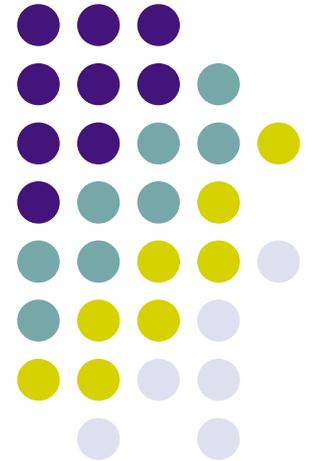


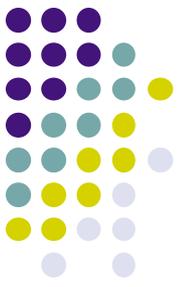


# Menopause and Cancer risk; What to do overcome the risks?

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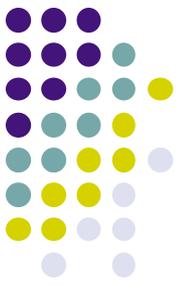
Fatih DURMUŐOĐLU, M.D





# Menopause and Cancer

- How does menopause affect a woman's cancer risk?
  - Menopause does not cause cancer. But risk of developing cancer as age gets older.
  - After age 55 increases a woman's risk of **breast** and **endometrial** cancer
  - Late menopause also may increase risk of ovarian cancer possibly because of more ovulations have had happened.



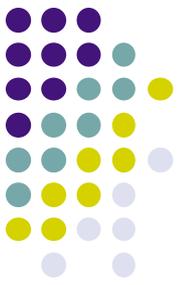
# Governing Principles-I-

- Consideration of MHT should be part of an overall strategy including lifestyle recommendations regarding diet, exercise, smoking cessation and safe levels of alcohol consumption for maintaining the health of peri and postmenopausal women.
- MHT must be individualized and tailored according to symptoms and the need for prevention, as well as personal and family history, results of relevant investigations, the woman's preferences and expectations



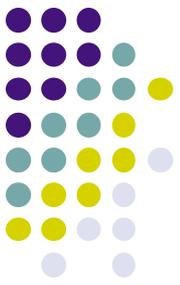
## Governing Principles-II-

- In women with premature ovarian insufficiency, systemic MHT is recommended until the average age of the natural menopause.



# Breast Cancer

- The possible increased risk of breast cancer associated with MHT is small (less than 0.1% per annum, or an incidence of  $< 1.0$  per 1000 women year of use)
- Lower than the increased risks associated with common lifestyle factors such as reduced physical activity, obesity and alcohol consumption.



## Breast Cancer-2-

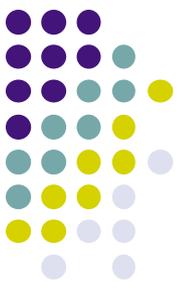
- Randomized controlled data from the WHI study demonstrated no increased risk in first-time users of MHT during the 5–7 years since initiation of treatment
- The WHI study also demonstrated that 7.1 years of treatment with unopposed CEE decreased the risk of breast cancer diagnosis and mortality in hysterectomized women.



# Breast Cancer-3-

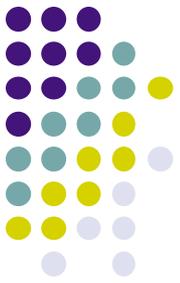
- The risk of breast cancer in women over 50 years associated with MHT is a complex issue.
- The increased risk of breast cancer is primarily associated with the addition of a progestogen .
- The risk of breast cancer attributable to MHT is small and the risk decreases after treatment is stopped.
- There is a lack of safety data supporting the use of MHT (estrogen therapy or estrogen–progestogen therapy) in breast cancer survivors.

