Advances in the Treatment of Ovarian Cancer
Webcast
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Dr. Robert Coleman

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Andrew:
Hello and welcome to Patient Power. I'm Andrew Schorr. Thanks for being with us once again. We are going to talk about one of the most serious cancers. All cancers are serious, but one that unfortunately is often caught later and then is more difficult to treat, but as with so much work that goes on at M. D. Anderson they are making real progress. On this episode of Patient Power we're going to talk about advances in the treatment of ovarian cancer.

But as I like to do I like to start with real people who have been affected by this. So I want you to meet Connie Hale. Connie is usually in Bay Cliff Texas, down on Galveston Bay, where she sells yachts, and I want to get a ride with you sometime Connie, but I know you're with us there near near Dallas. So let me see if I've got this right. Back in 2005 you had your annual physical, right?

Ms. Hale:
I did, Andrew.

Andrew:
And so while the tests were normal your doctor doing a physical exam felt something abnormal when she did, what was it, a pelvic exam where she felt something?

Ms. Hale:
Yes

Andrew:
Okay. And so what she wanted to do was have an MRI to see what was going on. And when you had the MRI what did it show?

Ms. Hale:
Well, it showed that I had a tumor. And we had discussed whether it was cancerous or what she thought, and she said it didn’t look as if it were. So I went into surgery thinking, I'm going to have a tumor removed and my ovaries and my tubes and I'm going to go home, and I'm going to be a well person.
Andrew:
Right. So she said I think we need to go in and get it, and you said, Sure, expecting it not to be malignant. But when you woke up from the surgery what did you find out had happened?

Ms. Hale:
Well, I found out that I had a cancer. And they weren't exactly sure if it was ovarian or if it was in the bowel, because it had gone into part of the bowel and they had removed part of the bowel and I ended up with a colostomy at that time.

Andrew:
Now, I know you have a very strong family and friends, nine sisters and one brother, do I have it right?

Ms. Hale:
That is correct.

Andrew:
So it's a tremendous blow. What's going on. You go to sleep for surgery and think, well, it won't be that big a deal, and then this word cancer comes up. So what happened then, because then you want to fight the cancer and you want to beat it.

Ms. Hale:
Well, I think the first thing that came to my mind--well, of course, when you come to and you find out all this you don't really--it's kind of hard to absorb, you know, and you're kind of in shock and disbelief and all the other things that you are. But after all this set in and I got my head about me and actually went home and decided what I wanted to do and that was to go to M. D. Anderson. And I had already had that in my mind, but when I went back to the doctor for her to release me, which was two weeks later, she said, Connie, if it were me, and you've been my patient for a long time, this is what I would do. I would go to M. D. Anderson. She said, I will send your file over. You need to call, just call in to this number, and she gave me the number to call. And that's what I did. And I got new patient and they took my information, and from there I met with Dr. Coleman.

Andrew:
Well, we're going to meet Dr. Coleman now, your doctor, who is a gynecologic specialist and a professor at M. D. Anderson, Dr. Robert Coleman. Dr. Coleman, thanks for being with us and joining Connie as we tell her story but also the story of advances in treatment as you're doing at M. D. Anderson. Welcome to Patient Power.

Dr. Coleman:
Thanks for having me. It's a great pleasure to be here.

Andrew:
Dr. Coleman, so Connie wound up with what was considered stage III ovarian cancer. Help us understand what the different stages are.

**Dr. Coleman:**
Sure. Ovarian cancer is a disease that we have a fairly good understanding of in terms of how it spreads, and staging is really a reflection of that. So that is as the tumors are limited to the ovaries we call that stage I. As they start to spread outside of the ovaries to the pelvic tissue we call that stage II. When it gets into the abdominal cavity and there are nodules in the abdominal cavity, then that is stage III. And then it's subdivided on the basis of the size of that disease in the abdominal cavity. So stage III C is the most usual diagnosis that's made when it's first diagnosed, and it reflects the fact that there are tumors that are larger than a couple centimeters in size or involving the lymph nodes. And then stage IV is the situation where it's actually involving a distant site or in the body of certain organs like the liver or the lungs. So it's basically a reflection of the distribution of the tumors.

**Andrew:**
Dr. Coleman, now, stage IIIC that's what Connie was diagnosed with. And, Connie, you didn't have any symptoms to that point, did you?

