the stomach. And those people who did not have a response to *H-pylori* antibiotic therapy — if they didn't respond, the Germans recommended, strongly that the doctors needed to go back and look and see if the patient didn't also have a diffuse large-cell aggressive lymphoma component present, as well as the indolent lymphoma.

DR LOVE: And that was another thing that DR Hart was talking about as a community oncologist dealing with lymphoma and everything else and that is his perception, that it's very important to make sure you have expert pathology when you have a lymphoma case. Do you often see that when your pathologists at MD Anderson rereview or provide a second opinion, that it might be different than the diagnosis that the patient comes in with?

DR HAGEMEISTER: We used to see it a lot more commonly than we do these days. Let me just say maybe — pick a number — 10 years ago — I would guess that at least a third of the patients who came to see us had a very significant change in their pathology, in looking at their slides. We called it something very significantly different from what outside pathologists had called it. Nowadays, because we have better studies to look at those cells — in other words, not just by having the pathologist look at it with his eyes, but also to do special stains now — because of those special stains and better technology that's used to analyze these cells when they are on the slide, we now can make a better distinction, and pathologists in the community have a better chance of being able to make a diagnosis, which better characterizes the patient and puts them into a slot, as far as a diagnosis is concerned, much more easily.

DR LOVE: Now, can you talk a little bit about how you approach these patients who have diffuse large B-cell lymphoma in the stomach?

DR HAGEMEISTER: Oh, sure. There have been studies that originally realize that, because you could cut out the disease and remove the disease surgically, surgeons were the persons who originally saw these diseases and treated them. That was years ago.

DR LOVE: That was kind of like the way a typical cancer of the stomach might be approached: Take it out.

DR HAGEMEISTER: Correct. Remove it. That's the same in many sites where the disease presents outside of lymph nodes. For example, the testes, the ovary, perhaps even lung. It's been done in the past, removing the lung, as you would a lung cancer. It's been done in brain disease as well and perhaps even sinuses or parotid or thyroid, in that you do surgery to remove the disease.

DR LOVE: And that's kind of based on the model of the primary tumors that usually occur in these organs, which, in some cases and in many cases can be cured by surgery.

DR HAGEMEISTER: Right. So obviously, that's the model. However, that's more than 30 years ago. And as time went on and it was recognized that radiation therapy was effective treatment for a lot of patients who had localized disease, radiotherapy was being used more as adjuvant treatment after surgery and, ultimately that means to try to get rid of the disease, keep it from coming back after surgery had been done, and ultimately, when chemotherapy became available, especially effective chemotherapy, for large-cell lymphoma, for aggressive lymphomas, then finally it became that chemotherapy became a standard of care for these patients.

Nowadays, surgery is not at all the treatment of choice for these patients, and it hasn't been for at least 10 years, a minimum of 10 years. Everyone would select chemotherapy as being the first treatment for such a patient with involvement of the stomach.

DR LOVE: And why is that? Is that basically because in the other types of more common tumors, you're hoping it's going to be just in that area, but in lymphoma, that's not really what's going on?

DR HAGEMEISTER: Well, perhaps. But more than that, results seem to be better when you give chemotherapy, whether you do surgery or not. In other words, patients who were treated with surgical removal of the tumor and then got chemotherapy did better than the patients who got surgical removal of the disease. So for a long time, oncologists have recognized it, investigators have figured out that chemotherapy is the mainstay of therapy for these patients. So the only question has been whether radiation therapy should be used.

DR LOVE: What have you seen in terms of the effects of chemotherapy in these tumors?

DR HAGEMEISTER: Well, the patients go into remission on a regular basis. This is no different, probably, as far as response is concerned or complete remission is concerned, than it is in any other site. In fact, my general observation is that patients with gastric large-cell lymphoma tend to do better than patients who have other kinds of localized large-cell lymphoma, perhaps. And there are some studies that suggest that may not be true, in that, if you look at whether someone who has gastric lymphoma in a large series, because there aren't that many patients, you may not see very much difference. But if you look at series that have given chemotherapy with or without radiation therapy, results are extraordinarily good.

DR LOVE: What about the selection of chemotherapy? I know there are a number of different kinds of treatments. This man got one type of treatment. What's the spectrum of chemotherapy that's used in this situation?

DR HAGEMEISTER: R-CHOP has to be considered. I think that results with R-CHOP are so good, with or without radiation. Radiation therapy should be considered, and should be probably considered as standard. The only question is, how many cycles of chemotherapy do you administer, more than what regimen do you administer.

DR LOVE: Can you sort of dissect out the R-CHOP regimen, maybe starting with the rituximab?

DR HAGEMEISTER: Well, rituximab is one of those drugs that, fortunately, side effects are not 100 percent, but are, let's say, 95 to 96 percent of the time limited to only the time that the patient receives their first infusion. In other words, while the patient's actually receiving the treatment in the clinic or in the hospital for the first time, over that, say, four- to six-hour period of time, that's the only time the patient will have a side effect. They consist of chills, perhaps a drop in blood pressure. Very rarely, a patient will have some kind of trouble breathing or some other more significant side effect. And those side effects disappear once the rituximab is stopped or the infusion is slowed.

DR LOVE: What fraction of patients have those reactions?

DR HAGEMEISTER: Somewhere around 50 percent will have some minor — that is, Grade I or II — side effect. Grade III or IV side complications or side effects are really, really rare.

DR LOVE: And what's going on? Is this an allergic reaction? What's actually happening?

DR HAGEMEISTER: It's the interaction of the rituximab with the immune system. You think of it that some doctors have said, "Well, that's a good thing, that your body is reacting to the rituximab." But what it really is is just that it's recruiting cells that — say that rituximab is interacting with cells that cause those side effects. It's that the rituximab is interacting with the immune system. And when it does, those cells are called into action, and they release certain cytokines and certain proteins that happen commonly. For example, when you get an infection, those cells are also activated. Rituximab activates those cells. And therefore, a patient can get fever and low blood pressure.

DR LOVE: And why is it that usually you only get it for the first time and, when you give it again, it doesn't happen?

DR HAGEMEISTER: That's a really good question. I don't think we know the answer to that, to be honest with you. One would think that it would mobilize those cells again in order to act in patients who receive that therapy, but it doesn't happen a second time or a third time. In fact, the more that — of the rituximab you receive, the more your body's cells are accustomed to having been exposed to it. So the first infusion reaction is pretty clear. But after that, the rituximab presumably is around still, some. It hasn't disappeared completely from your body. It's still in lymph nodes, perhaps, or wherever it's hiding. There's still, rituximab is present when you receive your second dose of rituximab the week later or after three weeks.

In fact, there's a really interesting study that was just looked at in Canada, where they tried to reduce the rituximab infusion to one hour and they demonstrated that you don't get any more side effects with the second, third, or fourth administration of rituximab, as long as you're giving steroids along with it. So that when you're giving R, rituximab plus chemotherapy, you can actually reduce the infusion to an hour, rather than giving it over, say, three or four hours; therefore shortening the time in the clinic, thereby saving money. And of course they're interested in doing that in Canada, because of their healthcare payment system.

DR LOVE: Well, I mean everybody's interested in getting out of the oncologist's office as soon as possible.

DR HAGEMEISTER: Everyone is, absolutely.

DR LOVE: Is that something you're now doing, the one-hour infusion?

DR HAGEMEISTER: We haven't adopted that policy yet, although we have a policy where, if patients are receiving are not having a side effect the second time, we do shorten the infusion. So it is shortened. Rituximab is administered more rapidly. But this is the first study that I know, that's looked at it in a really prospective fashion, that has said, if we give rituximab after the first time it's been administered, the second and subsequent times it's given, as long as it's given with chemotherapy that includes a steroid — let's say prednisone — as in this particular patient, you can reduce the infusion to one hour, and you don't have any additional side effects, as if you just gave it over three or four hours or something like that.

DR LOVE: It was interesting when I talked to this patient and his wife that they sort of thought rituximab was chemotherapy. They didn't realize what it was. Can you talk a little bit about what the difference is and sort of how rituximab works, compared to how chemotherapy works?

DR HAGEMEISTER: I'm not sure that I know what the differences are between the way rituximab works and the way chemotherapy works. They probably both work through some similar pathways in the cell, meaning that ultimately, they induce apoptosis. That means the cells implode rather than explode. They don't just suddenly burst open and die. Instead, the DNA, the machinery that keeps the cells alive, the cancer cells alive, the DNA disintegrates, and it disintegrates with both rituximab and it disintegrates

with chemotherapy. All of this takes place through a final pathway that's known as a Bcl-2 pathway. That's apoptosis, and that means that the cells implode. And Bcl-2 is one of those mechanisms whereby cells undergo this degeneration, this DNA degeneration and, eventually, implosion.

So rituximab, when it's administered with chemotherapy, actually potentiates those effects. And in that case, rituximab is probably not acting strictly as a monoclonal antibody to get rid of the disease but is, instead, interacting with the chemotherapy to make the cells implode.

DR LOVE: You said it's a monoclonal antibody. Can you describe what that is?

DR HAGEMEISTER: Yes. In order to make rituximab, they took a part of a lymphoma cell, known as CD-20. It's a protein that's on the surface of a lymphoma cell. They injected it into a mouse, and the mouse knew that it was of human origin and made an antibody against it, against the CD-20. It was known as a monoclonal, rather than a polyclonal or multiple different kind of clones of cells were involved, and still just one particular lymphocyte in the mouse made all this antibody, which is all lymphocytes do, anyway. B lymphocytes just make antibodies.

And in this mouse in which they injected the CD-20, it made a monoclonal antibody. They tried, then, to use this antibody, after it was purified, to treat human beings. However, human beings made an antibody against the antibody. And becau —

DR LOVE: Because it was from a mouse.

DR HAGEMEISTER: Because it was from a mouse. The human being knew that this was of mouse origin and said, "Well, I'm going to make an antibody and get rid of that, because I don't want that around."

So what the company that eventually came up with rituximab did is they took off the portion that the human being recognized as being of mouse origin and substituted a human portion — a human antibody. In order to do that, they had to fuse the DNA from the mouse that made the portion that attaches to the CD-20 with DNA from the human being that made the portion of the human being antibody that would make it unrecognizable to the human being as being a foreign protein, fuse those two pieces of DNA and then, now they have a piece of DNA that will make this antibody that is known as a chimeric antibody. A chimera, from Greek mythology, is a creature that's made up of two different kinds of creatures — for example, an eagle and a lion. Well, that would be a chimera — a lion with wings, for example.

Well, this is a chimeric antibody, meaning that is an antibody, a monoclonal antibody that is made up of part mouse and part human. It is not any longer recognized by the human being as being a mouse antibody. The human being does not make antibodies against it, doesn't destroy it. So you can give it multiple different times and it doesn't get destroyed.

DR LOVE: And what happens once this substance goes into the body? It then seeks out or hooks up with the CD-20 antigen sticking out from the lymphoma cell?

DR HAGEMEISTER: It immediately attaches to those sites, to where CD-20 is. The only problem that investigators haven't really understood is what the reservoir is for this drug, because normally, this drug should disappear in a relatively short period of time, because all gamma globulins — this is just a globulin, a gamma globulin, if you want to think of it that way. It's an antibody, a gamma globulin that normally does not last for a very long time in the human beings, say a month or so. Maybe less. But this antibody, when you give four doses once weekly, can last as long as six months. So there has to be a reservoir. There has to be some place in the body where rituximab sits. And it isn't destroyed as a normal antibody or doesn't degenerate as a normal antibody would in the body. Instead, it's got to sit around for a while. So no one has yet described where that is. That may be normal lymph nodes. It may be in normal lymph nodes that the antibody is still preserved. It may be in lymphoma cells that haven't decided to die yet.

DR LOVE: Now, most people, you know, understand the idea of an antibody, you know, being produced by the body to deal with infection, and that's how, you know, a lot of infections sort of go away. Is this sort of the same kind of action, but just targeting the lymphoma cells, as opposed to, say, bacteria?

DR HAGEMEISTER: Sort of. I don't think it's quite that simple. There's a theory about monoclonal antibodies. Theoretically, you, Neil Love, were born with all the lymphocytes, perhaps thousands of different kinds of lymphocytes, one of each kind of lymphocyte, to combat all the viruses or bacterial infections that you might encounter during your lifetime, and that whenever you are exposed to those viruses, you are challenged to have those normal lymphocytes manufacture an antibody. They proliferate. They then manufacture an antibody that specifically goes to control that infection.

Well, you also have lymphocytes that also control whether you are exposed to somebody else's cells or somebody else's tissue, because those lymphocytes are there to protect you from what is not you. And in this particular circumstance, this is an antibody that is given to you in a passive sense. It's not a normal antibody that you're going to encounter in yourself. It's not one that you're making up. So it's something that's a passive antibody that's now being administered to you to get rid of a specific target in your body.

