Kintalk Podcast Questions with Dr. Mindy Goldman, MD

Hi and thank you for joining us today for our Kintalk podcast series, “Ask the Doctor”. I’m Megan Myers, genetic counselor and Kintalk Specialist. Today we will be talking with UCSF’s own Dr. Mindy Goldman about Surgical Menopause. Dr. Goldman specializes in women's health care and gynecology issues for women with breast cancer and those at risk for cancer. Dr. Goldman works with women who have an increased cancer for gynecological cancers and choose to under go risk reducing hysterectomy and bilateral salpingo oophorectomy, which is the removal of the uterus, both ovaries and fallopian tubes.

Dr. Goldman, when we see women with the diagnosis of Lynch syndrome or Hereditary Breast and Ovarian Cancer in our clinic, we talk about the risk for gynecologic cancers in this syndrome. Women with Lynch syndrome have up to a 60% life time risk for endometrial cancer and up to a 12% life time risk ovarian cancer. Women who have Hereditary Breast and Ovarian Cancer Syndrome (HBOC) due to mutations in their BRCA1 or BRCA2 genes have up to a 40% lifetime chance of developing ovarian cancer. Due to these increased gynecological cancer risks we often discuss the potential of undergoing risk-reducing hysterectomy and bilateral oophorectomy (the removal of the uterus, ovaries and fallopian tubes) to dramatically decrease the risk of these cancers. However, it is important to add that while these surgeries prevent cancers, they can also greatly change a woman’s body physically and emotionally. Women should be aware of the side affects and prepare themselves before their surgery.

Our Kintalk members, as well as our patients here at UCSF, often have many questions about the surgery, the recovery period and the side effects of removing these organs both before and after menopause.

I am hoping you can shed some light on these issues for our listeners.

Question 1.
A woman who is diagnosed of Lynch syndrome or HBOC but has never had a diagnosis of cancer should consider talking about risk-reducing gynecological surgery. What advice would you give her about when she should have the surgery?

First I want to clarify that the recommendations for surgery are diff for Lynch syndrome vs HBOC. But in both of those syndromes we talk about thinking about risk reducing surgery once a women is done with child bearing as early as age 35 and for sure by age 40. With the lynch syndrome patients the ovarian cancers can be seen at an earlier age so we really do try to talk to people about seriously considering this by age of 40. Some of the things that are important to think about when people are considering undergoing these surgeries is preparing themselves for the onset of surgical menopause both recovery from the surgery and what is it going to be like to recover from the surgery itself. Now typically in Lynch syndrome patients when people are ready to have their risk reducing surgery it involves hysterectomy as well as the removal of both tubes and ovaries. For patients who have HBOC the surgery involves the removal of both the tubes and ovaries, what is most important when people are considering that is where are they going to have it done and cuts in the pathology because the crucial thing about both of those surgeries is its very important for the pathology to be cut in a very specific fashion where a microdisection is done of the tubes and ovaries and also of the uterus so the pathologist can make a very close assessment for cancer and that's different from the way pathology is cut in for different routine surgeries that we do when we are doing hysterectomy or removal of ovaries. So that's one of the things I talk to patients about is asking sure the pathologist due cut in their specimen in the special risk reducing protocols. The other thing that I talk to patients about is whether they have both completed child bearing and whether they are emotionally prepared for issues surrounding surgical menopause. Even though the recommendations are to think about this as soon as someone has completed child bearing or as early as age 40 certainly there are many patients that have a lot going on in their lives and they are not ready to have the surgery yet. One of the newer things that is sort of interesting and doesn't have a lot of data yet is that there is some data that suggests that all ovarian malignancies may actually begin in the tubes and given that there is a thought that if someone is not yet ready to be thrown into surgical menopause from removing the ovaries that you could remove their tubes once they have completed child bearing and at an older age come back and remove their ovaries which will throw them into menopause. Now I caution because there really is not long term data to say is this going to be effective in decreasing someone's risk at getting these cancers but there are many gynecologists and gynecological oncologists that are talking to these high risk patients about potentially doing these types of surgeries in a two stage process. I think in terms of preparing, I think particularly if someone is going to become menopausal there are so many side effects and the side effects are often times more intense when someone is thrown into menopause acutely, that is with surgery, I think going into surgery in the best physical and emotional shape is most helpful. Making sure someone is exercising, that they are sleeping well, that they are eating right so they feel both physically and emotionally that they are in a good space and ready to have this surgery.

Great thank you. Just one quick question to clarify, if women are interested in having a salpingectomy is that for women who have HBOC or for women who have Lynch syndrome, or for women of both groups?