**Ms. Hale:**
Well, I did, but they were so minuscule. You know, you make all these excuses. My stomach had extended, of course, and I probably had more gas and that kind of thing. But it's all things that you make excuses for. Hey, I've got to go on a diet. I'm eating the wrong things. So thinking back, yes, I did, but it was nothing that I could put my finger on and say I think there's something wrong. But as far as pain or anything like that, no, I did not.

**Andrew:**
So, Dr. Coleman, it's because the symptoms can be very vague and could be other things that ovarian cancer is typically diagnosed later, right?

**Dr. Coleman:**
That's right. I think that her story is very typical in that her symptoms are not very specific to anything in the ovarian or GYN track. It's just that it oftentimes involves the abdominal organs and so the symptoms are very abdominally related or are a reflection of like pelvic pressure. So another common symptom that we hear about with patients who have pelvic tumors is that they have frequency of urination or they feel this pelvic heaviness, difficulty having bowel movements, etc. Those are all very classic symptoms, but there could be a whole range of things that happen to be in the pelvis or abdominal cavity. So nothing specific.
Andrew:
Is there now some research that's helping doctors look at a grouping of vaguer symptoms and saying, well, that needs to be worked up that it could be ovarian cancer developing?

Dr. Coleman:
That's a great question. And I think what's happening in maybe the last three years or so is we've got a better handle on what the constellation of symptoms are. So the ones that you mentioned or that were brought up earlier, the abdominal pain, the frequent urination, or the pelvic heaviness and these abdominal bloating complaints are present across the spectrum of patients. But when they collectively come together and they are persistent, then that usually indicates that there's something other than a completely benign condition going on, and it certainly requires investigation.

So, unfortunately, we don't have a cookbook approach to say that if you have symptom A, B or C then you need to have this done because that's the next step for diagnosis. It's more that when we look at this in patient cohorts the patients who ultimately had ovarian cancer had these symptoms usually collectively more severely and for a period of time that would ultimately bring them to the attention of the doctor. So, unfortunately, we don't have a very straightforward way to tell patients that if they have these to come in, but they should certainly be monitoring them if they come together in groupings and certainly if they are persistent.

Andrew:
Okay. Let's go back to Connie's story. So Connie, you go see Dr. Coleman and you end up getting on, I guess, combination chemotherapy. Did you have surgery first?

Ms. Hale:
Well, I'd had already had surgery when the I went to M. D. Anderson, when I went to Dr. Coleman.

Andrew:
That's right.

Ms. Hale:
So I had already had the surgery.

Andrew:
And then you had cycles of chemotherapy?

Ms. Hale:
I did. What's what happened next.
Andrew:
And you also ended up being in a clinical trial where some newer medicine was
being tried as well.

Ms. Hale:
Yes, I did

Andrew:
So how have things worked out? We're more than two years later now.

Ms. Hale:
Well, I'm cancer free

Andrew:
Yaay.

Ms. Hale:
And I feel wonderful, and I have a great life

Andrew:
Yaay. Dr. Coleman, let's put Connie's case in perspective. So she had surgery
already, but is the first approach, let's say when somebody comes to M. D.
Anderson to see can you sort of debulk the disease with surgery and then you
follow with drug therapy?

Dr. Coleman:
Right. So the standard approach to this disease is that as soon as we have
indication that it's ovarian in nature or pelvic in nature is for us to make sure that
the patients are optimal for a surgery which could be quite entailed and be fairly
intensive. So what we'd like to do is make sure they're medically fit for surgery,
knowing that we may take out a fair amount of tumor and it may be quite a long
procedure. So the majority of the patients, though, that we see are good
candidates for surgery, and the intent there is to try to remove as much tumor as
possible.

So, like Connie, the typical patient that we see that ultimately has a diagnosis of
ovarian or peritoneal or primary fallopian tube cancer is that they'll have a mass in
the pelvis that's not necessarily enormous but it's enlarged, and then they'll have
large sheets of tumor that are dusting the inside of the abdominal cavity. Some of
these are confluent enough to make a large mass in the abdominal cavity and along
the diaphragm. But usually it's along the surfaces of the underlining of the
abdominal cavity or along the intestinal mesentery or the intestinal surface itself.