Others have tried to come up with antibodies that are also useful, that

are made in, for example, other types of animals — for example, monkeys. There's one that's being made in monkeys right now that may turn out to be something of value. But there are other mouse antibodies that haven't turned out to be quite so good. And maybe it has to do with the target; maybe it has to do with the fact that they're not very good antibodies. I just don't know. Rituximab seems to be the one that probably here to stay. But it's not quite as simple as saying, "Okay. You happen to have this antibody that's protecting you from a virus." In fact, the lymphoma cell is made up of not only some abnormal DNA, but it's also made up of your normal DNA.

DR HAGEMEISTER: So that's a problem in considering antibody therapy for lymphomas. It's also a problem in considering vaccine therapy, in that you're not going to end up having a vaccine developed just against any kind of virus. You may have that against a virus, but you're not going to get that against a cancer cell, because every person's cancer cell is that one person's cancer cell and not everybody else's cancer cell.

DR LOVE: Now, why is it that you see side effects like hair loss or nausea and vomiting with chemotherapy and you don't see that with rituximab?

DR HAGEMEISTER: Rituximab doesn't appear to affect actively growing cells, for one. Chemotherapy, in general, has different mechanisms of action in order to get to that final degradation pathway. It doesn't just interfere with DNA in cancer cells, whereas rituximab targets specifically B CD-20, B-cell CD-20 surface antigen. And so hair cells don't have CD-20 on the surface of them.

DR LOVE: You used the word "targeted," and, to me, I hear that talked more and more about with these agents like rituximab, which are very, very specific to the cancer cell, whereas chemotherapy is not quite as specific. Is that the way you sort of conceptualize it?

DR HAGEMEISTER: It would be a nice way of putting it in a sort of easy way of understanding it. There's a lot more that's involved. For example, chemotherapy interacts with the DNA directly, whereas rituximab doesn't interact with the DNA directly. So, for example — and methotrexate acts differently from doxorubicin or Doxorubicin or in cyclophosphamide. They all have different sort of mechanisms of action that do interfere with DNA. But these drugs interact and combine with the DNA differently than does rituximab. Rituximab doesn't do that. Rituximab, instead, targets just something on the surface of the cell and then causes what are known as downstream effects. In other words, effects after it interferes with that surface molecule. Then those molecules play a very important role in the cell machinery. And eventually, the DNA degrades because of that attachment of rituximab to the CD-20.

Case 2: Ms M

A 65-year-old woman who received R-CHOP therapy for diffuse large B-cell lymphoma

DR LOVE: The second patient presented by Dr hart also was diagnosed with diffuse large B-cell lymphoma, which is the most common lymphoma subtype and is considered a quote aggressive form of the disease compared to more indolent subtypes like follicular lymphoma. This 65-year-old woman presented initially with difficulty breathing.

DR HART: She presented to her physician with some respiratory symptoms, shortness of breath, was found to have a large pleural effusion and also a mediastinal mass.

DR LOVE: And pleural effusion being sort of fluid around the lung.

DR HART: Right.

DR LOVE: Mediastinal mass inside the center of the chest.

DR HART: Correct. There's large numbers of lymph nodes there, and many cancers, including lung cancers or breast cancers, other cancers, can spread to those lymph nodes and make them enlarged. Lymphomas can certainly do that, too. So that's one of the diagnoses that is considered a lot when a patient presents like this. Obviously, another common diagnosis that would do this would do this would be a lung cancer.

DR LOVE: So these are the lymph nodes kind of around the bronchus and the lung and the heart, in the middle of the chest.

DR HART: Right. And that is a serious place to have involvement, because, obviously, they can press on either the airway passages, or they could press in the blood vessel leading to the heart or they can actually get into the sac around the heart, which is called the pericardium, and collect fluid there, too.

DR LOVE: And when you first saw her, what kind of condition was she in?

DR HART: She was having some respiratory symptoms. She had already undergone what's called a thoracentesis, where a needle is put into the pocket of fluid to drain it out and —

DR LOVE: That's sort of in the side of the chest?

DR HART: Yes, it's put through the chest wall into this pocket of fluid. Sometimes you can take out a liter or two liters of fluid. And the patients will usually feel better very quickly after that, because then their lung on that side has more room to expand. You can exchange more air and you feel instantly better. So she was feeling somewhat better from that, because I think that fluid collection what was causing most of her symptoms.

DR LOVE: And how did you approach her treatment or her workup at that point?

DR HART: We referred her to the thoracic surgeons, which are the chest surgeons that are expert in doing operations. Lymphomas are almost never cured with an operation, but we sometimes will do small operations to try and make a definitive diagnosis. It's very important with lymphomas that you have big enough biopsies so that the pathologist can classify the different types of lymphomas.

DR LOVE: And what happened?

DR HART: Well, they went in and did what's called a mediastinoscopy and did a biopsy of some of those lymph nodes. And that showed that this was what's called a diffuse large-cell lymphoma, which is a common type of lymphoma. The large cell just means that it was an aggressive-type lymphoma.

DR LOVE: So that was similar to what you described for Mr S.

DR HART: That's correct. This is the same general type of lymphoma, which is a very — it's one of the two most common types of lymphoma that medical oncologists deal with.

DR LOVE: So did she have it anywhere else in her body?

DR HART: She did have some lymph nodes in other places that you could see. She had some in the periaortic region, which is down in the upper part of the abdomen, near the aorta, or the large blood vessel there. So she had some involvement in those areas, too.

DR LOVE: And so you saw those on the scans?

DR HART: Right. Those were seen on the scans. Those were not biopsied. Usually we biopsy the most important site or the most accessible site and then we look at the other sites and try and check them with scans.

DR LOVE: And did you do a bone marrow biopsy in her?

DR HART: Yes. She did have a bone marrow biopsy done. And hers was felt to be negative.

DR LOVE: So what kind of therapy did you think about for her and discuss with her?

DR HART: Well, I decided with her to give her the rituximab antibody and also a regimen called CHOP, C-H-O-P, which was very similar to what was given to Mr S. In her case, she was a younger woman. I felt that she had certainly a bulkier, more potentially life-threatening lymphoma. So she needed to get basically the full-court press.

DR LOVE: What do you usually see in terms of side effects with CHOP — certainly, it's a very common, maybe the most common, form of chemotherapy in lymphoma — and also rituximab?

DR HART: Well, with rituximab, the main side effects that we see are related to the infusion, commonly with the first one. It does not tend to cause effects later on, but you certainly can get fevers or chills. It depends a little bit how much is the burden of cancer in the body. The more cancer the patient has when they start, the more likely they are to get effects. A patient that has a lot of lymphoma cells in their bloodstream is obviously going to get a much higher chance of a reaction. So often in those patients, we will give them just the chemotherapy first and come back with the rituximab once we have killed off quite a bit of the cancer cells.

So rituximab is otherwise very easy to tolerate aside from that. So we run it in very slowly for the first treatment, over about six hours. We can sometimes shorten it to four hours for subsequent treatments.

DR LOVE: When they have these kinds of reactions, sort of how bad are they?

DR HART: They usually will respond to slowing down or stopping the rituximab. We will sometimes give the patient some medication with a drug like diphenhydramine, some Acetaminophen. Occasionally, we will need to use some corticosteroids, something li — there's several drugs that can be given that are sort of prednisone-type drugs, too. So it's rare to have a patient who absolutely cannot take rituximab. I've had two in my career that I absolutely could not get any rituximab in, even under, you know, putting them in the hospital and dripping it in very, very slowly. But that's a rare exception. The degree of reaction can be — if you're not used to it — can sometimes be very scary to the patients, sometime to the nurses and physicians. But since the drug is so widely used now, I think most oncologists and most oncology nurses are aware of this and are able to deal with it.

DR LOVE: Now, is it true that usually, by the time the patient goes home, they feel fine?

DR HART: Yes. Absolutely.

DR LOVE: And that, in general, it tends to stop after maybe one infusion, or maybe the second one?

DR HART: Yes. That's absolutely true. That's why we can almost always go ahead with the second infusion and subsequent infusions a little bit faster.

DR LOVE: Now, do you see the same kinds of side effects that you see with chemotherapy, the hair loss, nausea, vomiting, et cetera?

DR HART: No. Rituximab has essentially no hair loss and no nausea or vomiting, because I tell the patients, "This is not chemotherapy. It is a targeted agent, which is an antibody to a protein that is on the surface of the lymphocytes." So actually, we don't know exactly all of its mechanisms of action. That's still being worked out. But it does target the cancer cells and may help the immune system recognize the cancer cells better, to get rid of them.

DR LOVE: You mentioned before sort of how the treatment of lymphoma has evolved and particularly how things change when people started to utilize rituximab. And I guess that was really in the '90s. What did you sort of observe as you started to add that into your treatment with the chemotherapy?

DR HART: I just observed a lot more patients being in complete remission after we finished, say, six cycles of CHOP chemotherapy.

DR LOVE: In other words, the tumor going away?

DR HART: Yes. So a lot more patients that had no evidence of cancer at that time. And so I think it's one of those innovations that I think, the studies came out. The drug was released. Once practicing doctors started working with it, it probably took it just a few months to become basically, at least in America, the absolute standard treatment. This is one where the drug was good enough that the doctors, I think, even leaped ahead of what the studies had shown, because they felt this does not add a lot of side effects. It really boosts the effect of the treatment.

DR LOVE: Now, not to get too far off on a tangent, but a lot of patients such as, basically, the first two that we've talked about so far, receive chemotherapy plus rituximab. What about using Rituximab alone, without chemotherapy?

DR HART: That is done quite frequently for patients with the slower-growing types of lymphomas. The diffuse large-cell lymphoma, which is the most common type of aggressive lymphoma, in general can certainly be helped by rituximab alone, but it is too aggressive a lymphoma to be permanently cured with the rituximab treatment alone. Remember, one of the paradoxes that I try to explain to patients with lymphomas is that the slower-growing lymphomas are almost never cured, whereas the aggressive lymphomas put your life at risk, but you can often cure them, also.

DR LOVE: So these first two patients really fit into that category of having the aggressive tumor, where hopefully you'll be able to cure them. If not, it's a big problem. Whereas the other, the more indolent ones that you were talking about, even if you don't cure them, the patients may do well for a very long period of time.

DR HART: They may do well for many, many years. And if they're an older patient, I tell them that if we can control this, even if we can't cure it, you may be able to live out your normal life expectancy.

DR LOVE: Getting back to Ms M, can you talk about how she tolerated the treatment and what happened in terms of the tumor?

DR HART: She tolerated the treatment very, very nicely. She did not require any hospitalizations. She is a much different affect than Mr S. He's sort of a quiet and reserved person. She's much more open about things and will come in and feel free to complain about anything she wants to in the office and does not keep anything back. So that was refreshing to deal with, also.

But she did quite well with her treatment. She had the expected hair loss. She did not have very significant problems with nausea. Her blood counts did decline some with her treatment. We did use some of the growth factor support in her treatment. We have drugs now, which will boost up the white blood cell and the red blood cell count, and they're commonly used. One's called filgrastim or pegfilgrastim, and there's one called epoetin alfa, which is commonly used for red blood cells. Those have also been one of the major breakthroughs in cancer treatment in the last 15 years or so, where we can now support these patients so they — even if their white count declines — and I tell the patients especially on CHOP chemotherapy it will decline, unless you use shots not to keep it up.

DR LOVE: What happened to the tumor?

DR HART: Her tumor did very, very well. And we got a CAT scan after two or three cycles that showed a great improvement. And she completed her six cycles, and follow-up CAT scans done since that time — this is about a year and a half or two years ago now — continue to show no evidence of recurrent disease. With these aggressive lymphomas, I usually tell patients that if you are cancer free at the three-year mark from the treatment, that there's a reasonable chance, a very good chance that you're going to stay free of cancer.

DR LOVE: Now, can a patient have completely normal scans and yet still have the cancer come back?

DR HART: That can certainly happen. There's no scan that can find one cancer cell or 10 cancer cells or 100 cancer cells. So the only absolute test is the test of time. And I always try to explain that to patients, that if they're looking at me feeling well a certain number of years after diagnosis, then at least in the large-cell lymphomas, we can give them a reasonable guarantee that they're going to stay free of cancer.

DR LOVE: How did you see Miss M sort of responding emotionally, coping with this situation?

DR HART: My impression of her was that she did well and tolerated things. So she has a very close family. Like I said, she's very close with her daughter and her son-in-law. I think that she tolerated things well. I'm sure that there were things that she wanted to do that she couldn't, but as a physician, there wasn't that much that I recall her talking about as being devastatingly bad side effects. So I think that she went through things and tolerated things pretty well, because she also had, in a different way from Mr S, she also had some good emotional strength.