I think most people talk about it more often with HBOC but because lynch are also at risk for ovarian cancer and data is suggesting that ovarian malignancies are beginning in the tubes that it is appropriate that could be considered for those patients as well. It's important to realize that when this is done it is a similar procedure that is done under general anesthesia and so people need to realize that it is going in for a surgery that can be done as an out-patient procedure but it does need to be done under general anesthesia.

Question 2.
Please tell us about surgery that you would perform on women who have a diagnosis of Lynch syndrome or HBOC but has not yet gone through menopause. Are there different types of approaches you would recommend to different women? Generally, how long is the recovery? Is the recovery period different for each type of surgery? What determines the type of surgery? (TAH/BSO, TAH or BSO, laparoscopic vs open)

The surgical approach is similar to the surgical approach that we do for all women, we try to do the least invasive procedure as possible. For HBOC because that involves just removing the tubes and ovaries and there is not the need to necessarily do a hysterectomy that is something that is done laparoscopically, it's an outpatient procedure, it takes about an hour and a half, people are watched in the hospital for a couple hours afterwards and the recovery period is relatively quick, most people feel that they are back to themselves within a couple weeks. We usually recommend people taking off 1-2 weeks from work, we can give up to 3 weeks from work but most people find they are doing well a couple weeks from surgery. For people with Lynch syndrome however that involves removing the uterus as well as the tubes and ovaries so that is a bigger surgery. That can be either be approached laparoscopically, abdominally or vaginally. The issue surrounding approaching this vaginally is that it is relatively straight forward to remove the uterus from the vagina but sometimes you cant always get to the tubes and ovaries and its crucial in these patients that all of the tubes and ovaries are removed so the pedicels that we take or the specimen that we take we actually cut the pedicels a little higher that we do in a surgery that is done for someone that is not at risk for these types of cancers. So that usually means that someone starts with at least a laparoscopy to get the tubes and ovaries and then they might go down below in the vagina to complete the hysterectomy. If someone has a very large uterus that is filled with fibroids, which is very common because as many as 30-40% of women have fibroids and they are more common in certain groups like African Americans, if they have a very large uterus it might be something that is not amenable to doing a laparoscopic procedure and someone might need to have an open procedure with an incision. These days however laparoscopy has evolved just like every field of technology has evolved and there is so much more we can do through the scope. Some surgeons also will choose to do it robotically assisted and there may be times where that can be very helpful if someone has lots of adhesions or if they have significant scarring from endometriosis but all of those still begin with using a laparoscope. When someone has these minimally

invasive surgeries the recovery time is short, so the whole reason we do this is to allow people to get back to their normal life sooner. With laparoscopic hysterectomy's most people stay in the hospital over night and then usually people feel pretty well by 2-3 weeks after surgery and certainly after 4 weeks people are back to themselves. If you compare this to when women have an open procedure often times its 6 weeks before people are feeling back to themselves. The benefit of laparoscopy, it sort of cuts that recovery period down, almost in half it really allows people to return to their normal lives sooner.

Question 3.
One of the greatest concerns we hear from women with LS is the fear of removing their uterus and ovaries, losing their natural female hormones abruptly and suffering the physical and emotional side effects of this loss. These side effects can include:

Sexual issues (including dryness)
Bone density
Aging
Mood/Depression
Urinary issues
Hot Flashes
Cardiac Disease

Would you address the concerns about the role of hormone replacement for these women. Is hormone therapy effective in preventing the effects of surgical menopause?

Before I talk about hormones let me talk about some of the health issues that I think are really important when you are talking about making someone surgically menopausal years before they would naturally go into menopause. The average age of menopause is 50-51 and we are recommending doing these surgeries as early as 35 so it's upwards of 10 years before someone would naturally go into menopause. If you look at some of the health issues related to aging, we know that the risk of heart disease is higher in men than women until menopause and then the risk of heart disease goes up in women after menopause. Heart disease is actually the #1 cause of death in the general population. There is a thought that the estrogen that is produced by the ovaries protects against heart disease in women. So one of the concerns if you are making someone menopausal earlier is are they going to be at higher risk for heart disease. So let's say you are saving a woman from getting a cancer but let's say they are going to be destined for a heart attack and instead of having a heart attack at 70 they are now going to have a heart attack at 60. ***In this patient population (women with Lynch syndrome or BRCA1 or BRCA2 gene mutations) we feel the benefits of surgery outweigh the risks and there are things that can be done to help protect against heart disease.***

