ABOUT US
The Angeles Clinic and Research Institute was established by a group of physicians who came from academic backgrounds and sought to establish an environment where world-class patient care was the top priority. The Clinic's physicians include widely recognized oncologists and leaders in cancer medicine who, together with expert radiology services, radiation oncology, specialized oncologic nurses, and a dedicated support staff, have created a state-of-the-art center for oncology in the Los Angeles area. In addition to superb clinical care, our physicians are known for their world-class clinical research. The Institute has earned an international reputation for developing new cancer therapies, providing the best in traditional and experimental treatments, and expertly guiding and training the next generation of clinicians and researchers.

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PREVENTING CHEMOTHERAPY INDUCED HAIR LOSS—A Patient’s Perspective

By Ms. Roxana Lissa

I have always had the same curly hair and pretty much the same haircut. I think I cut it short only once. I don’t particularly love my curls. In fact, I always wanted to have straight hair, but I got used to them. Some friends think that my hair is part of my personality - and I guess they may be right about that.

When I was diagnosed with breast cancer in November 2012, the first question I asked my surgeon was if I was going to lose my hair. She held my hand and said with a smile, “Yes, but you will have your life.” The reality was that given the type of cancer I had (triple positive) and that it had spread to the lymph nodes, I needed to start chemotherapy right away and I would be bald in a matter of days. A dear friend of mine who is also a breast cancer survivor made an appointment for me to try on wigs. Our little 3 year old daughters were with us. While I was excited to try different styles of wigs with bangs and straight hair, I could see my daughter Sienna’s little face full of worry when she asked me, “Mamma, why are you changing your hair?”

In my battle against cancer, the one thing I most needed to hold on to was for my two kids and my husband to see me as normal as possible. Little did I know at the time how hard this battle was and how many tears they would see. I also wanted to continue to work. As a public relations professional and owner of a fitness/spa studio, appearance is a big deal and my hair was a big part of it. My husband Franco encouraged me to shave my hair and he wanted to do it with me at the same time. A wig seemed the only available solution, until something amazing happened.

After my diagnosis, I met with Dr. Cathie Chung at the Angeles Clinic and Research Institute. She is now my oncologist. As we were discussing chemo and the side effects she said with sadness in her eyes, “And you will lose your beautiful hair.” A few minutes after she noticed my hair, she handed me a brochure about the “Penguin Cold Caps” and told me there might be a way to reduce my hair loss.
I learned that the Penguin Cold Caps (www.penguincoldcaps.com) is a technique that reduces chemotherapy-induced hair loss by cooling the hair capillaries and reducing the metabolic rate of the hair follicles to a hibernated state, reducing the absorption of chemo drugs in the hair bulbs of the scalp. The way this works is that while you are getting chemo, you wear the very cold “cold caps”, changing it every 30 minutes. You continue doing this for 4-5 hours after chemo that day only. This sounded difficult and complicated compared to shaving my hair, but I knew it was perfect for me and I was willing to take the risk. I researched and saw articles and news pieces on many women who tried the cold caps and didn’t lose all their hair; and while there are no guarantees, I was ready.

While my journey with the cold caps wasn’t easy, given the special care your hair needs during and after chemo, the shedding that is part of the process and the big dose of patience that is required to go through the process during the chemo treatments, I am so happy I did it. After 8 rounds of chemo with some of the most powerful chemo drugs that cause immediate hair loss, I kept about 50 percent of my hair. Fast forward two months after my last chemo, my hair is now growing stronger and is fuller. I might need some extensions or another cut but I was able to maintain the long length, and I never became bald or wore a wig. And what’s more important, my kids got to see their mom “almost normal” and in the end, that’s what mattered to me the most.