And so what our goal there is is to try to remove absolutely as much as possible
that's safe. And, in general, we're getting better and better as we do more
aggressive surgery to get more of this tumor out. But our intent ultimately would
be to remove all tumor that's visible. That happens about 25 percent of the time. About 75 percent of the time, so another 50 percent of the time, we're able to remove the tumor down to about a centimeter of any individual size around the abdominal cavity. And then the remaining 25 percent have disease that's in a distribution that's not either safe to take out or it's just involving structures that are not able to be taken out. So that's our first goal.

And then once that's done and the patient has recovered enough to have chemotherapy, then we'll go ahead and administer the chemotherapy. And there's a lot of options for treatment at that point

Andrew:
Okay. Let's understand that. So the name of the game in drug therapy has been often combining different agents that are effective in one way or another, seeing whether a certain combination is right for patient A or a different combination for patient B. And so where are you now in what you have to offer somebody with even more advanced ovarian cancer knowing it's often discovered when it's advanced in trying to accomplish what we have with Connie?

Dr. Coleman:
Right. Boy, there's a lot of work going on in this setting. I think that one of the real joys of being involved in drug development at this stage of the game for ovarian cancer is that there are so many new regimens that are coming down the development path that are ultimately ending up in this primary treatment arena that makes it a very exciting place to work and study in.

Right now, for patients that are newly diagnosed there are some studies that are stratifying patients on the basis of how good a surgery they had. Some of them are also stratifying patients on the basis of whether or not they even had surgery first. So we do have several options for women who come for therapy. One of the ones that right now--a very large study which is ongoing throughout multiple sites around the country and here as well is to look at the addition of two interventions in the management of this disease.

One is to add a biological drug called bevacizumab, or Avastin, to the standard chemotherapy regimen in the hopes that it will do a better job with the primary tumor reduction on therapy. And then that trial also has a secondary phase which would be administering either observation or the continuation of that drug for a long period of time after their first sets of chemotherapy infusions are done. So it's a very exciting trial. We don't know how this is going to pan out, but in many solid tumor this combination has been quite successful.

And then we're also looking at new versions of the drugs that we consider the staple of our primary treatment regime, and that would be the taxanes, paclitaxel and a platinum, carboplatinum. So we're looking at new derivatives of these two
new compounds. One of which we have ongoing right now is looking at a new drug called Abraxane, which has been approved for use in breast cancer patients, and that's being combined with a platinum.

**Andrew:**
I was going to say what I'd like to do is get into greater detail about it. And also as we continue in our next segment understand where we're heading as far as personalizing treatment to the exact situation a woman presents with and what you're beginning to understand about the biology of ovarian cancer tumors too.

So we'll be back with more with Dr. Robert Coleman, who is a specialist certainly in ovarian cancer and a professor of gynecologic oncology at M. D. Anderson Cancer Center and his patient, Connie Hale. It's all coming your way as we continue Patient Power right after this brought to you by M. D. Anderson Cancer Center.

**Break**

**Andrew:**
Welcome back to Patient Power as we continue learning about advances in the treatment of ovarian cancer as done at M. D. Anderson Cancer Center. Andrew Schorr here with Dr. Robert Coleman, professor of gynecologic oncology and an ovarian cancer specialist, and his patient Connie Hale, who joins us today as she's visiting a friend in Bartonville, Texas.

Dr. Coleman, before the break you were discussing about clinical trials and biologic therapy, targeted therapy on top of the more traditional chemotherapies used in combination for many women, and you've also said that there are other drugs in development. So is what you're doing trying to figure out what is it about ovarian cancer cells that allow them to keep living and proliferating and figuring out what that quality is and then developing a drug that can kind of short circuit it?

**Dr. Coleman:**
Yeah, that's exactly right. I think, ultimately, if you can envision this, I've often made the statement that I think we'll be looking back on this era of the standard therapy or empiric therapy days as really the ancient days and that we'll come up with a cocktail that's so specific for an individual patient that our success rates will be so much better and our toxicities so much lower. So, yeah, that's really the Holy Grail here, is to try to figure out the exact processes that are going awry in ovarian cancer, or in any cancer for that matter, and then target those drugs specifically to that process.