DR LOVE: How did both of these patients sort of recover from chemotherapy? You've talked about, you know, football players missing a season. How long did it take Miss M to sort of get back on her feet from what you could tell?

DR HART: Several months. I think it took her several months to get back to things. I mean, I usually tell them, "As your hair is growing back, your energy level will be recovering, too. So think of it coming along at the same time. Your hair grows about an inch a month, and your energy level is going to be increasing up over that amount of time."

Most patients are somewhat anemic after they finish their treatment. It's important for patients to understand that it takes a while for this to happen. It takes a while for the body to recover. Sometimes it can be upsetting to patients, if they think, "Well, I finished my chemotherapy. Life goes on now. I should be ready to go." They have to give themselves time to recover from that.

DR LOVE: I'm curious about the spectrum of the types of cancers that you treat in your practice and where, sort of, lymphoma fits in, in terms of is it a rare cancer for you to see? Is it as common as some of the more well-

known ones, such as breast cancer? How often do you see lymphoma patients?

DR HART: We see quite a bit of it. It is not the most common cancer by any means. It's certainly not in the big four of cancers, like breast and lung and colon and prostate, which are the ones, you know, the most common adult serious cancers. Lymphomas have been going up in their incidence in the last 10 years or so, as opposed to some other cancers, which have been declining. We're not sure why that is.

Most lymphoma patients do get referred in at some point to see a medical oncologist. So I think, as a medical oncologist, we do see almost every patient in town who has a diagnosis of lymphoma, whereas we don't necessarily always see every breast cancer or prostate cancer patient.

DR LOVE: Do you think that most oncologists in practice, such as yourself, who's well read and keeps up with things, you know, is in as good a position to take care of a patient with lymphoma, as somebody at an academic center or university?

DR HART: I think there's no reason that they should not be. I think the pitfalls that you can run into in private practice taking care of lymphomas, one of the things that can happen — and this can happen in academic places, too — and I've been in both camps at various times in my career — is with not having the pathology ascertained and reviewed. So I certainly would tell patients that lymphomas are one of the more difficult pathologic diagnoses, and even very experienced pathologists who look at lymphomas all day long and have done so for 30 years can have differences of opinion about them. So it's gotten a lot better recently, with some of the new, fancy molecular techniques and things that can be done. Those can be done pretty much at almost any hospital. So I think you need to be sure about the diagnosis. And they need to be sure that they're having high-quality radiologic studies done. I think the standard treatment, such as the CHOP-type chemotherapy and rituximab, there's no reason for a patient such as that to have to go to an academic center.

It's also important to remember that the staging needs to be characterized for all patients. And there is a prognostic index now, which a well-trained medical oncologist should be fairly familiar with. Several factors that can really help predict what the patient's chance is of being cured with this standard type treatment. And there are patients that will have a better than 50-50 chance of being cured with that. And there are patients that will have a 20 percent chance of being cured with the same exact treatment. So if the patients turn out to be one of the ones at the low end of that spectrum, then those are patients that should be potentially considered for some type of novel or new type of treatment or if you want a clinical trial.

I think it's important to assess the patient at the start, but you also need to look at the patient in the — fairly early on in their treatment, because these are very cancers. They should be very responsive to chemotherapy and almost — I tell patients with lymphomas, we should start to see big changes right away. This is not something that's going to take, you know, six months before you see any change. You should see something happening. If you have a palpable lymph node, with the first treatment we should start to see that going down.

DR LOVE: Is that what you saw with her?

DR HART: Yeah. She felt better, you know, right away. She pretty much felt, aside from losing her hair, she felt pretty much back to normal with the first treatment.

DR LOVE: What about the role of second opinions, seeing a second oncologist? Where does that fit into oncology practice?

DR HART: Well, I think any physician should allow their patients — should never discourage a patient from having a second opinion. Now, I tell my patients there's two ways that we can do that. One would be to get a second opinion, which I very frequently do, and I encourage quite a bit, and I do very often, is to get a second opinion on the pathology. And that is easily done and does not usually cost the patient anything themselves, because the pathology specimens are kept, for the most part, permanently and can be easily sent someplace else. So I will often, because of the difficulties with classifying lymphomas, even by very good and competent pathologists, I will often get a second opinion on the pathology, to make sure that people agree. Is this a fast or slow-growing type of lymphoma? So that's one thing that can be easily done, and I often do that in general. I think that's always a good — good idea.

And then, as far as going for a treatment second opinion, I'm certainly very willing to do that. And I always like to tell the patients that over the years in my practice, I've certainly met excellent lymphoma doctors in almost every major city in the United States, and I'd be very happy to pick up the phone and get them there at any time. Some patients, if they are very ill from an aggressive lymphoma, they might not really be in condition to travel. So I will usually tell a patient like that, that my recommendation, although I'm certainly willing to send them at any time for a second opinion, but my recommendation would be to take the standard Rituximab plus CHOP-type treatment, if I think that I have a reasonable chance at taking care of things, if they are looking that it's going to be such a difficult chance, then I will sometimes encourage them to go on a clinical trial at the start. But for a normal-risk lymphoma, I think a large, large majority of American oncologists treat them very similarly now. So I think there's not that much difference.

Ms M

Side effects of chemotherapy and rituximab

DR LOVE: I spoke with this patient, who recounted for me her experience at first diagnosis.

MS M: I saw Doctor Hendrick. And he said, "we did all your tests, and it looks like you have non-Hodgkin's lymphoma." And I just said, "Oh, yeah. Oh, cancer. Yeah. That's fine," not a big deal.

DR LOVE: Were you surprised?

MS M: You know, all the while, I thought I had pneumonia. I just figured, "I need an antibiotic. What's the big deal," because I'm not a sickly person. I didn't have any health problems. I've exercised. I've watched my diet.

DR LOVE: So, when the doctor brought up the thing about lymphoma, that was the first time you'd thought about it?

MS M: Yeah. Never had a clue. Even with my arm being swollen. My thoughts at that point, having it, I was thinking, "Oh, my God. This is going to be so costly." That's all I could think of. I don't know why I wasn't concerned too much about the disease. Because my mother had a breast removed, and she had colon cancer, so it was almost like it happened to someone else, but not you.

DR LOVE: Was she cured of that?

MS M: Oh, yeah. My mom just turned 89.

DR LOVE: But your first concern was cost?

MS M: Yes. Because I'm divorced and I didn't want to be a burden to my children. So I'm independent. I have a great family, so I knew they would do everything. But I didn't want that inflicted on them. So when they said non-Hodgkin's lymphoma, I thought, "Oh, yeah. Okay. That's fine." And he said to me, "Are you okay?" I said, "Oh, yeah. It's not a problem."

DR LOVE: Were you really okay?

MS M: I don't know. I think I was kind of like shocked. And then I was like, "Oh." I don't think it really ever sunk in. I knew I had to go through some stuff, and yet I didn't want to go through a lot of things, if the end was going to be the same as it is for everybody else, dying. I mean, I've heard of people being deathly sick and not having a good quality of life. And I thought to myself, "That would be not so much horrific for me, but for my family."

DR LOVE: So that was kind of what you were thinking as this all —

MS M: Yeah.

DR LOVE: — got started.

MS M: Yeah.

DR LOVE: Once they had all the tests done and were ready to start treatment, can you talk about what happened, what was explained to you?

MS M: It was really kind of fast, because Doctor Hart said that there was going to be someone to come in to start CHOP and chemo in the hospital.

DR LOVE: What exactly did you experience when you got the CHOP chemotherapy, and then what exactly did you experience the next day when you got rituximab?

MS M: I didn't experience anything. I —

DR LOVE: No side effects?

MS M: Uh-uh.

DR LOVE: From either one?

MS M: From either one of those treatments, and I never had any reaction to any other treatments until the day I finished my chemo.

DR LOVE: What about your hair?

MS M: You know, I got to about the

twelfth day, and I thought, "Man, I'm lucky. I didn't lose my hair yet." And then I took a shower and washed my hair, and then it just came out by the clumps full. And I thought, "Oh, well. They told me this was going to happen to me." They had explained how I should watch my food as far as rare meats, eating out, mixed salads, salad bars. When my white count was down, not to be in a crowd and stuff like that. So I was very cautious of that. No yogurt and the fresh fruit and stuff like that.

DR LOVE: Did you use a wig?

MS M: You know, it was amazing. The day I come out of the hospital, both my daughters said, "Okay, Mom. We're going for a wig," and I was like, "Already a wig. You know. Why? I'm not going to lose my hair. I'll probably be fine." And so off to the mall I went and got two wigs. So immediately when my hair fell out, I just called my hairdresser and she shaved my head, because it was all over the place. And I went into a wig, and away I went.

DR LOVE: What was that whole thing like for you, with your hair?

MS M: I thought, when I've heard of other people, it would be, like, traumatic for me. I thought, "I'd sooner die than lose my hair." And then someone said to me once, "Oh, you don't really know. You wouldn't want that to happen to you." So when my hair fell out, because everything was explained to me, I just thought, "Well, it's just one of the things that's going to happen to you." And so when that went, I thought, "Okay. Now we're starting, and I probably might be expecting all these other symptoms people talk about, like vomiting and diarrhea," but it never happened to me. And I thought, even after I had my first chemo treatment in Doctor Hart's office, I thought, "Okay. When I finish, is tonight the night I'm going to wake up sick, or tomorrow?" Anticipation of it. But they gave me my medicine to take, you know, so I wouldn't have vomiting and stuff. And it was fine.

DR LOVE: Some people also, the first or second time they get the rituximab, have a reaction during the infusion. Did you have anything like that?

MS M: Never.

DR LOVE: Nothing, just like water going in there.

MS M: Yeah. It was really a very fine experience for me. Not that you should have cancer, but I guess between all the years — well, like Doctor Hart said, they have improved so much on different things.

DR LOVE: Were you surprised by the lack of side effects?

MS M: Yes. I kept thinking in my heart, "I bet they didn't get it. Because I don't have all of these symptoms that other people have talked about," I thought, "Hmm. I wonder if that drug is really working on me."

DR LOVE: Up to that point, you hadn't been feeling well. You described all these symptoms that you were having, pains and feeling tired.

MS M: Mm-hmm.

DR LOVE: What happened to all that?

MS M: It left. The pain in my back was because I had so much fluid in my lung and behind my heart, I guess that's why I had the pain in my back. That went.

DR LOVE: Went away?

MS M: Mm-hmm.

DR LOVE: Now, as this was going along, what kind of information were you getting from Doctor Hart in terms of what was going on with the lymphoma?

MS M: Actually, it wasn't 'til after I had my first CAT scan and chest x-ray that I knew that I was doing very well, you know, as far as my condition was.

DR LOVE: What were you told?

MS M: That it was gone, you know, basically, that it was not there. And so I just continued to finish my — I don't remember if I had my last CAT scan after my chemo or during it. It seemed like I had it, I think, three months, and then six months later.

DR LOVE: How long was it that you had the first CAT scan after your treatment, a couple of months?

MS M: I think it was maybe three months after.

DR LOVE: At that point, they said, "The tumor's gone."

MS M: Mm-hmm. It was gone.

DR LOVE: Were you surprised?

MS M: I was thrilled. Yeah. I just figured that everything worked and everything was in order and...

DR LOVE: Initially, when you found out about this, before you kind of got a lot of information, I guess there was a gap between the time you found out that this was lymphoma until the time they said, "Here's the situation. Here's the treatment." And maybe it was a few days or a couple of weeks.

MS M: Immediately.

DR LOVE: Okay. So this was happening quickly.

MS M: Yes.

DR LOVE: So initially, at the very first point when you found out about this, were you expecting that you were going to be cured or that this is going to be really a problem?

MS M: I thought it could be a problem, but I thought the way medicine is today and having medicine in my family, that it probably wouldn't be a big deal.

DR LOVE: Did Doctor Hart kind of say to you, "I think we might be able to cure this"?

MS M: Mm-hmm. I think, even from the first time I was told I had it, they said it was like 50-50; you know, you had a 50-50 chance. You have an open window, I think, of five years. I've heard that from other people who had lymphoma.

DR LOVE: How did that strike you?

Ms M: Huh. I thought I better live and be happy as long as I can, up until any point.

DR LOVE: Was that sort of better than

what you had generally thought about in terms of cancer treatment?

MS M: Yes. Mm-hmm.

DR LOVE: Of course, your mom had been cured of breast and colon cancer. Have you had any other treatments, other than the chemotherapy and the rituximab?

MS M: No, not at all. I've had chest x-rays and a lot of blood work and a CAT scan.

DR LOVE: Tumor's never come back?

MS M: Well, no. Not that I know of. I don't have those symptoms.

DR LOVE: What happened in terms of your hair? I imagine your hair continued to not grow while you were getting the chemo?