PREVENTING CHEMOTHERAPY INDUCED HAIR LOSS—A Doctor’s Perspective

By Cathie T. Chung MD, PhD
Director of the Breast Cancer Program
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Chemotherapy induced hair loss (alopecia) is an unintended side effect from chemotherapy, which can be the most traumatic aspect of treatment for many patients with breast cancer. As opposed to other bystander effects of chemotherapy, such as bone marrow suppression (lowering of the blood counts), alopecia can be distressing to patients because for some, it is a visible reminder of illness which can impact perceptions of self-identity, sexuality and social interactions. For patients with cancer, hair loss goes beyond vanity because it can induce anxiety and fearfulness at a time when patients are already faced with the challenges of being diagnosed with cancer. As with any other physical side effect from chemotherapy, the development of alopecia can negatively impact quality of life and impair the psychosocial wellbeing of patients.

The likelihood of developing chemotherapy induced alopecia (CIA) is influenced by several factors, including the type of chemotherapy given and treatment dosage. Generally, hair loss begins within 2-4 weeks from the start of chemotherapy. For the most part, it is reversible. The hair will usually start to re-grow 3-6 months after the end of treatment. Little is known about the molecular mechanisms of CIA in humans but, in general, it is thought that chemotherapy induces apoptosis (programmed cell death) of hair follicles. As such, within 2-4 weeks of exposure to chemotherapy, hair shafts break off almost as soon as they emerge from follicles. Additional insult from chemotherapy on mitotic (cell replication) and metabolic processes in actively growing hair follicles leads to thinning of hair shafts, rendering them fragile and susceptible to fracture. Ultimately, continued exposure of hair follicles to chemotherapy induces regression of the follicles and transition to a resting state.

To date, there are no FDA approved therapies for the prevention of CIA because of the scarcity of research in this area. In fact, there are few randomized clinical trials or rigorous scientific studies on prevention of CIA; possibly, because historically, there was concern that strategies used to prevent CIA might negate the therapeutic effects of chemotherapy. In addition, research on CIA has been difficult to do for several reasons. First, rodent models of CIA have not been particularly applicable to humans and studies directly in humans (for example the performance of scalp biopsies during exposure to chemotherapy) face ethical concerns. Second, while subjective reporting scales exist to measure the terminal event of severity of hair loss, there have been few quantitative metrics developed to study early hair injury, as a way to examine the pathophysiology of CIA and identify potential strategies to counteract it. In this regard, newer technologies have been developed, including the use of cross-section trichometry to assess hair mass index as an indicator of chemotherapy-induced injury. Finally, metrics to assess the success of interventions to prevent CIA have not been uniform across studies, although in general, the parameter of need of use of a wig or head covering has been considered an acceptable clinical endpoint.
While there are no FDA approved therapies for the prevention of CIA, the most widely used strategy to prevent CIA has incorporated methods of scalp cooling or hypothermia. This approach has been in existence for over thirty years and stems from the hypothesis that cooling the scalp diminishes the delivery of chemotherapy to hair follicles by constricting the blood supply to the scalp. The first and only study which examined the effects of cooling on CIA, in relation to degree of cooling of the scalp, was published in 1982. This study, which only involved 24 patients, demonstrated that hair could be preserved if the scalp could be cooled to below 22°C and maintained at this temperature for 20 minutes before injection of chemotherapy. Cold temperature may do more than affect chemotherapy delivery; it may also reduce the metabolism of hair follicles, rendering them less susceptible to injury from chemotherapy.