And so we've come a long way into figuring out a way to understand the relationship, which is really the hardest part of this, is that we can find out that there may be a thousand mutations in a specific cancer cell but we need to
understand how they relate to each other. And the relationship is really the heart of trying to find out the right drugs that will fit into that scenario that will be most effective for patients.

Andrew:
When you talk about these genetic mutations, so a cancer cell, it's got all this--it's like somebody wearing bad clothes. They've got an ugly sweater and a terrible pair of pants and shoes that are dirty and all that kind of stuff. And so you see these qualities of a cancer cell, and so what you're looking for is what's at the heart of it to just knock it off, right?

Dr. Coleman:
That's right. And we do so so that we don't knock off the good cells. So we want to make sure that if there's a process that's driving a cancer process that it's also not the same process that's controlling the heart rate, you know, or the blood pressure or the immune function. And that's where all the details are coming. So right now we've just begun to launch into that type of molecular--we call that field molecular theranostics. So we're trying to figure out the specific details that have gone awry in the cancer cell and then target the new drugs to those processes.

Andrew:
Okay. I've got auto term for you--and I think what our listeners need to understand is when you say, We're looking at it, so much of this work is going on in the labs right there at M. D. Anderson, so that while you're bringing this benefit and the trials that come out of it right to your patients right there. So I think that's important to know.

What does this mean, if I get this right, is it short interfering RNA? Did I get that right?

Dr. Coleman:
That's right. Uh-huh.

Andrew:
What is short interfering RNA therapy, and what does it mean for ovarian cancer?

Dr. Coleman:
It's been a very exciting field to live in and to watch this evolve. But what we found about less than a decade ago is that the body has a natural way of controlling the way genes are expressed. And the body itself makes these very short little fragments of RNA which will have is the exact kind of complementary arrangement with a gene, and if they bind with that gene it's kind of shuts it off. And so it keeps things from going crazy. What we've discovered is that that's a very powerful technique to understand different biology processes in the lab so that if we want to understand, for instance, a specific gene in a mouse model of cancer or ovarian cancer or other cancers we can actually shut the gene off and see what happens.
And so what we've found is that there are a few critical genes that seem to be relevant for ovarian cancer, as well as some other tumors, and we can direct these interfering segment of DNA or RNA in the setting to those genes to shut them off. And that seems to be a therapeutically valid strategy in the lab. And so we've been very excited here at M. D. Anderson as we've been able to figure out a way to get that kind of therapy into the body systematically. Right now there's no way to do that and many people recognize the real value of this type of gene silencing, but there's been no way to get it systematically into the body or into where the tumor cells are.

So some of my colleagues here at M. D. Anderson and myself have been working on this process for the last couple years, and we think we have now a product that we will be able to deliver to patients, and so we're developing those first in human trials, hopefully to launch the first part of next year.

Andrew:
Well, this is maybe music to the ears of people who have been told that they have advanced ovarian cancer. And obviously not everybody qualifies for a trial and has certain criteria, but it's the kind of thing that goes on at M. D. Anderson on all the time.

Connie, you were in a study. I bet you're glad you were.

Ms. Hale:
Absolutely.

Andrew:
Because here you are.

Ms. Hale:
Well, you know, when you end up in that situation--or for me, anyway, you know, they offer you these opportunities to help yourself plus other people, how can you not? I mean, you know, how could you not participate? So it wasn't even a question for me.

Andrew:
And I was in a clinical trial too and I know it's worked out. And the treatment I received a number of years ago at M. D. Anderson is what most people receive now.

Now, one other thing I wanted to ask you about, Dr. Coleman, is tumor profiling. So in so many cancers we would say we used to assume that the biology of the tumor, not that we could did much about it because we had these kind of shotgun approaches, was just the same in everybody. But when we say ovarian cancer are we possibly looking at different biology for different people?
Dr. Coleman:
Yeah. It's very clear that different processes govern the growth of different tumors. There's some commonality to them, and certainly, you know, if you can imagine if there is a common pathway for cell death and that common pathway is interrupted it can be interrupted by a number of different ways. And so it's kind of like the work-around. You step on one part of the hose and there's another part of the hose that feeds the tumor. It kind of works its way around there. So what we try to do is get to a point where we can identify what the dominant process is in the cell and then hopefully go after that.