MS M: No. It didn't grow, but when it seemed like the chemo was ended, my hair grew fast, and it came in curly.

DR LOVE: And how long did it take to see your hair grow back?

MS M: Oh, probably by — I finished my last chemo in February, and I remember playing in a golf tournament in October, and I had curly hair and had it trimmed a couple of times. So it didn't seem like a long period of time.

DR LOVE: A few months.

MS M: Yeah. Well, I have fast-growing hair, also.

DR LOVE: And what about your energy level, you know, in terms of how it was when you started the chemo, how it was when you finished the chemo and how it is now?

MS M: My energy level, I think, was really well. I was off of work about a year in that time I had the chemo and everything. When I went back, my energy level was good. It's well now, except after four days of working and putting in 40 hours, I tend to be a little tired.

DR LOVE: Yeah. Well, that's not too unusual.

MS M: But I expect more out of myself.

DR LOVE: Yeah. I mean, Fridays are kind of tough for most people, I think. What kind of interactions and reactions did you get from your coworkers?

Ms M: My coworkers are wonderful, and I can't tell you how nice the patients were in the office, sending me "Get Well" cards and letters, calling, flowers, gifts. And the doctor I work for is a really great guy and offered me my job back, same salary and everything. It was really — and I was glad to go back to work. I'm a people person.

DR LOVE: What was it like to walk in there after a year?

MS M: Like going back home again. Really good. Feeling that now I'm well and, you know, because I knew I was really kind of annoyed and tired when I was sick.

DR LOVE: So you got the chemo roughly over a period of about six months.

MS M: Mm-hmm.

DR LOVE: And every time you got the chemo, would you get the rituximab?

MS M: Yes. And it was, you know, like I said, I wasn't sick. I expected to be sick, because that's what I heard and, you know, how people, vomiting and diarrhea and not being able to eat, but my family insisted that I eat, so I did.

DR LOVE: How did your weight do during the chemo?

MS M: I didn't lose any more. Actually, I — yes, I did gain, because I remember looking in the mirror and think, "Oh, I don't have any wrinkles. My..." I may say a little heavy.

DR LOVE: So you had lost some weight before the treatment?

MS M: Yes. Actually, once they tapped my lung. I think when I went to Doctor Cordonite, I was up to 132 pounds. And once my lung was tapped and everything, I was down to 118 pounds.

DR LOVE: And what was your normal weight?

MS M: I could go 126.

DR LOVE: So you had lost close to 10 pounds by the time you started treatment.

MS M: Mm-hmm.

DR LOVE: And then you actually gained weight on chemotherapy and rituximab?

MS M: Oh, yeah. I was having a good time eating, mm-hmm.

DR LOVE: You had a good appetite?

MS M: Mm-hmm. I had a good appetite. I ate. My family insisted that I eat, and I did.

DR LOVE: And what's your weight right now?

MS M: Do I have to tell you that?

DR LOVE: No, but did you regain the weight that you lost?

MS M: Oh, I regained that and some. I might be up around about 147 —

DR LOVE: You don't —

MS M: — pounds.

DR LOVE: That's okay.

MS M: I tell you, honestly — well, maybe not.

DR LOVE: Well, you look very healthy.

MS M: I feel healthy. I feel good.

DR LOVE: I would imagine that it might be interesting for you to tell people that you had six months of a pretty intense chemotherapy and looking as healthy as you do.

MS M: You know, people come in the office and patients who see me, "You look the best you've ever looked. Do you feel good?"

"I feel great, you know." And they're like, "Do you really?" And I say, "Yeah." And they go, "Boy, you had a horrible, miserable time," and I said, "Mmm, not really." And they look at me. I said, "I don't know. I think it was the other woman who had all that chemo. It wasn't me," because I went through it so well. And they're like, "You really did?" And I go, "Yeah, I did. I can't sit here and lie and tell you,

'Oh, my God,'" because it wasn't that way for me.

DR LOVE: How has this experience changed your perspective on things, if at all?

MS M: I think I don't let as much bother me. I'm glad to be up and running every day. And I want to see and do as much as I possibly can and, if anybody offers me a trip, I'm going. You know, I just want to be happy and enjoy. I think I'll probably live into my nineties. My mom has longevity in her family, so I want to enjoy and be happy and look forward to seeing my grandchildren and my kids and working.

DR LOVE: Do you think that you kind of have returned to the way you were before? You're about as happy as you were? Or do you think in some way you're different?

MS M: I think I'm different and better.

DR LOVE: In what way?

MS M: I don't know. I think I just look at life and appreciate it a lot more. It just seems like when you work and time is going on, you're just busy and doing and that kind of thing. And now I'm, like, happy to see the day coming and spend the day and do whatever comes.

DR LOVE: What was going on inside the family as this was all moving forward?

MS M: I think my family was really upset and concerned. I think kind of more than I was. I know my son and daughter flew in from Philadelphia immediately to see me. And I think they were more concerned than I was.

DR LOVE: Is that kind of your personality in general, that you're kind of easygoing? Because I'm more —

MS M: I'm always easygoing, yeah.

DR LOVE: Well, and you know, I — I'm surprised, because I've talked to a lot of patients with —going through experiences like that. And most of them describe that in the beginning, being really disoriented, almost in shock, you know, very upset. As you describe your story, it doesn't sound like that's the way you felt.

MS M: I didn't. I don't know why. Like I said, I think sometimes I had an out-of-body experience. I was going to do what I was told to stay healthy, to get through this. And I was going to do every single thing I had to do.

DR LOVE: Would you say that, in general, as, you know, throughout your whole life, you've kind of maybe worried a little bit less about stuff than the average person?

MS M: No. Before this, I worried about everything.

DR LOVE: Huh.

MS M: I worried about not saying the right thing, being in the right place, doing the right thing, not doing enough.

DR LOVE: So something changed in you.

MS M: Yeah. I don't know. It's kind of like a calmness or something. And, no, I did worry all the time, constantly, about everything.

DR LOVE: Did you worry about the lymphoma a lot, once you knew you had it?

MS M: No. I think at some point, talking to people long before I ever had that, it was something that I knew that was pretty curable.

DR LOVE: Where does spirituality and faith fit in for you?

MS M: Ninety-nine percent of the time. I'm happy to be alive. I'm on my knees every morning thanking God that I'm here and given me this opportunity to be around. And I think in my heart, for the grace of God and the doctors, I'm here today and well.

DR LOVE: Any advice you might give to a person kind of just starting out the path that you've already been through?

MS M: To have faith in your doctors and think very positive, that this is just one little thing. It kind of cannot maybe be forever for you, but it's just at the moment. And take care of the moment and get through it.

DR LOVE: What do you do for fun? What are the things that you enjoy the most?

MS M: Being with people, golfing, spending a lot of time with my family and grandchildren, just interacting with a lot of people. I like people.

DR LOVE: Did you continue that during the chemotherapy?

MS M: I did play a little bit of golf. Not too much, because of being out in the sun, which I did enjoy. I was occupied with a friend of mine, helping to do some remodeling on a condo. That occupied my time. Being with people when I was healthy, you know, going out to lunch and that. And friends visiting, family visiting, being able to visit my family out of town. Being active.

I don't know if you could ever say it was a great experience for me. I just don't know how to explain it to anybody else, except that it wasn't all that bad. And that's all I can tell you.

DR LOVE: Well, I think maybe one of the things that I've seen in people who have stories like yours, who've had success with treatment is you've triumphed over one of the great adversities that people have to face.

MS M: Yeah.

DR LOVE: That's the way it looks to me.

MS M: I can't explain to you why I received it the way, you know, and I just thought, "Well, whatever they tell me, I'm going to have to do it, if I want to live." You never know how strong you are until you have to, and so I just thought, "Well, it's another thing you have to go through, to get through." And that's basically what I did.

Mr H

39-year-old man with chronic lymphocytic leukemia (CLL)

DR LOVE: The third patient presented by Doctor Hart was a 39-year-old man whose actual diagnosis is chronic lymphocytic leukemia, which turns out to be very much related to the other lymphomas. As recounted by Doctor Hart, this young man had a very unusual initial clinical presentation.

DR HART: He was one of the most interesting patients that I've seen in a long time. I got a call from the emergency room physician about this patient, and he said, "We have a gentleman in the emergency room that has a white count of 800,000." Now, the normal white count being four to 8,000. This was 800,000. Of course, I said, "I'm coming right in."

And this person, interestingly, was about 35 years of age, too. So there was something in his picture, which just, when I first got the phone call, seemed to be something unusual. Because, number one, we would not usually see such a young person with a chronic lymphoid leukemia. And the white count was extraordinarily high. So I went in to see him. And he indeed had a white count of somewhere between 800,000 and a million, but he actually did not look — he looked somewhat pale, but he — and he definitely had large lymph nodes and a very large-size spleen. But he didn't actually look that sick otherwise, although he had lost some weight. He looked chronically sick, but not like he was going to pass away in the next hour.

DR LOVE: Where did you feel the lymph nodes?

DR HART: He had lymph nodes in his neck and his armpit area.

DR LOVE: How big were they?

DR HART: They were moderate size, couple of inches in size. So in his case, I was — because I'd actually — the second white count they got on him was already a million. And I felt until we got confirmation of all of this — and obviously, we're sending off specimens of his blood for analysis by this — when I mentioned this flow cytometry, where they can analyze exactly what the cells are and do a lot of studies on them, I decided I was concerned about his white count being that high. So what we did to get sort of the ball rolling for his treatment was to do what's called a leucophoresis, which means there's a machine that will actually wash the white blood cells from the blood. So he was put on this machine, which looks sort of similar to a kidney dialysis machine. And it basically — your blood goes through the machine, and it sort of pulls out a good number of the white blood cells, which are then discarded, and returns everything else back to the patient. So it takes a few hours to do that. And it's not as difficult as it sounds, if you have the machine available. So I called in the pathologists and they did this. So we did that a couple of times, just to sort of take the edge off his white blood cell count until I could get a little more information.

Looking at his blood under the microscope, it did look like it was mature lymphocytes. So I felt, although this person was extremely young and I had never actually had a patient prior to this, in their thirties, with chronic lymphoid leukemia, I thought that's probably what he had and, indeed, that was what his diagnosis was.

DR LOVE: And how did you confirm that diagnosis?

DR HART: He had typing done on his lymphocytes. And we, you know, did a bone marrow, also. And his lymphocytes were typed. And there

are certain features that these sort of cells have. When you look at them under the microscope, they look closer to normal lymphocytes than these very immature blast-type cells from acute leukemia. And all of the typing pointed towards this being a chronic lymphoid leukemia. He did have some features of a more aggressive type, which I didn't really need the machine to tell me that he had a more aggressive illness, because he presented with the highest white count that I've ever had in my career, as well as with enlargement of the organs.

So I felt he needed to start on treatment right away. And there are different choices that you can do for these. In general, this disease, chronic lymphoid leukemia, is very similar to what we used to call a well-differentiated lymphocytic lymphoma. So, this — I often have patients with these sort of lower-grade lymphomas, that always ask, "Do I have lymphoma, or do I have leukemia," and I tell the patients, "Well, you sort of have both. It depends where you look. They're basically the same disease." So there is a indolent lymphoma, which is similar to this chronic lymphocytic leukemia.

DR LOVE: Can you kind of talk a little bit about what the difference is between, quote, a leukemia and a lymphoma?

DR HART: Well, a leukemia, by definition, is malignant white blood cells in the bloodstream. And so if you find the cells in the bloodstream, it's called a leukemia. They can either be lymphoid types or they can be what's called myeloid types, which is another type of white blood cell. So the broad classification of leukemias is either the myeloid or the lymphoid. And with — in either one of those, there can be the acute types, which are very, very serious illnesses and need heavy doses of chemotherapy immediately, and the chronic types, which we often treat without any chemotherapy or either with some mild treatment.

And a lymphoma is basically, by definition, what you find in an enlarged lymph node or another piece of solid tissue. It does not necessarily have to be a lymph node. So — but there are many similarities and sometimes you can actually have the same cells, and it's really the same disease. It just depend which part of the body you're looking into.

DR LOVE: And what about the other types of leukemia, for example, the acute myelocytic leukemia? How is that different than chronic lymphoid leukemia?

DR HART: Well, much, much different. Chronic lymphoid leukemia can have, in its early stages, a survival of over 10 years, sometimes 15 or 20 years, and sometimes needs no treatment, whereas an acute myeloid leukemia is one of the most serious human illnesses that requires an aggressive treatment. Generally speaking, when we first diagnose those patients, unless we feel that they are too ill to treat, we put them in the hospital. They're in the hospital for anywhere from — they usually take about one full week of continuous chemotherapy. They're often in the hospital for two or three weeks afterwards. And they sometimes then go on to bone marrow or stem cell transplant.

