Hello. My name is Tilu Ninan. I am a nurse practitioner at the Cancer Prevention Center at The University of Texas MD Anderson Cancer Center. I’m going to be talking to you about Etiology of Breast Cancer today.

The objectives of this lecture is that upon completion of this lecture, the participants will be able to: understand the etiology of breast cancer; and list the risk factors for breast cancer; and understand the hormonal factors that increase the risk for breast cancer.

We’ll talk about breast cancer facts. Breast cancer is the most common cancer in women in the United States except for skin cancer. It is also the second leading cause of cancer death in women. The first leading cause of cancer death in women is the lung cancer. According to American Cancer Society there are 2.5 million breast cancer survivors in the United States.

Risk Factors for Breast Cancer: We’re going to go through this slide just listing the risk factors and then I’ll talk about each one of them in detail in the coming slides. So, gender, age, hormonal factors, lifestyle factors, family history, personal history of malignancy --- malignancies, therapeutic radiation to the chest, proliferative breast disease, increased mammographic density, and increased bone mineral density. All of these are risk factors for breast cancer.

Gender: Being female is the most common risk factor for breast cancer. Male breast cancers are only one percent of all breast cancers. And this may be because females have more breast cells and their breast cells are exposed to the female hormones, estrogen and progesterone.

Age: Increasing age is the most important risk factor for breast cancer. Most females with breast cancer have no other risk factors other than age.

Let’s look at the hormonal factors. Long menstrual history: that would include a woman starting her menarche at an early age and going through menopause at a late age. Not having children or having children after the age of 30 also increases the risk for breast cancer. Having many pregnancies or having children at a young age is thought to reduce the risk. And this may be because it reduces the total number of menstrual periods that [a] woman has over her lifetime. Recent use of oral contraceptives also increases risk for breast cancer. But this risk is thought to go back to normal once the oral contraceptive is stopped. Use of combination hormone therapy after menopause is also a risk factor for breast cancer.

The women’s health initiative looked at estrogen-progesterone combination versus placebo on the breast cancer incidence and mortality in postmenopausal women. The estrogen-progesterone combination was given to women with a uterus and this study showed that there was an increased incidence of invasive breast cancer in the --- in the group that was given the hormonal medication. Although these breast cancers were similar in histology and grade of breast cancer compared to the placebo group. But the
breast cancers were more commonly node-positive in the hormonal group and there was also more breast cancer-related deaths in the hormonal group compared to the placebo group.

The study also looked at the effects of estrogen alone, where it says “placebo” on breast cancer and mammographic screening in postmenopausal women. These women were women with a history of hysterectomy. There was no increased incidence of breast cancer in the hormonal group in this --- in this group. And there was also increased incidence of mammogram requiring a short-term follow-up.

Lifestyle Factors: Obesity and being overweight, especially after menopause, increases the risk for breast cancer. Weight gained as an adult is also associated with increased risk. After menopause estrogen is produced by our fat cells in the body. So if a woman is obese they may have more fat cells producing more estrogen, so --- so thereby having higher levels of estrogen and the risk may be from that. Sedentary lifestyle: Physical activity reduces the risk for breast cancer. American Cancer Society recommends 45 to 60 minutes of intentional activity, five or more days a week. Alcohol: Risk associated with alcohol increases with the amount of alcohol consumed. If a woman is drinking about two to five drinks of alcohol per day, they are thought to have about one and a half times the risk than a woman who does not consume any alcohol at all. American Cancer Society recommends no more than one alcoholic drink per day for a woman.

Family History: 70% of all breast cancers are sporadic, meaning that there is no association with family history. 15 - 20% are familial. Only 5 – 10% are thought to be hereditary.

Let’s look at the her --- hereditary syndromes associated with breast cancer. Mu --- in the heri --- hereditary syndromes, there will be multiple generations affected by the same or related types of breast cancer. For example, there may be multiple relatives with breast cancer or ovarian cancer or breast and ovarian together. In this group, there wi --- the age of diagnosis will be much younger than the average population. There will be --- there may be [the] same individual with multiple primary cancers as well.

Hereditary Breast and Ovarian Syndrome or HBOC: This is a syndrome with a mutation in the BRCA1 or BRCA2 gene, and the individuals may have a 40 to 85% of estimated lifetime risk for breast cancer. They are also at increased risk for ovarian cancer. And this is --- the syndrome is most commonly seen in the United States in the Ashkenazi Jewish --- women of Ashkenazi Jewish descent. Cowden’s syndrome: This is a syndrome with a mutation in the PTEN gene. And this increases the risk for both benign and malignant breast tumors. Li-Fraumeni syndrome: This is a syndrome with a mutation in the p53 gene or in the CHEK2 gene. With the Li-Fraumeni syndrome there is increased risk for other cancers as well, like leukemia, brain tumors, and sarcomas.

Ataxia Telangiectasia: In this syndrome, the mutation is in the ATM gene and they also have an increased risk for breast cancer. Peutz-Jeghers syndrome: The --- This is a
mutation in the STK11 gene. And these individuals may develop pigmented spots on their lips and in their mouth and polyps in the urinary tract and GI tracts. And they also have increased risk for many cancers including breast cancer. The last one is hereditary diffuse gastric cancer or HDGC: In this, there is a mutation in the CDH1 gene. And they may develop a rare type of stomach cancer at an early age. And they're also at increased risk for invasive lobular breast cancer.

Familial Breast Cancers: In this group of people there would be --- the family history of cancer is greater than what would be expected to be seen by chance. But age of diagnosis of cancer --- is --- is similar to the average population. And there is no clear pattern of inheritance.

Personal history of breast cancer increases the risk for second primary breast cancers.

Therapeutic Radiation to the Chest: Women who received radiation to the chest as a child or a young adult have an increased risk for breast cancer. The risk of breast cancer depends on the dose of the radiation received and the age at which the radiation exposure occurred. This --- this is considered --- they are considered at increased risk if their radiation was from the age of 10 to 30. Breast cancer develops many years after the radiation exposure.

Proliferative breast dis --- Breast Disease: Atypical ductal hyperplasia and atypical lobular hyperplasia are considered risk factors for breast cancer. And they increase a woman’s risk by 4 to 5 times for breast cancer. Lobular carcinoma in situ increases the risk for breast cancer by 8 to 10 percent --- 8 to 10 times.

There are two types of lobular carcinoma in situ – classic and pleomorphic. Classic lobular carcinoma in situ increases the risk for breast cancer. And it is thought as a risk factor and they have increased risk in bilateral breasts for breast cancer. Pleomorphic lobular carcinoma in situ is treated just like ductal carcinoma in situ. And these women would be treated with excision and radiation.

Mammographic Density: Increased mammographic density increases a woman’s risk for breast cancer. Women with dense breast tissue in 75% or more of the breast have 4 to 6 times’ greater risk for breast cancer compared to women with little or no dense breast tissue in the breast. Mammographic density also makes detection of breast cancer difficult and increases the interval development of breast cancer in between two screening mammograms.

Bone Mineral Density: High bone mineral density is thought to be a risk factor for breast cancer. And women with high bone mineral density have an increased risk for breast cancer, whereas women with low bone mineral density is thought to have an incidence lower incidence of breast cancer. There has been several studies looking at this and showing a range from 2.5 to 4.5 times’ increased risk for breast cancer in women with high bone mineral density.
Summary: Breast cancer development may be a multifactorial interaction between different risk factors such as genetic factors, personal, and family history, hormonal factors, and lifestyle factors. Thank you for your time, and we welcome your feedback.