*There are modifiable risk factors and non-modifiable risk factors****. Someone can't change if they have a family history of heart disease but they can make sure that they are at a healthy weight, they don't smoke, their blood pressure is under control and***

that their cholesterol is okay. *In a 40 year old we often don't think so much about checking their cholesterol BUT we do think about checking cholesterol in these patients once we have removed their ovaries. We talk to them about regular cardiovascular exercise and we make sure that their blood pressure is under control and that they are non-smokers. The other big issue is bone loss, women reach peak bone density at age 30-35, everyone has a loss after that but the major rate of loss which is about 2-3% per year occurs in the immediate menopause. The concern is if you make someone menopausal earlier are they going to develop something like osteoporosis sooner.* ***So we talk about ways to prevent osteoporosis, which includes regular weight bearing exercise, at least 30 minutes 3 times a week and one calcium supplement per day.*** *Sometimes these patients will need to get bone density tests earlier than we do in the general population because they are made surgically menopausal at an earlier age.*

Now the issue of hormones comes up primarily from a treatment standpoint. There is a lot of controversy over hormone replacement therapy but most of that controversy really relates to looking at the use of hormones for the prevention of disease. 20-30 years ago hormones were standardly given to prevent heart disease, and to prevent osteoporosis, with the knowledge that it was the most effective treatment for hot flashes. We now know its still the most effective treatment for hot flashes but it's not clear whether hormones should be used for prevention of disease. The large Women's Health Initiative study that looked at healthy older women who did not have established heart disease. This study did not show a benefit of hormones for prevention of heart disease and showed an increased risk of blood clots and strokes. However, one of the problems with that study is the average age of the women studied was 63 and the average age of menopause is 50-51 and we are talking about making these women menopausal as early as age 40. There is a thought that if you give women hormones early before the age of 63 that maybe hormones would have a benefit from a cardiac standpoint and would prevent heart disease. There is actually research going on now looking at that but currently there is no organization in the United States, not he American College for OBGYN, American Cancer Society, North American Menopause Society, none of the large organizations have said, "take hormones to prevent disease" they will say, "take hormones for treatment of symptoms using the lowest dose for the shortest duration possible" so its sort of an unknown question whether we should be giving these women hormones after putting them into surgical menopause to prevent heart disease and to treat bone loss.

Certainly we know it will help out with their symptoms. As long as someone doesn't have an underlying cancer and they are undergoing this surgery as a preventative procedure if they don't have other reasons they shouldn't take hormones. Having a prior blood clot in the leg or the lungs or having underlying liver disease or some people that may have a clotting disorder would be a reason a women should not take hormone replacement therapy. ***As long as they don't have any contraindications I think hormone therapy can be very helpful at alleviating the symptoms of surgical menopause. For many of my patients I will actually start them on hormones while they are on the recovery room to try and minimize both dealing with the effects of surgery and the effects of surgical menopause, which I think can be even more intense.*** *I think*

that at least in the short term, hormone therapy can help alleviate the most common symptom: hot flashes. Other things that women will often complain about are sleep disturbance and some of that may be related to hot flashes because for many women their hot flashes are more common at night. So if you treat their hot flashes that may help out but there is also the thought that menopausal women do have other primary sleep issues, so hot flashes isn't all of it.

Some of the other issues that we will sometimes see in menopausal women is mood disorders that doesn't mean that menopause causes depression but if someone is susceptible to depression menopause is a time in their life when they are more apt to see depression or more apt for depression to occur. Hormones do not fix that, if someone has a major depressive episode that's something they need to see their primary care physician about or psychiatrist and make sure that is evaluated and treated appropriately. For someone who has mild mood changes associated with menopause sometimes hormone replacement therapy may help out with that.

Hormone replacement therapy would also be beneficial for protecting the bones and it may help out with some of the sexual issues. Much of the sexual issues that we see are related to dryness and libido. The area of female sexuality is becoming a real science and good quality studies are being done and we know that much of female sexual functioning is actually psychologically based. Any of the studies that have looked at female sexual dysfunction, if dryness is an issue, the thought is that you should treat the dryness first because if it hurts to be touched or have penetration its automatically going to set something up that you are not going to want to have sex. So hormone therapy is one way to treat some of the dryness. Additionally, I will talk in just a minute about some of the alternatives and if libido is an issue in of itself and someone doesn't have vaginal dryness there are sometimes things we can use to treat that. Sometimes we can use compounded male hormone testosterone and sometimes antidepressant Wellburtine can boost sex drive.