DR LOVE: And can you talk a little bit about the therapy that you recommended to Mr H and why you decided on that?

DR HART: Once we had gotten his blood counts down slightly from using the machines, and I felt that he was not going to have an immediate problem, I decided to get him started on chemotherapy. I was very reluctant to use any antibody treatment immediately in this gentleman, because he had such a large burden of cancer cells in his body. Remember, we talked about having reactions to rituximab or the antibodies. And those reactions are much more common. So I felt he would be very likely to have a severe reaction. So I actually gave him CHOP chemotherapy, which is also effective in these lower-grade lymphomas, too, if patients have more of an aggressive treatment. So he actually came down nicely with this. And after the first cycle or two, we did add rituximab in.

And so he continued to improve. His spleen shrank. His lymph nodes came down. His white count was gradually going down. Obviously, it started up extremely high. And it gradually worked its way down. However, he was certainly not in a complete response. After a number of cycles of CHOP plus rituximab, he was not in complete response.

Given his young age and the fact this was an unusual case — and we talked somewhat about second opinions. I felt, in his case, I did want to get a second opinion. He did have a brother — because of his young age, I had him do what's called tissue typing, where his blood cell type is actually checked out. And his brother checked out, too, and turned out to be a match with him. So I felt that would mean that his brother could potentially be a donor for bone marrow or stem cells, if this patient, Mr H, were to need a transplant at some time in the future.

And since he was slowly responding to treatment, I felt that we should at least investigate this. So I referred him to a major medical center, which was about two hours away, a medical school, and he was evaluated there by their bone marrow and stem cell transplant program. You know, they felt that he should continue on treatment, and we would save the possibility of a transplant for sometime in the future, if he were to have a relapse. But they certainly did not recommend an immediate treatment with that.

So at this point, we changed him from this CHOP regimen to another drug, which is commonly used in the lower-grade lymphomas and leukemias, called fludarabine. And that's one of the more — fludarabine is a newer drug that has come out, which works somewhat differently and has a pretty good toxicity profile. I wanted to have

him seen first, because fludarabine is one of those drugs that can make it slightly more difficult sometimes to use the patient's own bone marrow, if you were going to do a transplant that way. So — but we already knew he had a match with his brother and we could do that as sort of the ace in the hole, so to speak, if we needed to.

So I gave him some cycles of fludarabine, and he continued to respond. His white count normalized. He did quite well. No serious infections, although that's the one thing with these lower-grade lymphomas and CLL, particularly; you have to be on the very careful watch for infectious problems. These patients are very prone to many types of infections with unusual organisms.

So he did quite well and has just recently completed a consolidation with an antibody called alemtuzumab, which has been recently released for use in patients with CLL. And he is now — as far as we can tell in his blood, in complete remission. In the next week or two, I am going to send some marrow and blood to assay, to see if there are any few little leukemia cells left or not. It's called minimal residual disease, and I'd like to see if we've wiped that out or not.

DR LOVE: Do you consider him curable?

DR HART: That's a very good question. According to a textbook would say not. I have to tell a patient that there's not any proof that a patient such as he can be cured, but I do think that, because of the progress that is now being made in CLL that potentially he is curable. Now, I should just back off a little bit from that. There have been patients who received bone marrow transplants or stem cell transplants from another person, who can be said to be cured from these sort of low-grade lymphomas. Without a transplant, the question is: Could he be cured? In the past, the answer to that would be definitely no, but I do — I guess I'm an optimist by nature, and I think, with the advent of some of these new antibody treatments — you know, the data on no patient being cured is based on the last generation of treatments. With the new generation, I do have hope that we'll be able to do that in people.

DR LOVE: From a practical point of view, what's it like to treat a patient with CLL now, compared to 10 years ago?

DR HART: Well, the treatments are getting very, very exciting to me. I think the advent of the antibody treatments, especially, is very, very nice and give us a lot of new things that we can do. You know, when we just had conventional-type chemotherapy to do, it was a harder decision, I think, about how much good are you doing the patient and should you even try to get the patient in remission? I mean, what we were thinking about in the past was just — if you had to treat them, just treat them for a little bit, get them kind of out of the danger range and get their counts down, but not really try and get somebody in; we didn't even talk about remission in CLL. I mean, no one ever even spoke of somebody being in remission, of somebody being — you know, having no leukemia cells found in their bone marrow was just not heard of. So it's very nice to be able to get to that, because we've certainly gotten so we can talk about that in the people with the aggressive lymphomas. And now, in these lower-grade lymphomas and leukemias, I think that we're going to get — it's controversial, still. I do think that there will be people that we can cure.

DR LOVE: Now, how did he tolerate these therapies?

DR HART: He did very, very well with almost everything. He is a young healthy person. And he is an unusual person who at various times had a radio show and other things and has a lot of friends in town. And he leads a very active life. So he has felt somewhat tired. He tells me that he doesn't do as many wild and crazy things as he used to.

But other than that, he's done quite well. His white counts are now entirely normal. He's not even the tiniest bit anemic. He has no more palpable lymph nodes. I'm getting ready to redo all of his tests and see if he's in a molecular remission. I certainly hope that he is. I'm keeping my fingers crossed.

DR LOVE: What do you expect from the future with him?

DR HART: Well, right now, he looks perfect. I would say he is 100 percent his normal self. He's doing pretty much all of his regular activities. So I'm trying to treat him with the intention of either curing him or getting him into a very prolonged remission. And I'm hopeful that he will be in a prolonged remission. I'm not going to know for sure until we get, you know, some further analysis, looking for very low-level residual disease. And obviously, there's a reasonable chance that he still may have low-level residual disease then. So I'm trying to keep up to date with the progress of this field about — you know, there's many articles coming out frequently now, what to do with these patients. So he could be retreated with antibody, other things. And obviously, somebody this age, I'm trying to keep him free of disease for as long as possible and do whatever I need to do to do that.

DR LOVE: Now, from your point of view, do you consider him kind of within the realm of non-Hodgkin's lymphoma, even though he has a leukemia?

DR HART: Yes. I think this is in the same realm, because we're basically using some of the same drugs that we use. This is also a B-cell, low-grade type of cancer. So there are many similarities between this B-cell type chronic lymphocytic leukemia and non-Hodgkin's lymphoma. So I consider them as part of that same spectrum.

DR LOVE: What's the difference between a B cell and other kinds of cells?

DR HART: Well, a B cell is one of the two major types of lymphocytes, the other one being a T cell. And this — sort of, this depends what part of the body they mature in. The B cells eventually turn into what are called plasma cells, which are little factories that make antibodies, which are a liquid part of the blood that helps to fight infection. They're proteins in the blood that go to kill off bacteria and viruses.

DR LOVE: Now, on our first patient education program, we talked about the difference between the aggressive lymphomas. And John Leonard talked —

DR HART: Mm-hmm.

DR LOVE: — about that versus the indolent or nonaggressive lymphomas, like —

DR HART: Right.

DR LOVE: — follicular lymphoma. And —

DR HART: Right.

DR LOVE: — Brad Kahl talked about that. Would you say that sort of chronic lymphocytic leukemia is kind of similar to the indolent lymphomas?

DR HART: Yes, it is. It's definitely in that category. The people at the very early stages — and I have family members of mine who were at this very early stage, who, you know, I don't even use — with this one sort of family member of mine, I don't use the "L" word at all with him. I don't even use the leukemia word with him. I just sort of tell him that he has a lympho-proliferative problem of some mild type, because he just has a white blood cell count, which is slightly above normal, with lymphocytes. I did send testing on him. He has exact same process as my patient, Mr H, had, but he is exactly the opposite end of the spectrum. He has a white blood cell count just a little bit above normal, with no lymph nodes and nothing else. He needs no treatment, and hopefully he never will. He just needs to get his blood counts checked once every — you know, once or twice a year. And the other end of that spectrum is like Mr H, who has the whole picture of everything going on. But they still are slow-moving cells, in general.

We're getting better, with some of the new tests. There are some new tests that the readers may hear about from their doctors. And one called ZAP-70, has a long, funny-sounding name, which is a way of looking indirectly into how aggressive this type of leukemia is. So we call it nonaggressive, but what the patients always want to know is, "Well, you say it's not aggressive, doctor, but how am I going to be doing five years from now or 10 years from now?" And in addition to this Wrey classification, which is still quite useful, we now have some of these more fancy molecular techniques to help us sort of fine tune things in there. And I found that to be kind of helpful now in talking to patients.

DR LOVE: You know, it's interesting, too, thinking about these tumors or these cancers, such as CLL and indolent lymphoma, that can have a very long history without you being able to eradicate them.

DR HART: Right.

DR LOVE: And you kind of get into the idea of what really is cure. And if you can remain without symptoms from the cancer and live long enough to die of something else, kind of, it has the same effect as being cured.

DR HART: I tell my patients that all the time. The oldest patient in my practice ever was a 100-year-old gentleman with CLL who I never treated and eventually died, I assume, of old age. He just didn't come back one winter to see me. But I doubt very much that he needed any treatment.

So certainly, in the practical sense, if you live to be an old person and die of something else, then, to you, personally, that's a cure, and if you don't have symptoms of your disease. So I think we're going to be, in the next 10 or 15 years, making a lot more cancers like that. I think we're certainly seeing now breast cancer patients who are like that. And we're not quite there with colon cancer and some of these other cancers, but it's moving in that direction.

Dr Hagemeister: Discussion of cases 2 and 3

Indolent versus aggressive lymphoma; difference between CLL and lymphoma; recovery from chemotherapy

DR LOVE: The first two patients have so-called diffuse large B-cell lymphoma, and I asked Dr Hagemeister to review this disease and how it differs from the so-called indolent lymphomas and chronic lymphocytic leukemia.

DR HAGEMEISTER: Diffuse large-cell lymphoma, B-cell type, is the kind that, at least in the United and Europe, is the most common type of lymphoma. But even in that type of lymphoma, there are special subtypes. And even in that lymphoma, there are special clinical — not just only – not just pathologic, but also clinical — subtypes. So perhaps in that one particular disease, diffuse large B-cell lymphoma, there are probably many different forms of it that we still don't understand.

DR LOVE: One of the concepts that I have — and you can tell me whether you, this is what you teach your fellows or how you conceptualize it — is that these tumors often are growing rapidly. They can be curable. And if they're not curable, they're kind of difficult to treat. Would that be a good summary of them, in general?

DR HAGEMEISTER: I think so. Usually, if a patient develops a recurrence in a very short time, let's say while on treatment with chemotherapy or within a year, certainly within six months of having had therapy for their large-cell lymphoma, it's going to be very difficult to manage that patient, ultimately, and to keep them free of disease or get rid of their disease, especially when they're treated with good curative-intent chemotherapy to start with.

If, however, they develop a recurrence more than a year — more than six months, more than a year — I don't think the jury is out yet, exactly what the number is. But if they've gone at least a year without having a recurrence of their disease, there's still a good chance that they can be cured. But they have to do through high-dose therapy followed by stem cell rescue in order to be able to do that. That is a bone marrow transplant, if they have relapsed disease. And there's just not really any question about that these days. You have to induce them into remission with the second treatment, which is usually not so difficult, and then do a bone marrow transplant. So it's not impossible to cure some patients with aggressive lymphomas should they develop recurrent disease. But a lot of that depends upon how long they remain free of disease the first time when they get treated with chemotherapy.

DR LOVE: Now, we have talked before about rituximab. How did rituximab affect, overall, the treatment of these aggressive B-cell lymphomas when it came along in the 90s?

DR HAGEMEISTER: Changed the prognosis for patients with all aggressive histology lymphomas, at least primarily diffuse large B-cell lymphomas. There are studies in the United States, as well as in Europe, that demonstrated that patients with large-cell lymphoma, B-cell type, all had better time to treatment failure. That is to say, they remained free of disease longer. And they also survived longer than patients, when they received rituximab along with chemotherapy, rather than just receiving chemotherapy alone. And on top of it, other regimens, newer regimens that were attempted — there were a lot of different regimens that were attempted to try to cure these patients, giving more intensive chemotherapy, giving dose-dense — that is to say, giving chemotherapy more frequently, giving cycles more closer together. There were those attempts. In general, there was some success, but not universal acceptance.

Then, once rituximab came along and was administered in addition to the chemotherapy, all of the results went up. All the results got much better and significantly better. And so much so that now there's a lot of confusion about whether additional drugs to the R-CHOP regimen or whether giving more intensive chemotherapy or any kind of other change in the treatment program is really going to result in any improvement post — after whatever rituximab has already added on top of it.

DR LOVE: Are there other agents like rituximab, targeted agents or antibody therapies, that are coming along for diffuse large B-cell lymphoma?