# Recommendations for Clinical Care for Breast Cancer



- Routine screening for breast cancer is indicated for midlife women.
- Genetic testing for BRCA mutations should be recommended for women at high risk for breast cancer on the basis of family history. (Level I)
- Weight gain is associated with an increased risk of breast cancer recurrence, and a low-fat diet is associated with improved survival
- The dose and duration of MHT should be consistent with treatment goals, such as symptom relief, and should be individualized
- Women at increased risk for breast cancer should be counseled regarding the potential benefits and risks of tamoxifen and raloxifene for breast cancer risk reduction. (Level I)

# Endometrial Cancer



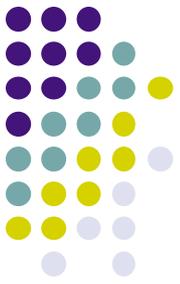
- Women with a uterus should have progestogen supplementation to counteract the unopposed estrogen effect .
- Continuous combined estrogen–progestogen regimens are associated with a lower incidence of endometrial hyperplasia and cancer.
- SERMs other than tamoxifen do not stimulate the endometrium and do not increase the incidence of endometrial spotting or bleeding compared to women not using any hormonal therapy

# Recommendations for Clinical Care for Endometrium Cancer



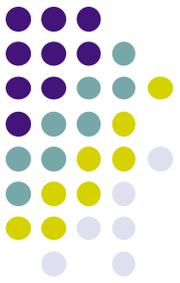
- In postmenopausal women, any bleeding should be promptly and thoroughly evaluated. A thickened endometrium must be biopsied.
- Transvaginal ultrasonography, hysteroscopy, and sonohysterography are useful to identify focal abnormalities. (Level I)
- Postmenopausal woman with an intact uterus using systemic estrogen-only therapy are at risk of developing endometrial hyperplasia and cancer.
- Treatment with adequate progestogen reduces the risk of endometrial cancer in women using ET.

# Recommendations for Clinical Care for Endometrium Cancer-II



- Women using estrogen combined with bazedoxifene do not require a progestogen.(Level I)
- Atypical endometrial hyperplasia should be treated with hysterectomy and bilateral salpingo-oophorectomy.
- Conservative management with progestogen therapy and close follow-up may be an option for reliable younger women seeking to preserve fertility or for poor surgical candidates. (Level I)

# CERVICAL CANCER



- When detected at an early stage, the 5-year survival rate for women with cervical cancer is 92%.
- In women aged older than 65 years with cervical cancer, 42% had never been screened.
- Risk factors for cervical cancer include human papillomavirus (HPV) infection, sexual intercourse at an early age, multiple sexual partners, smoking, and immunocompromised states, including HIV infection.
- Almost all cervical cancers are related to infection by the sexually transmitted, high-risk (oncogenic) types of HPV. Two vaccines are available to prevent infection with the HPV types that cause most cervical cancers.



# Cervical cancer & MHT

- Long-term cohort studies have shown no increased risk of cervical cancer with MHT use.
- In the WHI RCT, there was no increase in risk of cervical cancer with MHT use.

# Recommendations

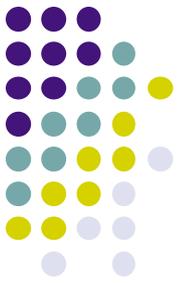
## Clinical Care



- Vaccination for HPV is recommended for girls aged 13 to 26 years and for boys aged 13 to 21 years. Women immunized against HPV should follow routine cervical cancer screening guidelines. (Level I)
- Cervical cancer screening should start at age 21 and is recommended every 3 years for women aged 21 to 29 years.
- For women aged 30 to 65 years, co-testing with cervical cytology and HPV testing every 5 years is advised, although screening with cytology alone every 3 years is acceptable. (Level I)
- Women who have had a hysterectomy for benign disease with removal of the cervix should no longer be screened for cervical cancer, unless there is a history of cervical dysplasia (cervical intraepithelial neoplasia [CIN] 2 or higher). (Level I)

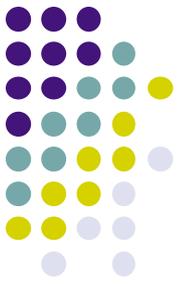
# Recommendations

## Clinical Care-II-



- Women with a history of cervical cancer, HIV infection, immunocompromised state, or diethylstilbestrol exposure in utero require increased screening. (Level I)
- Screening should be discontinued after age 65 years in women with adequate negative prior screening and no history of CIN2 or higher in the past 20 years.(Level I)
- Abnormal uterine bleeding or a cervical abnormality identified during a pelvic examination may be a sign of cervical cancer and should be promptly evaluated.(Level I)

# Ovarian Cancer



- Ovarian cancer is the tenth most common cancer in US women but the fifth most cause of cancer death.
- Risk factors for epithelial ovarian cancer include genetic predisposition (BRCA mutations, Lynch syndrome), older age, nulligravidity, endometriosis, early menarche, and late menopause.
- Protective factors include oral contraceptives and tubal sterilization, each of which decrease risk by 50%.
- In summary, long-term, estrogen-only therapy may be associated with a small attributable risk of ovarian cancer of 0.7 per 1000 women per 5 years of use,
- A significantly smaller, or no, increased risk is seen with combined estrogen plus progestogen therapy.