In the past, the success rates of scalp cooling to prevent CIA have been variable, leading to a decline in use of this methodology. In addition, fueled by initial concerns that scalp cooling may be associated with an increased risk of developing scalp metastases, this strategy was largely abandoned. In retrospect, however, the lack of uniform efficacy of scalp cooling to prevent CIA probably resulted from technical limitations associated with lack of precision of cooling and reproducibility. For example, earlier methods of scalp cooling were quite rudimentary, consisting of the application of bags filled with crushed ice, to later use of frozen cryogel packs and packs with an endothermic cooling reaction. In addition, in many of the earlier small studies evaluating scalp cooling to prevent CIA, there was no standardization of post chemotherapy infusion cooling times, which is now known to be critical for achieving high success rates for hair preservation. With the advent of more recent and effective methods for scalp cooling, such as with the development of cold caps and continuous cooling machines, there is now resurgence in the use of scalp cooling to prevent CIA. Additionally, this resurgence is supported by reviews of all the compiled data to date which do not support an increased risk of scalp metastases or brain metastasis with scalp cooling in patients with breast cancer. For example, a retrospective review of 553 patients with early stage breast cancer who received chemotherapy and underwent scalp cooling and 87 patients who did not and who were followed for 5.8 years, showed that the incidence of scalp metastases was 1.1% among the group who underwent scalp cooling and 1.2% in the group that did not. Moreover, the development of scalp metastases in this study was never the first single site of recurrrence but was diagnosed either concurrently with other sites of distant metastases or after the development of other known sites of distant metastases.

With advancing improvements in technology, clinical trials will be needed to determine the most efficacious method of scalp cooling to prevent CIA. In general, scalp cooling is well tolerated, with the most common side effects being headache and discomfort from coldness. While the option of hair preservation is an individualized decision, particular to each breast cancer patient requiring chemotherapy, it is hoped that such options may reduce the fear of chemotherapy for some patients and enhance their quality of life during treatment.

References:
Clinical Trials Cont’d …

- treatment of subjects with unrespectable pleural or peritoneal malignant mesothelioma
- Eligible patients:
  - Patients with unrespectable pleural or peritoneal malignant mesothelioma who have received no more than 2 prior systemic chemotherapy
- Newly opened: Second line Alk inhibitor (LDK378) in patients with ALK-positive advanced NSCLC
  - Patients should have been treated with either crizotinib or a platinum doublet previously
  - Patients to be randomized to LDK378 versus chemotherapy. Crossover allowed to LDK378 if progression on chemotherapy

Solid Tumors:
- Genentech Protocol PCD4989g – anti PD-L1 antibody for solid tumors
  - Currently evaluating:
    - Triple negative breast cancer
    - Bladder cancer
    - HPV negative head and neck cancer
    - Gastric cancer
    - Serial biopsy cohort with cutaneous or subcutaneous disease amenable to a biopsy
- Amgen Protocol: AMG 337 - A Phase 1, First-In-Human study Evaluating the Safety, Tolerability, and Pharmacokinetics of AMG 337 in Adult Subjects with Advanced Solid Tumors
  - An oral c-met inhibitor open to all solid tumors

Breast Cancer:
- Protocol M12-895-A Randomized, Phase 2 Study of the Efficacy and Tolerability of Veliparib in Combination with Carboplatin and Paclitaxel versus Placebo plus Carboplatin and Paclitaxel in Subjects with BRCA1 or BRCA2 Mutation and Metastatic Breast Cancer
  - This is a three arm randomized clinical trial for patients with metastatic breast cancer and a documented deleterious BRCA 1 or BRCA2 germline mutation. The trial consists of three treatment arms:
    1. Chemotherapy alone, with carboplatin and paclitaxel
    2. Carboplatin and paclitaxel with Veliparib
    3. Temozolomide (a single chemotherapy agent) with Veliparib
  - Veliparib is an experimental therapy known as a PARP inhibitor. This drug inhibits the activity of an enzyme known as PARP, whose function is to repair damaged DNA for example, by chemotherapy. As such, in the presence of Veliparib, breast cancer cells which undergo DNA damage by chemotherapy are unable to survive because they lack a mechanism to properly repair their cellular DNA to permit continued cell growth. This lack of ability to survive DNA damage is particularly enhanced when cells are also BRCA deficient because of a deleterious mutation. This is an exciting new clinical trial that is specifically targeted against BRCA-associated metastatic breast cancer and takes advantage of the inherent cellular repair mechanisms by which these breast cancer cells are normally able to proliferate.

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