DR HAGEMEISTER: Yes. There are two that are out now, which are very, very interesting. They are radioimmunotherapy. They are monoclonal antibodies that are also directed against CD-20, which contain a radioactive component. In other words, the cells are not only treated with the monoclonal antibody, which attaches to the cell, but then also the radiation therapy also radiates the cell. And a recent study that was completed in Europe, administering Zevalin to patients with large-cell lymphoma in relapse, a significant number of these patients had a complete remission to treatment, meaning that they had a great response to therapy when they received this radioimmunologic agent.

In the United States, this agent and the other agent, Bexxar, are only approved for treatment of relapsed low-grade, or indolent, lymphoma, slow-growing lymphoma. And it wasn't even thought that it might be of really great benefit for patients who had aggressive lymphomas. But it was tried in Europe and, in view of the responses that patients had to that particular drug and knowing that radiation therapy is effective treatment, at least locally — when you give it locally, you can get control of the disease locally — that means in the area where the nodes are or where the involvement is, by giving radiation, it seemed logical to give this drug to patients systemically and to give the drug intravenously. So it's intravenous radiation, if you want to think of it that way.

DR LOVE: But targeted to the tumor cell.

DR HAGEMEISTER: Targeted to the tumor cell. It also, of course, had side effects and can cause low blood counts and patients can get low platelet counts, as well as low white blood cell counts. But they generally recover. And so now there are a number of studies, not only in patients who have relapsed disease, but also patients who are receiving front-line therapy, administering chemotherapy with or without rituximab. Most of them are with rituximab, followed by radioactive therapy, that is to say, intravenous radiation in the form of either Bexxar or Zevalin. And those studies are going on in the United States, as well as in Europe.

DR LOVE: So that's still kind of in the experimental mode. What are some of the other things coming down the pike?

DR HAGEMEISTER: There are other drugs that are being tested. It's a catch 22, I think, about these particular new monoclonal or targeted agents in the treatment of these disorders. And that is that some of the other monoclonal antibodies that are being developed have to be administered along with rituximab. The problem is is that rituximab seems to be a drug that just is here to stay. It's such an effective agent. It's been of value in all kinds of B-cell lymphomas, not only aggressive B-cell lymphomas but also slow-growing lymphomas, so much so that it's impossible to do a study without including rituximab as part of the trial.

DR LOVE: You mentioned indolent lymphoma. Can you talk a little bit about, you know, sort of the spectrum of indolent lymphoma and how that integrates with the concept of chronic lymphocytic leukemia?

DR HAGEMEISTER: Yeah. You mentioned a chronic leukemia as being another lymphoma. It is, in fact, a lymphoma. But there is an artificial distinction between what CLL, or chronic lymphocytic lymphoma, is and what small lymphocytic lymphoma is. Patients who come to my clinic often will ask, "Do I have lymphoma or do I have leukemia? I don't understand."

And the diagnosis of leukemia in one sense, to some patients, might be, "I have a really fast-growing terrible disease," and that happens to be a particular kind of leukemia, acute myelogenous leukemia, which is primarily a disease of younger persons, gains a lot of notoriety because it's a very aggressive, severe form of the disease in which patients often don't survive and for which there's been a lot of investigations. And it's not a lymphoma. It's not a lymphocytic leukemia. It's instead a leukemia that's made up from bone marrow cells or other white blood cells that are cancerous.

In chronic lymphocytic leukemia, instead, there are a lot of lymphoma cells that involve the bone marrow. And they escape into the blood stream. But they're very, very slow growing. In fact, in a particular study that's been looked at, the number of cells that decide to grow in one year — 95 percent of the cells in chronic lymphocytic leukemia decide to grow in a year. So the turnover of these cells is very, very slow. The growth of these cells is very, very slow. So in general, chronic lymphocytic leukemia is aptly named. It is a chronic disease. It is a disease that tends to grow very, very slowly, not progress very rapidly, and many patients can be monitored without any therapy, without any real major complications. The problem happens that whenever the bone marrow happens to be extensively involved or the spleen gets big or the nodes get big, that — then patients require treatment. And when they do, there have been a lot of studies that have been recently developed at our center, showing that rituximab also benefits these patients, but only if they receive it along with

chemotherapy.

So the kind of chemotherapy appears to be best, a fludarabine-type regimen. And at our center, there's a study known as rituximab plus fludarabine plus cyclophosphamide, which appears to render these patients into complete remission much better than just any of the drugs by themselves or even in other combinations. So currently, that's an active program that's ongoing.

Now, the difference between CLL and SLL —

DR LOVE: And SLL being?

DR HAGEMEISTER: SLL being small lymphocytic lymphoma, which is another kind of slow-growing lymphoma, which is relatively uncommon. It's much less frequent than other kinds of lymphomas, but still, it's composed of small lymphocytes that are malignant, which are slow growing. Patients will have nodes. They will often have bone marrow involvement, but it's minimal marrow disease. And that is to say they just have a little bit of marrow involvement and they don't have a lot of cells in their bloodstream. So they don't really have the, quote, leukemic, unquote, picture, that is to say, with a lot of blood involvement. And "a lot," in this context, is greater than 5,000 malignant cells. But it's an artificial distinction.

Mike Keating just presented at Lugano, a sort of a mini symposium, looking at — sort of summarizing the differences between SLL and CLL, these two different forms of the disease. And bottom line, there is no difference, except for the clinical presentation. Molecularly, genetically, DNA-wise —

DR LOVE: Response to treatment.

DR HAGEMEISTER: — response to therapies, they are the same. So what makes one person develop a leukemic picture with more than 5,000 lymphocytes versus one person who has just lymph node enlargement — and you can even get bulky disease, bulky nodes, greater than five, even 10 centimeters, and still have just SLL. What makes one person do that versus the other person do the leukemic picture, we don't know. We don't know why. And it may have something to do with adhesion molecules, molecules that make the cancer cells stick together. It may be that simple, that keep the cells together and not make them show up in the blood stream. We don't know.

DR LOVE: Let's talk a little bit about some of the side effects and risks that are seen with the common therapies for lymphoma. Let's start with rituximab.

DR HAGEMEISTER: Rituximab appears to induce no further toxicity when it's administered along with chemotherapy than just the chemotherapy itself. So when you do a randomized study giving R-CHOP versus CHOP chemotherapy alone, the complications are no different between those two groups of patients. Rituximab, of course, we already talked about, first infusion reactions. Those still occur, but they are limited and a very limited toxicity, which is the reason, in part, why rituximab has become so widely accepted as being an effective therapy. And that it's not just effective in getting good responses, it's also effective in that patients do not have the same types of toxicity that we expect to see with other drugs.

DR LOVE: What about the chemotherapy, you know, particularly, for example, CHOP, one of the common common regimens? Do you see a large number of patients going through that without nausea and vomiting pretty well, or is that a spectrum?

DR HAGEMEISTER: Well, nausea and vomiting nowadays is so well controlled with the antiemetics that we have. It just depends on where you are and at different centers, certain drugs are used in one center more than others, but there are very effective antiemetics. And actually, CHOP chemotherapy doesn't really cause that much nausea. It's only moderately — what we call moderately emetogenic. It only causes modest nausea and vomiting.

DR LOVE: You mean even without the antiemetic.

DR HAGEMEISTER: Even without antiemetics. It's not a very potent combination from the standpoint of inducing nausea and vomiting. I mean, sure, you get some nausea and vomiting after the chemotherapy is administered, perhaps a day later or especially with the Cyclophosphamide. But it's very easily controlled with standard drugs. Rituximab doesn't cause nausea and vomiting at all. I mean, it's very, very rare that you'll see a person who gets nausea. It does occur in patients with a first-infusion reaction, but still, it's relatively limited and not very serious. You're not going to see much nausea and vomiting because of the antiemetics.

There are other regimens that are much more severe in their causing nausea, especially with Cisplatin or platinum-type therapies. These are much more emetogenic, cause a lot more nausea and vomiting.

DR LOVE: What about other quality-of-life issues, fatigue or just feeling bad? What do you see, particularly, with the common regimens with lymphoma?

DR HAGEMEISTER: Fatigue is actually the number one complaint that patients have. There have been some very interesting studies that have looked at what complications the physician thinks are important versus what the nurse thinks are important versus what the patient thinks are important. And in some of those studies, it's really interesting that the physician thinks that pain is the most serious problem that the patient faces. And I think that might be that the physician thinks that he can give pain medications and get rid of it, so it's the most important issue that the patient has, so he can get rid of it.

Nurses, in some cases, have thought that hair loss was the most important feature that the patient had to face, which, of course, I've never had a patient say or really panic over losing

their hair, except, perhaps, for young women, I mean, 20-year-old women for whom their appearance is even more important than getting rid of their cancer, which might be hard for some of us to believe, but there are some young girls who are like that.

And yet the patients clearly make it very clear to us that fatigue is their number one problem that they have when they receive chemotherapy. Fatigue is a complex issue. It involves not only — actually, their anemia, which is a major issue. It may involve an effect on the brain that's separate from the anemia, what we call chemo brain. It may involve that, in part. It may involve emotional side effects, for example, depression, anxiety, tension during the day that one might experience, because you're on chemotherapy or because you have your disease. That's another issue that relates to fatigue. And finally, there may be actually side effects of the chemotherapy that directly cause fatigue, that we don't have a real good handle on. So fatigue is the number one, number one, far and above, side effect most patients complain of.

DR LOVE: What I heard from these three patients was some fatigue. You know, for example, the first patient, in his mid seventies, who's used to working out all the time and doing a lot of activity was able to continue working out, but not quite as hard. So some impact, but not sort of totally life altering. Is that sort of the average?

DR HAGEMEISTER: I don't think that is. I think very few patients end up doing the same kind of physical activity or just slightly less physical activity that they did when they receive R-CHOP chemotherapy. Most patients have to adjust. I tell all of my patients to try to keep their lifestyle as, quote, normal, unquote, as they possibly can. I actually don't think there's any benefit for staying away, out of crowds. That kind of thing is all theoretical. And, besides, if you're going to get an infection, you get it from bacteria that are on you already. I think perhaps that's a secondary concern about whether I'm going to expose myself to infections or whether I could bleed or something like that. I think they worry about that a little bit, and it's a secondary concern for them.

DR LOVE: Well, you're saying most patients have more fatigue than this patient described?

DR HAGEMEISTER: I think they do. And I think that it's not at all common for a patient to feel, "I've been a lot — really tired."

And the more chemotherapy they take, the greater the number of cycles of treatment that they receive, the greater their risk of fatigue. It probably also has something to do with where they were as far as their activity is concerned, before they went into treatment. Perhaps weight issues, comorbid issues. For example, heart disease, pulmonary disease. Smokers, perhaps.

DR LOVE: So, in this man, nonsmoker, he's working out, you know, a retiree, but very, very active lifestyle. Are you saying maybe that contributed to the fact that he sort of tolerated the chemo better?

DR HAGEMEISTER: Abs — absolutely. I think what you got going into the treatment means that you're going to take the treatment a lot better. We call that performance status. And perhaps performance status should be adjusted, not just zero, which means you're asymptomatic and walking around with cancer. But maybe there ought to be a minus one, meaning that the man or woman who is actually in better shape than stated age. That person probably tolerates their treatment a lot better than do people who are going into with, already, some element of frailty. So I don't think age plays a role here. Your patient, who's over the age of 70, who has this illness, probably stands as good a chance of getting through treatment as does a patient who's under 60 even, if they remain vigorous.

DR LOVE: The last thing I want to ask you about was a very interesting observation in these three people, which is a little bit about their attitude and how they dealt with this situation. And it was kind of an, almost an interesting theme that was evolving, of — at least in these three people. You know, sort of after an initial period of kind of shock and trying to figure out what's going on, settling in on the concept of, "I'm going to be positive about this." I heard a lot about trying to continue to do things that were fun, to enjoy their life. What do you see in terms of the spectrum of how people sort of respond to this, emotionally and lifestyle wise? And do you think there's any correlation between that and how they do?

DR HAGEMEISTER: There absolutely have been studies that have looked at this issue. And they are in conflict. Some studies have suggested that people who maintain a positive outlook actually have better chances of survivals. But they are few. The studies that have demonstrated that are few. Most studies have demonstrated that there is no difference, as far as your treatment outcome, if you have a positive outlook or a negative outlook. And I look at patients sometimes when they come into my clinic, and I say, "Oh, this patient's not going to do well."

And the ones that I think are not going to do well are usually those patients who I see not wanting to take an active role in their treatment. Okay? So it doesn't have to necessarily do with how active they are or what their attitude is, as far as their survival. It's instead, how do they adhere to the treatment program. And if they have a positive attitude, they're more likely to adhere to the treatment program and become involved in their care. And I think that patients who actually are involved in their treatment programs and try to adhere to them as carefully as they can and don't avoid therapy don't say, "You know what? I'm not going to do what the doctor says. I'm

not going to follow this program," or, "It's okay if I do this and skip this this day." I don't think that's a good idea. I think that those patients who are more willing to follow the program and — because they have a positive attitude and say, "I am going to get through this. I'm going to go through that." That's where the positive attitude comes in, in that they're willing to go with their treatment program.