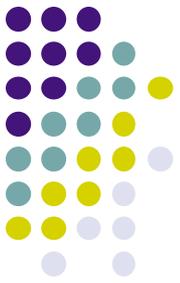
# Ovarian Cancer-II



- In normal-risk women, ovarian cancer screening with cancer antigen-125 or ultrasound is not effective and is not recommended.
- Signs of ovarian cancer are subtle and include early satiety, abdominal bloating, abdominal pain, pelvic pain, and urinary frequency occurring daily for weeks.
- Women with suspected ovarian cancer should undergo definitive surgical procedures with gynecologic oncologists as outcomes are superior.

# Recommendations

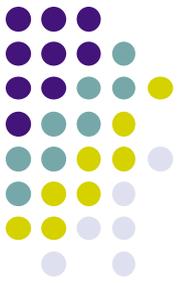
## Clinical Care



- Women should be informed of the symptoms of ovarian cancer and advised to inform their healthcare providers if daily symptoms persist. (Level III)
- Family history of breast, ovarian, colon, and pancreatic cancers suggestive of increased hereditary risk should prompt referral for genetic counseling. (Level II)

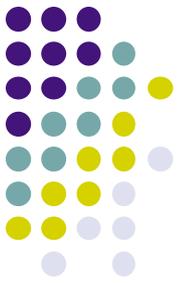
# Recommendations

## Clinical Care-II-



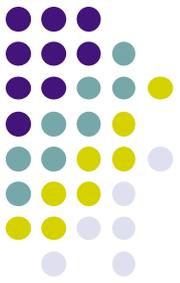
- In high-risk women, screening may be offered
- Risk-reducing surgery (bilateral salpingo oophorectomy or possibly bilateral salpingectomy) or medications (eg, oral contraceptives) should be considered to decrease ovarian cancer risk. (Level I)

# Lung Cancer



- Lung cancer takes many years to develop, with an average age of diagnosis of 71 years.
- It is the leading cause of cancer death among in many races and the second most common cause of cancer death among Hispanic women.
- Most lung cancers are believed to be caused by cigarette smoking.
- Other risk factors include exposure to asbestos, radon, second-hand smoke, and other environmental agents.
- Among nonsmokers, women are more likely than men to develop lung cancer. Smoking cessation reduces lung cancer incidence.

# Lung cancer-II-



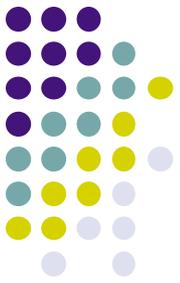
- Studies on the effect of hormone use on lung cancer incidence and survival are limited, with inconsistent results.
- Large observational studies have shown protective effects of oral contraceptives and hormone therapy on lung cancer risk.
- However, in the **Women's Health Initiative, use of estrogen-progestogen therapy was associated with an increased risk of death from lung cancer, with an additional 9 cases per 1,000 women after 5.6 years of use plus 2.4 years of additional follow-up.**
- An increased risk of lung cancer was not seen with the use of estrogen alone.
- Additional research is needed on the association between hormones and lung cancer

# Recommendation Clinical Care



- Women should be asked about smoking at all comprehensive visits and smoking cessation advised. (Level I)
- Women using HT, particularly those who smoke, should be informed that EPT was associated with a small increased risk of death from lung cancer in the WHI, with no increased risk associated with the use of estrogen alone. (Level II)
- The US Preventive Services Task Force recommends annual screening for lung cancer with low-dose computed tomography in women aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.
- Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability to have curative lung surgery. (Level I)

# Colorectal cancer



- Colorectal cancer is a leading cause of death for women.
- Risk factors for colorectal cancer include age, smoking, presence of colorectal polyps, inflammatory bowel disease (eg, ulcerative colitis or Crohn disease), family history of colorectal cancer, personal history of breast cancer, and certain genetic diseases (eg, Lynch syndrome/ hereditary nonpolyposis colorectal cancer or familial adenomatous polyposis).
- Colon cancer has been linked to a high-fat, low-fiber diet and to a high intake of red or processed meat.