So, yes, the profiling gives us a lot of new questions to ask and to go after. What we're trying to do is to figure out what are the most relevant processes that are targetable and then start there.

Andrew:
Right. Let me ask you a common question I'm sure you get, and that is the CA-125 test. This came in from Charlene, who's right there in Houston. She says, "My sister-in-law was recently diagnosed with ovarian cancer. Her CA-125 is 600. She's awaiting an appointment for surgery. What does the CA-125, a 600 indicate?" And I'd even say, what's the CA-125 test?

Dr. Coleman:
That's a really great question, and it's something, imagine--you go back to the history of this, and I was fortunate to interview the person who discovered CA-125 who's actually the vice president of translational research here at M. D. Anderson, Dr. Bob Bast. I interviewed him about this specific question to put together a piece on this compound.

But if you go back to the '70s what they were doing is they were trying to figure out an immunotherapy for ovarian cancer, and they found this antigen called what ultimately turned out to be the CA-125 on these tumor cells. And when they targeted this new therapeutic to this antigen they found out that it just fell off the cell. And fortunately they were able to measure it in the blood. And so they realized that, hey, although it's not a great therapeutic strategy it's certainly something that may be measuring what's going on in ovarian cancer. And initially what they thought was that this would be the way to diagnose ovarian cancer when it was in the smallest form, because it's a very sensitive blood test.

But as it turned out, we found out that not all ovarian cancers actually produce the CA-125, and it's not necessarily related to cancer when it's elevated, and in some cases it may reflect the volume of disease but a lot of times, for a lot of situations it actually doesn't reflect the ultimate volume of tumor. So 600 or more than 500, let's say, or 400, doesn't necessarily mean there's more cancer there, but it just means that the tumor that is there seems to be releasing this antigen into the blood so it can be measured.
The CA-125 itself is used in a lot of situations. We use that to help prognosticate how patients may potentially respond to therapy, and if it's elevated it provides a very nice tool to monitor response to primary treatment and to follow the patients once they're done with their therapy and the surveillance.

Andrew:
Right. Well, that leads to my next question and that is, what is your sort of after care surveillance to see, you know, is there a chance that the cancer is coming back? Like in Connie's case, what's your lookout to make sure things are staying good?

Dr. Coleman:
And that's usually a fairly long conversation, as Connie can attest to. When we finish that primary treatment we have a lot of options in front of us, and one of the common questions that come up is that now that the security blanket of chemo is gone what do you do to keep track of things. So like what we did with Connie is we will come up with some kind of a plan to monitor more intensely the first couple years after the treatment is done if we decide not to do any kind of therapy. And that usually involves monitoring with some physical exams, CA-125 and some periodic imaging like a CT scan or an MRI. And that's mainly just to determine whether or not there's early recurrence of the tumor or some indication that the tumor might be coming back.

Andrew:
Okay. And then what about maintenance therapy? Now, Connie, you're not taking any medicine, is that correct?

Ms. Hale:
No, I am not. I finished chemo.

Andrew:
Right. So Connie is not taking any medicine, but there are certainly studies of some people doing it, and you mentioned it earlier, too, related to Avastin. So where are we now with maintenance therapy after all those earlier surgery, chemo, other treatments to try to keep the cancer at bay should it raise its head again?

Dr. Coleman:
Sure, and this is also again a common problem that--or a common discussion that we have with a lot of patients. You know, we--unfortunately, the natural history of ovarian cancer is that patients who are fortunate enough to get into a remission after their first go-round with chemotherapy that a significant proportion of these patients will ultimately have a recurrence. And so we have felt that maybe there's a way that we can affect that probability by introducing therapy after the completion of their first-line treatment plan. And it's a very logical concept.
Unfortunately, we have studied many different compounds and many different modalities in this setting, and we have not been able to show that a therapy that's administered after a patient has enters into their remission that will extend their life overall. So that's the overall survival end point. But what we do know is that we have seen some studies for some therapies that will extend an intermediate end point, which we call the progression-free survival, and that's the time from the initiation of the treatment until, if the patient recurs, that time point.