Mr H

Coping with chemotherapy and monoclonal antibody therapy

DR LOVE: The last patient interviewed for this program is a whimsical and entertaining young man who, like the first two patients, was able to reach inside and find the strength to deal with this intimidating situation.

MR H: This whole experience hasn't been unpleasant for me. You know, I've thrown up a few times when I first got chemo. And then I never threw up again. So it's really been not bad. I mean, I've had worse flus in my life. It's just been real manageable. I've been real lucky to have a treatable disease, anyway. It's not that it's curable, but it's treatable.

DR LOVE: What was sort of your reaction or your mental state when you first found out about the problem?

MR H: Freaked out. A lot of crying. Didn't want anyone to know. You think you're going to die. I remember being in the hospital and thinking I wouldn't wake up. So I'd never go to sleep. I was always up. And so they had to shoot me with lorazepam, which really calmed me down, and I could go to sleep or stay up. It was a real mellow — whatever it was — anxiety reducer. And I kept wondering — it just didn't seem right to me that I was going to die. And I had all these things I wanted to do, so I just suddenly became — it's either you keep living in this misery of death around the corner every day, or you get real positive and go and do things that you've always wanted to do, that you were always scared to do before. And so in the hospital, I made that decision that I was going to be positive and proactive about it and not dwindle in the scary part. And since then, I've done a lot of things I've always wanted to do. I have my own TV show now — I always wanted to do that, but for some reason never had the balls to do it. And so I do a lot of things like that. I'm a lot more aggressive in business and life, and I do a lot more fun things that I've always — I don't know. It just — when you think you might die, your whole life changes. And all those little problems and things you were scared of before are all out the door. So it's a real kind of freeing experience in the same way as it's a very scary experience.

DR LOVE: Who were you sort of sharing this with? Who were you talking to at that time?

MR. H: My friends, I guess, and my family. I had a bunch of people who were always coming to see me every day. And it was a little, like, room full of people. And it was good that everyone was always positive and up, and they weren't — like, my mom was with me every day, and my ex-girlfriend. And all these people who flew in were staying with me and my brother. If any of them would have showed emotion, it would affect me greatly. But everybody was really good and not to be sobbering and crying. And it kept me that way, too. You know, you're an emotional wreck, the first stages of realization. But the quicker you get to the positive part, the better you can help yourself. And I really felt like that was a big deciding factor in me getting better, was me deciding that I was going to get better.

DR LOVE: Had you ever faced a serious health or safety problem before?

MR H: No.

DR LOVE: So this was all new?

MR H: Yeah. It was completely new. I never really get sick, either. So it was a very new experience for me.

DR LOVE: How long a period of time was it that you were kind of — I don't know — in limbo, or before you were able to find the sort of strength you're

describing?

MR H: I would say a few days into it, I decided if I was going to die, I was going to go out being happy. And that's a very hard thing to decide upon, for some reason, because you think you're going to die every day. I just decided — and I had another friend that went through it, too, and she was real positive. And she's through it. You know, I'm not saying that's a cure by any means, but it's definitely a cure to a good ending of a life, you know. You can be scared and freaked out or you can just be happy and you go do things you want to do while you can do them. And I just really had a feeling like there was something else meant for me, that I needed to do. And that kept coming back to me. And then I realized I had to just go with that and see what happened, be positive and get through it as best you can.

DR LOVE: As you were sort of thinking this through and sort of coming to terms with it, again, I'm just kind of curious. Was it more an internal process going on or was there somebody or some people that you were discussing this with?

MR H: It was more internal, because that's the one thing about it. It's — you're the guy sitting in the bed in the hospital room, surrounded by all your friends, looking out at them instead of looking at your friend in the bed. And you go on the internet, and then it starts showing you the fatality rate and the odds, which freaks you out. So you have to just take that kind of with a grain of salt, also, and decide your own path. But it was a lot of me, by myself, figuring through it.

DR LOVE: Again, during that initial period, what was explained to you, specifically, in terms of the kind of therapy that you'd get and sort of what to expect from the future?

MR H: It was explained to me that there's no cure and it was a slow-moving disease, and I was a younger person to be getting an older man's disease, and they said if there were treatments — I wasn't responding to treatments, I could always do a bone marrow transplant, which is kind of like a last-ditch effort. And the odds of that still aren't that strong, you know, of it taking.

So I always knew there were some desperate roads I could take, but I also knew there were a lot of things I could do right away with treatment that my doctor's taking me through now. And I – I'm lucky that I respond to these things really well. And I seem to be healthy enough to handle them.

But while I was getting treatment, sitting in the room in your Lazy Boy chair, you know, I see one of my buddies across the room, an older guy, who's a lawyer in Fort Myers, and he has the same type of disease. And he's had it for 25 years. So talking to him, I was like, you know, "How do you deal with it? I mean, do you ever think you're going to die or something?"

And he said, "There's always," he said, "I'll go into remission; I'll come out. I'll be good for a month; I'll be good for six months. I'll come back out. I'll get some other," – he said, "There's always been a silver bullet treatment that comes up that I can take." You know.

Anyways, he's had it for 25 years, which I thought was really impressive. And I feel like there's going to be something like that for me, also. And if it comes down to a bad situation where I'm not responding anymore, I have a bone marrow match, which is my brother, and hopefully, by then, there'll be a little better odds of it taking.

DR LOVE: Are you in treatment right now?

MR H: Mm-hmm.

DR LOVE: What kind of treatment are you receiving?

MR H: I'm on Alemtuzumab right now, which are just shots I get every other day. I'm getting 36 of them. And I think I'm around 28 now, or 26. So I've got a couple more weeks, three more weeks or so. And then they'll stop me, I'll get a break, and they'll just keep checking my blood to make sure my levels stay down.

DR LOVE: How's that been?

MR H: It's been pretty good. It's very easy to do. It's not like other treatments where you're getting hooked to an IV and you have to sit there for six hours or whatever, all day, and then you can leave. This, I can come in, get a shot. Then I can leave, kind of like Epoetin alfa a little bit. And it's been a really good drug. I've had no side effects from it, that I'm aware of, and my numbers are really good right now. So I'm very fortunate for that. And he also said, if it doesn't work, there's some really new good stuff coming out, you know. So there's a little promise of other things they can do later. So that's good. And it's a real easy treatment.

DR LOVE: What other therapies have you had?

MR H: Well, I'm doing this alemtuzumab now. Before that, I did rituximab.

DR LOVE: How was that?

MR H: Before rituximab, I came off my main chemo, my first chemo I did for six months. Then they started doing me with rituximab. And so I kept comparing it to the chemo regimen. And it was similar, but, you know, I was there, I think, for maybe 45 minutes instead of being there for five hours sitting, getting chemo. And at first, I had reactions to it. I think the first time I got it, I remember getting a real big heat rush through my body and feeling a little faint and started sweating. And the nurses noticed I was getting red, so they stopped the treatment, laid me back and just let me relax for a little bit. And I came out of it. And they hooked me back up 20 minutes later and kept it at a slower rate and administered it like that. And that happened one more time, and then it never happened again.

DR LOVE: Now, by the time you finished the rituximab infusion and went home, were those symptoms gone?

MR H: Yes.

DR LOVE: So it was only during the infusion you had those —

MR H: Yes.

DR LOVE: How about the chemotherapy? What was that like?

MR H: It wasn't that bad. I always — you hear it's a nightmare, but like I said, I threw up in the hospital a couple of times, and once at home. Then I never threw up again. There was some new nausea medicine that came out within that time. And once I got that, I never had any problems again. And, you know, the feeling — when you first get it, you feel real tired and weird. It's a real alien feeling. It's kind of similar to flu symptoms, but something I definitely never had felt before. But, you know, you just chill out for a night, go to sleep, and, hopefully, the next day you feel a little better. Sometimes, the next day I'd feel that way, too. But by the next night, I'd always be back to normal — not normal, but feeling okay.

DR LOVE: How about hair loss?

MR H: I lost most of my hair. I didn't lose all of it, which was odd. But I just shaved my head. I didn't care. I'm a guy, anyways. And I kind of liked not having hair on my body for a little bit. It didn't bother me.

DR LOVE: Have you gotten to know other cancer patients?

MR H: Mm-hmm. Oh, yeah.

DR LOVE: What's that been like?

MR H: Really interesting. I like it. With me, I'm a little younger, compared to all these people in the room. Sometimes they're younger than me, but there's mostly old people who sleep through their treatments. But there are some really interesting people that you meet. You know, I have a lot of really good friends now through it. Just really cool people that — you know, a lot of them don't talk. You kind of sit in your chair and got their own little thing going. But a lot of them want to find out about your story, too, because everyone wants to kind of relate their condition and get through it together. And I've really met some special people. I really have. And I've really enjoyed that part.

DR LOVE: Anything you've observed in terms of the kinds of people or situations where people tend to be able to adapt to this kind of situation, whereas people who are not able to adapt?

MR H: Yes. I think I've definitely noticed — you know, I don't know a lot with these older people that are so quiet that, and there's so many of those, that you see every other day or whenever. But, for people that I talk to, a lot of people ignore it and kind of just live another life besides it and don't like it. But the people that really want to get through it seem to get through it. I've just noticed that attitude is so much better than chemo. I believe that if someone doesn't fight it and kind of works with it, if they have a good attitude and a positive outlook, their condition is much better. And there's a lot of them that, like, complain about their doctors or the needles or whatever and kind of bitch at, you know, why they got it or whatever, but I keep seeing that you can't be that way. You know, you have to be positive and get through it in a positive manner, or you're hurting yourself more than you know. And I've noticed that with friends that I've met. The ones that are real care free and kind of open and want to talk and stuff seem to do better — of course, there's a lot of times where everyone's in pain and feeling real horrible. But you have to get through it with a good light. And it seems to be a lot better condition for you.

DR LOVE: Where do you think that comes from, being able to sort of find that strength through —

MR H: I think it's just being a strong person to start with. I think a lot of it is that, or you kind of learn to do it. I've seen that, too. You know, I see these introverted people that read a lot and don't really do things, and suddenly they're in these rooms full of people. And either they talk to you or they don't. And the ones that kind of reach out and just kind of experiment with their condition and try to meet people and do new things as best they can have a lot better condition of life, just because they're — I mean, some people will just go through the treatment and be their same kind of self. But the ones that kind of want to meet you and talk to you a little bit always seem to be a little better and a little up and normal.

DR LOVE: Is there anything positive that came out of this experience?

MR H: Oh, yeah. Just the fact that it drops all these social barriers for me was a really cool thing, a lot cooler than I thought. You realize the fear of dying really limited you before. Then suddenly you know you're going to die; you don't have that fear anymore, and you kind of look at things that you want to try and do. And I remember making a list of things, you know, like my top 10 things I wanted to do. And I've just gone and done them. You know, I rode a bull for my TV show. That was just the craziest thing I've ever done in my life. Entered a —

DR LOVE: You rode a bull?

MR H: Yeah. I entered a rodeo in the Professional Bull Riders, the PBA. And I had a buddy who was a rider, and so he got me in. And I didn't do any training. I just walked up to the rodeo, signed up and did it. I mean, it was by far the scariest thing I've ever done, but the coolest thing. You don't expect it to be fun. You expect it to be horrifying and you might die — and that was definitely there — but suddenly I'm sitting on a bull. There's this crowd screaming. The cameras are around me. And it was just a really cool experience. And, you know, I rode it for a few seconds and it threw me. But riding it for those few seconds was a cool moment that I would never have ever done that. And I was still on chemo at the time. But that was incredible.

And the TV show is incredible. That's something that I always wanted to do my whole life but never approached it, because I was doing something else,

or I think I was just a little scared to start the process. I decided I was going to do it. As soon as I did, people just came to me. I had investors. "Here's a program. We can buy this show," and I had a half-hour show I was doing every other week.

DR LOVE: What kind of show?

MR H: We called it Lounge Television. I used to do a live show and write a column in my town in Fort Myers, called "Ask Andy," and it was kind of a sex column. So I had lounge girls in the TV show, and it was just a variety show. I'd go out and ride a bull. I'd have a band every show. I had dancers, a DJ. It was a really cool, kind of fun variety show. And that show was a good example of something you can achieve once you get this release of worrying about dying. You know, I still don't like the fact that I have the death sentence hanging over me, or whatever, but it's really given me the power to not be afraid to do things, because it's — as relaxed as I've always been, and confident that I've always been in myself — and I've done a lot of crazy things — there's always been barriers that stop me from going over to talk to that person or to ride a bull or to start a TV show or start my own column or whatever. And after you get through the initial shock value, you realize you've been given a freed-up kind of feeling about yourself now, which is something new to me.