# Colorectal cancer-II-

- ❖ Screening for colorectal cancer has been shown to detect asymptomatic, early stage disease and improve mortality.
- ❖ Colonoscopy is the most accurate diagnostic test for colorectal cancer and allows for concurrent removal of polyps and biopsy of suspicious lesions.
- ❖ General screening guidelines include an initial colonoscopy at age 50, with repeat testing every 10 years until age 75. If polyps or other abnormalities are identified during screening, more frequent surveillance is recommended.
- ❖ Other methods to screen for colorectal cancer include annual high-sensitivity fecal occult blood testing, sigmoidoscopy, computed tomographic colonography, and double-contrast barium enema.

# Recommendation

## Clinical care



- The majority of observational studies show a reduced risk of colorectal cancer amongst users of oral MHT.
- Three meta-analyses have reported a reduced risk of colorectal cancer with MHT use with benefit persisting for 4 years after cessation of therapy. A typical effect was relative risk (RR) 0.80 (95% confidence interval (CI) 0.74–0.86) for ever-users and 0.66 (95% CI 0.59–0.74) for current users.
- The LIFT study demonstrated that tibolone was associated with a reduced risk of colon cancer in women aged 60–79 years.
- Results from the WHI randomized trial of estrogen-only therapy showed no effect of estrogen only therapy on risk of colorectal cancer.

# Recommendation

## Clinical care-II-



- In the WHI RCT of estrogen–progestogen therapy, colorectal cancer risk was reduced (RR 0.56; 95% CI 0.38–0.81).
- This effect was predominantly for local disease and, where spread had occurred, there was more node involvement and a more advanced stage at diagnosis amongst users of MHT.
- **MHT should not be used solely for the prevention of colorectal cancer.**· There are no data for an effect of non-oral MHT on risk of colorectal cancer

# Healthy Life Style



- ✓ Obesity (body mass index  $> 30 \text{ kg/m}^2$ ) affects over 20% of the population in many parts of the World .
- ✓ It can be associated with insulin resistance and thus increases not only a woman's risk of cardiovascular disease and diabetes, but also increases the risk for breast, colon and endometrial cancers and is associated with higher rates of depression and sexual dysfunction.
- ✓ Weight loss of only 5–10% is sufficient to improve many of the abnormalities associated with the insulin resistance syndrome.
- ✓ The basic components of a healthy diet are: several servings/day of fruits and vegetables, whole grain fibers, fish twice per week, and low total fat (but the use of olive oil is recommended).
- ✓ Consumption of salt should be limited and the daily amount of alcohol should not exceed 30 g for men and 20 g for women.

# Healthy Life Style-2-



- ✓ Smoking should be prohibited.
- ✓ Lifestyle modifications include socializing and being physically/mentally active.
- ✓ The public health awareness and multidisciplinary approach, starting from schools through to work places,.
- ✓ A new paradigm in doctor–patient relations is required, where the doctor becomes more of an advisor and the patient has to take the responsibility for his/her own health.

# Key Messages



## EXERCISE IN THE MENOPAUSE

- ❖ Regular exercise reduces cardiovascular and total mortality.
- ❖ Better metabolic profile, balance, muscle strength, cognition and quality of life are observed in physically active persons.
- ❖ Heart events, stroke, fractures and breast and colon cancers are significantly less frequent.
- ❖ The benefits of exercise far outweigh possible adverse consequences: the more, the better, but too much may cause harm.
- ❖ Optimal exercise prescription is at least 150 minutes of moderate-intensity exercise per week.
- ❖ Two additional weekly sessions of resistance exercise may provide further benefit.

A sunset over a body of water with a large, faint Turkish flag watermark in the foreground. The sky is filled with orange and red clouds, and the water reflects the colors. The Turkish flag, featuring a white crescent and star on a red field, is superimposed on the water in the lower half of the image.

*Thanks for your attention and patience*  
*Healthy and peaceful life for you all*