Other issues that we see in menopause include urinary issues. We know there are estrogen sensitive tissues around the portions of the bladder so they may experience irritative symptoms and hormones may help that out. In the studies that have looked at urinary issues, good qualitative studies have shown hormone therapy does not help urinary symptoms. However, for most women, anecdotally hormone therapy may improve some of the urinary symptoms. And this includes systemic or oral hormones. If you have someone who felt that they did not want to oral hormones and the risks associated with oral hormones we can sometimes give local hormones where almost nothing is absorbed into the blood stream. These can be given in the form of creams, suppositories and rings and this can help with some of the vaginal dryness as well.

If someone feels that hormones are not for them even in the short term then there are some prescriptions that can be available as an alternative to hormones that treat menopausal symptoms, specifically hot flashes. There are a number of studies that have looked at low doses of some of the antidepressants in about 1/10 or 1/20 of the dose for depression may modify hot flashes. There are 5 or 6 published trials that have looked at the neuropathic pain reliever Gabapentin that has shown to modify hot flashes. And there are a couple of published trials that show that antihypertensive

Clonidine may help with hot flashes. The one thing those all drugs in common are that they cross the blood brain barrier. We actually don't know what causes a hot flash but we think there is some temperature regulation zone in the brain and probably any drug that works centrally in the brain may have some affect with hot flashes. So there are definitely alternatives for people who feel hormone therpay is not the way for me. They can try some of these prescriptions as alternatives and there are certainly vitamins and herbal options including acupuncturist and potentially doing Chinese herbs. There are a number of herbal options like Black Cohosh that have been studied and vitamin E that may have a mild benefit. So there are lots of complementary and alternative options out there as well. ***I try to talk to my patients before they have the surgery so they know what to expect and what options exist and what seems like it might be a good choice for them so they are not recovering from surgery and having to make these decisions.***

Question 4

We have also heard from some patients who believe that some types of hormone therapies are better than others;
the so-called "bio identical" hormones versus the synthetic, manufactured hormones. Is there any scientific evidence that shows one type of female hormone is better than another?

I think that many people choose or want bioidentical hormones because they thought that because its natural it must be safe. I don't think there is good data to show that it is safer. If people want to use bioidenticals because that's suits them better that is perfectly fine. But in many ways you can argue that we know more about the synthetic forms of hormones vs bioindentical hormones. The Woman's Health Initiative studied the most commonly described synthetic form called Prempro and so the data that we know regarding hormone therapy is regarding the synthetic formulations. That being said, all of the large guiding organizations, American College of OBGYN and North American Menopause Society, have all come out with position statements regarding bioidenticals saying that, "Until we have good randomized control trial data showing that they are safer, people need to presume that hormone therapy is hormone therapy and the risks are similar." So when I talk to my patients about bioidenticals I will tell them I want to work with them and whatever feels best for them. I have no problems if a person wants to use bioidenticals. We know less about it. They should not be using it because they feel it is safer. ***There is no good data to say bioidentical hormones are safer****. It can be a little more difficult for patients who have not had hysterectomy (the removal of the uterus) too. In the patients with HBOC who have only had their ovaries and fallopian tubes removed if they are taking hormone therapy they need progesterone to protect them from uterine cancer. With bioidentical hormones its hard to know how much progestin they are getting to protect the uterus. With that being said* ***I still work with my patients to find whatever formulation works best for them.***

Question 5

Women with Lynch syndrome and HBOC listening to us today might wonder, “what is the best way to find a gynecological surgeon who has experience in doing risk reducing surgeries for women with this syndrome?”. Do you have any advice for them?

One of the most important things they need to find out if is if their surgeon will be working with the pathologist will cut the specimen in appropriate risk reducing fashion*. I think that is what is crucial. Patients come from far away to UCSF because they were told their pathologist at the local community hospital would not preform this specific protocol. Women need to make sure the pathologist that their surgeon works with is well aware of the type of protocol that needs to be done for cutting in the specimen for patients with LS and HBOC. I think that is really crucial.* ***Patients should talk to their GYN surgeon or GYN Oncologists to see if they do the risk reducing procedures****. The truth is the surgical procedure itself is similar to the surgeries of low risk patients. Pelvic washings are obtained and pedicels are taken a little bit higher up but from a technical stand point that’s not so different is the same but its making sure the surgeon has done with RRSO procedures and that they know their pathologist is going to do this risk reducing protocol with the specimen.*

Dr. Goldman, we thank you for sharing your wisdom with our Kintalk listeners today. And to our listeners, thanks for tuning in! Have questions? Feel free to post on the Kintalk Chat Feed or email us at info@kintalk.org.