DR LOVE: Any fears or concerns about the future?

MR H: Yeah, definitely. You know, I could die. I could get the flu out here today and, me being on Alemtuzumab, be real complicated. But that doesn't bother me. I could also walk out and get hit by a piano, you know, coming out of the building, or a car runs off the road. We all have that in our lives. And it's funny. I see more people dying from stuff like that, than people like me with cancer. I'm concerned that I might run out of silver bullets, but I'm not too concerned about that. You know, why worry about something that's so far off and iffy anyways? So I'm pretty positive about the future, and I've really, in a weird say, enjoyed the whole cancer process. I don't know if you've ever heard that before, but it's been kind of fun. It's been a bunch of new experiences for me. It's opened doors. I throw these huge benefits now in my town for other cancer charities, and I remember I wrote a column for my newspaper and it was edited because I was too cheerful about my condition. And they cut out some of my jokes, because they thought I was being too lighthearted about getting cancer and stuff. But I've kind of liked it in a weird way. You know, you're kind of like, "Whew. Okay. Now I know I've got it, so let's just live with it and move on, instead of worrying about it, am I going to get it."

DR LOVE: Has humor helped?

MR H: Oh, yeah. I'm a pretty weird person and I do a lot of funny stuff. And I've never changed that. But dealing with cancer in a funny way can be really fun, because people don't do that. So when you say jokes, people don't know how to laugh or whatever. So it's always funny to freak people out about that. And I remember in the hospital, the column I wrote was a true story, that I kept seeing this hot girl that one of the nurses said, "Oh, this girl has leukemia, too." And besides the fact of me wanting to meet her, she was this hot little 19-year-old girl. And every time she'd walk by my room, you know, with all her little, you know, pump and bags hanging — and I have to get mobile with mine — I could never catch her. And so it was like, I'm in my dress, walking around, trying to find this girl. And it was like this search to find this hot leukemia chick. And I imagined we'd meet in the library and our chemo bags would entangle, and I'd have some funny line to say to her. And I never got to do that, but I'm on my deathbed and I'm wondering when the hot nurse is going to come in to check on me. So there's a lot of funny situations like that, where I'm checking out nurses, wondering if I could meet them or go out with them, and I'm bald, you know, about to die. And so you meet really interesting people and you're put in some pretty funny situations sometimes.

DR LOVE: Has your reaction to this whole thing sort of surprised yourself?

MR H: Yeah, I think so. But it is true to my person, the way I've gone through this. I don't think I really changed greatly. I think I have become more positive. But I was a pretty positive person before and pretty optimistic. And I didn't let things bog me down, or I didn't stress out about stuff, but it surprised me a little bit that I've done so well through it, because you think, "You get cancer; you're going to die." But that's not the case. It really isn't. You can beat things and get through them. And fortunately, I have a disease that's treatable. So in that sense, I feel lucky that it's not some rare disorder that we've only seen one in a million times. There's no treatment, but we can try this. You know, I've been lucky to get the type of cancer that I have, so I'm fortunate for that.

DR LOVE: Do you see things differently now than before?

MR H: You definitely do. Your first right out of the hospital, it's just an incredible feeling to smell the air and see trees and plants. And my first night, I went to the beach and saw a sunset. And it was just like seeing it for the first time. And being out in the world, because you're kind of stuck in this bubble, you know, no bacteria, neutropenic environment, and you kind of get out of that alien, you know, floor you're stuck on. And it's so nice and freeing and you can just sit in a park and just be the happiest dork there, because you're just happy to be alive. And you really don't sweat the small stuff as much anymore. That's for sure.

DR LOVE: Any advice you would give to somebody else in the same situation?

MR H: Yeah. I mean, they're going to deal with it however they're going to do it. It's either you can cry and complain about it and cuss to God, or you can do something about it and make yourself happy and do things, you know, and be positive. And it definitely has an effect on how you progress through your condition. And I know it's hard to do it — or to see that way, but you really need to seek out positive things and know what you like and do the things you like. And if there's something you want to do, it's time to do it. And that's real good advice coming from someone who's always had things that I've wanted to do. Now, instead of putting them off, it's time to do those things. So go do them and have fun while you still can.

DR LOVE: What about exercise?

MR H: I exercise a lot. I've kind of become a freak now. But I thought it was very important. When I was on the cancer ward in the hospital, I was just doing laps all the time.

DR LOVE: Really?

MR H: Just, you know, get your little pump stand with all your bags and I would just walk around the halls. And I would do that as much as I could, and just stretching; stretches and massages were so helpful, and it kind of works oxygen through your system and kind of clears out all the junk that you're taking and they're putting in you. I remember the first few days, I was always doing laps, walking around. And the nurses were looking, "You can — other patients wear pants." I noticed I was in boxers my whole time, and everybody was — had, like, nice bed pants on. But exercise, definitely important. And I've exercised through all of my treatments. Sometimes, I take it easier, when my red blood cells are down. But even if I can't do something, I'll just stop it and move on to something else.

DR LOVE: What kinds of benefits have you seen from exercise, specifically? Does it help relax you? Does it help with that thing of positiveness that you said was so important?

MR H: Yeah, it does help with that. You actually start feeling good about yourself. You see results, too. You think you can't look better while you're in this bad state, but you really can. It's surprising. And you'd be surprised at how much exercise you really can do once you try it. I have noticed I'd go in to exercise, sometimes not feeling good, feeling a little tired from the treatments, and then once I've stopped working out, running or on the stair-master or lifting weights, after you kind of sweat it out, you feel good after that. And you get energy from it and it relaxes you in the same way. That was a huge benefit for me, and I really like it now. I mean, I keep asking the doctor, "Should I not be working out?" Because I work out as hard as I can now, and I'm right in the middle of treatments. And he's always like, "Go ahead and do it. If you feel good about it, do it, because it's going to be good for you to get your system moving like that." And it really has. And I've never had any trouble, even through chemo. You don't feel good, but you can do stuff. And any type of exercise, I think, is good, and I think people should be doing it.

DR LOVE: Any other sort of lifestyle things that have been helpful? What about things like music or meditation?

MR H: Yeah. I meditate. I have before, though, also. But I do notice when you think you're going to die, everyone's telling you all this information, all these books, these webpages and videos. You're overwhelmed with stress and information. It's real important to just, at one point, sit down, relax and try not to think about anything, and just be calm and concentrate on breathing. And once you come out of that for five or 10 minutes, you'll be blown away at how focused you are and relaxes, and how able you are to deal with situations now. That's really helped me.

DR LOVE: Do you think these kinds of things that you're talking about apply equally well to older people?

MR H: Yes, I do. I know a lot of older people are real fragile. And you can really see that when they're getting treatments and getting up and down. But I also think those people would be surprised at how much exercise they're able to do still. It's kind of the case where you have a sore shoulder, so you start favoring it, and you don't want to do too much with it, but you realize, "Jeez, I can do this move." And once you start stretching it out and doing something with it, it gets better on its own.

DR LOVE: What about food and nutrition issues?

MR H: I think it's important to be on a good diet, but I also think it's important to chow down on a Philly cheese steak, you know, if that's what you're craving right now. I think it's important that you go after any type of food you want to get when you feel like it.

Now, of course, once you start getting a little stronger and better, I think diet is really important. And it's probably the worst thing that I'm at right now. I mean, work out, but then I'll go home and have a milkshake and a cheeseburger. So it's really hard for me now to be a good eater, but I know that would be a major compliment to getting me better, would be a good diet.

DR LOVE: What about vitamins and supplements?

MR H: I think they're also great. I take them once a day. I don't know enough of what I should be taking. But I think that's important, too. Sometimes it's tricking yourself into making yourself better.

DR LOVE: Do you think that part of it is trying to regain some control, to feel like you're doing something?

MR H: Yeah. I don't really feel like I've lost control, but I do feel like I like to have any edge I can get. And so, any type of research stuff, I'm always into and interested about. And if something new, that someone's doing, that no one's really tried, I want

to know about. And I want to try it. As long as it's not going to hurt you, why not try it? Maybe it will hurt you, but if there's some avenue open, I think you need to explore it, and not just say, "Okay. I'm staying with conventional medicine." You know, maybe spiritual is going to help you. Maybe some witch doctor somewhere will help you. Different people, different treatments, even with the same diseases. I think that's a very true statement that some people aren't going to be open to things as they will to other things. And so if they feel more comfortable trying that, then they need to try it.

Evaluation Form:
Non-Hodgkin's Lymphoma Update for Patients — Issue 2, 2005

Research To Practice respects and appreciates your opinions. To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please complete this evaluation form. A certificate of completion will be issued upon receipt of your completed evaluation form.

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GLOBAL LEARNING OBJECTIVES

To what extent does this issue of *NHLU* for Patients address the following global learning objectives?

- Counsel patients with NHL about treatment options and ongoing clinical trials. . . . . 5 4 3 2 1 N/A
- Inform patients with NHL about the specific risks and benefits of various systemic therapies. . . . . 5 4 3 2 1 N/A
- Develop an increased understanding of the patient perspective on cancer information and treatment decisions in NHL. . . . . 5 4 3 2 1 N/A

EFFECTIVENESS OF THE INDIVIDUAL FACULTY MEMBERS

Faculty	Knowledge of subject matter	Effectiveness as an educator
Lowell Hart, MD	5 4 3 2 1	5 4 3 2 1
Fredrick B Hagemeister, MD	5 4 3 2 1	5 4 3 2 1

OVERALL EFFECTIVENESS OF THE ACTIVITY

Objectives were related to overall purpose/goal(s) of activity. . . . . 5 4 3 2 1 N/A

Related to my practice needs. . . . . 5 4 3 2 1 N/A

Will influence how I practice. . . . . 5 4 3 2 1 N/A

Will help me improve patient care. . . . . 5 4 3 2 1 N/A

Stimulated my intellectual curiosity. . . . . 5 4 3 2 1 N/A

Overall quality of material. . . . . 5 4 3 2 1 N/A

Overall, the activity met my expectations. . . . . 5 4 3 2 1 N/A

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Non-Hodgkin's Lymphoma™ UPDATE

Patient Education Series

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In addition, the following faculty (and their spouses/partners) have reported real or apparent conflicts of interest that have been resolved through a peer review process:

Dr Hart – Director of Research, Florida Cancer Specialists, Naples, Florida; **Speakers Bureau:** AstraZeneca Pharmaceuticals LP

Dr Hagemeister – Professor of Medicine, The University of Texas MD Anderson Cancer Center, Department of Lymphoma/Myeloma, Houston, Texas; **Consulting Fees:** Biogen Idec, GlaxoSmithKline; **Speakers Bureau:** Biogen Idec, Genentech BioOncology, GlaxoSmithKline, Ortho Biotech Products LP

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Non-Hodgkin's Lymphoma™ UPDATE

Patient Education Series

STATEMENT OF NEED/TARGET AUDIENCE

Counseling patients on the natural history, treatment options and personal implications of the diagnosis of non-Hodgkin's lymphoma (NHL) is complex and time consuming. The many variants of this disease make it a challenge to explain important information to patients in an understandable manner.

This audio CME activity focuses on interviews with clinical and research specialists in NHL and specifically reviews how these research leaders educate and counsel their own patients. The goal of this series is to help physicians better understand how to optimally discuss NHL with patients in their practices. Additionally, some of the programs will also include first-hand accounts of actual patients with NHL in order to provide listeners with another perspective on patient education.

GLOBAL LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

- Counsel patients with NHL about treatment options and ongoing clinical trials.
- Inform patients with NHL about the specific risks and benefits of various systemic therapies.
- Develop an increased understanding of the patient perspective on cancer information and treatment decisions in NHL.

PURPOSE OF THIS ISSUE OF *NON-HODGKIN'S LYMPHOMA UPDATE* FOR PATIENTS

The purpose of Issue 2 of *Non-Hodgkin's Lymphoma Update* for Patients is to support these global objectives by offering the perspectives of Drs Hart and Hagemeister on the translation and dissemination of complex information on NHL and its treatment into a format that would be helpful to patients diagnosed with the disease.

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HOW TO USE THIS CME ACTIVITY

This is an audio CME activity. To receive credit, the participant should listen to the CDs and complete the evaluation form located inside this insert or on our website. In addition, appropriately selected patients can utilize part or all of the materials contained on these CDs. The participant can distribute copies of the audio discs or direct these patients to download the MP3 files or read the transcript at **www.NHLUpdate.com/Patients**. The file for the transcript of this program is also included on the first audio CD. Kindly let us know whether this experiment in patient education works and how we can make it better. We welcome any feedback or questions to **Info@ResearchToPractice.net**.

Non-Hodgkin's Lymphoma™ UPDATE

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