So it's a complicated issue, and we could spend a whole lot of time talking about it, but we are studying this once again in a trial for which the standard of care is to do what we did with Connie, and that's observe with frequent follow up versus an administration of chemotherapy at a reduced dose, reduced frequency and for up to a year. So there's a lot of work being done in that arena to hopefully come up with a--at least settle the issue of whether or not more therapy at that one point in time actually will improve the overall survival.

Andrew:
I hope what people gather from our discussion with you, Dr. Coleman, is, as you said, there's a lot of work going on to try to know what questions to ask and look at what may be the most promising answers. And often since ovarian cancer is discovered later I know my recommendation just listening is I think a woman owes it to herself to consult with a gynecologic oncology specialist and I would suggest at a research institution such as M. D. Anderson, where some of this work is going on because you really want it to be brought to bear for you.

So what about that recommendation, if things are moving, Dr. Coleman, it's a little self-serving I guess, but it sounds to me that consulting with someone just specializing in ovarian cancer makes sense.

Dr. Coleman:
Oh, yeah. And it's hard to come up with data to actually show the merit of doing that, but we have actually. There's been several recent studies now that have shown that survival is actually impacted but who takes charge of the situation. But I think on a more personal level the one unique thing about GYN oncology as a subspecialty is that it's one of the only cancer subspecialties where the surgeon also is the person directing the chemotherapy or administering the chemotherapy in many cases, and also, if it's necessary, radiation therapy, they're involved with the consultation of that concept as well.

And so it's a unique opportunity for us and for I think the patients so they don't have so many cooks to go ask questions to that we can see this through the entire spectrum of its development, from diagnosis all the way through all of the multiple different therapy modalities. So it seems that that is the most efficient, and I think it's now bearing out that it's probably the best strategy for women who have a diagnosis of a gynecologic cancer.
Andrew:
And I would add certainly with the work you're doing, the groundbreaking work you're doing at M. D. Anderson, that M. D. Anderson would be an excellent choice. It was the obvious choice for you, Connie, and Dr. Coleman is your doctor who has guided you through so much of this. And I know you've told me at other times that how you felt that at M. D. Anderson not only was it good for your body but it was good for your heart. You just felt embraced and totally supported there.

Ms. Hale:
Well, I'm just going to say I didn't--at the time I didn't think about the outcome of what was going on with me, but had I at any point stopped and thought that I was going to end up--that I had cancer, I would have never--I would have automatically gone to M. D. Anderson. I just would have. That would have been my first thought. But what I can say to other women out there is if you are diagnosed with a tumor it doesn't make any difference if it's benign--in my case I wouldn't have cared if it was benign or not, now, looking back--I would automatically go and seek further options of just going in and having surgery like I did. I would have, and I should have, I guess--well, maybe not I should have because I'm okay at this point.

But I would recommend other women take a little bit more pragmatic approach, I would say, and do some more research. Get a second opinion. Go to M. D. Anderson and let them take a look at you whether you have cancer or not. I mean, that's what I would do now, looking back.

Andrew:
Well, Connie, we wish you all the best. I hope that I can come see you down on Galveston Bay and take a ride in one of those--

Ms. Hale:
I hope so too, Andrew

Andrew:
Snazzy yachts that you sell. So let's do that.

Ms. Hale:
I have one just waiting for you.

Andrew:
There you go. I don't have a big checkbook but I can certainly go for a ride.

Ms. Hale:
Well, I can take you for a ride.
Andrew:
So we'll celebrate. There we go. All the best. Connie, I want to thank you, your doctor, Dr. Robert Coleman, professor of gynecologic oncology at M. D. Anderson. Dr. Coleman, thank you so much, and we wish you all the best with your groundbreaking work with you and your colleagues there.

Dr. Coleman:
Thank you so much, Andrew.

Ms. Hale:
And I want to say thank you to Dr. Coleman, too.

Andrew:
Yeah, there you go. He's played a big role in your life.

Ms. Hale:
He has.

Andrew:
Yes, he has. That's what we do on Patient Power is really hear inspiring patients and often paired up with the physician who's part of the team that made a huge difference in their life, lengthening their lives and giving them back their lives, and that's the story of Connie and Dr. Coleman today.

Thank you so much for joining us, everyone on Patient Power. Remember, knowledge can be the best medicine of all. I'm Andrew Schorr. This has been Patient Power brought to you by M. D. Anderson Cancer Center.

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