August 2008

SGOP News

The Official Newsletter of the Society of Gynecologic Oncologists of the Philippines (Foundation), Inc.

Inside

From the Annual Convention Organizing Committee

All set for the 2008 Joint SGOP-PSCPC-PSSTD Annual Convention

Final arrangements are in place for the August 1-2, 2008 Joint Annual Convention of the Society of Gynecologic Oncologists of the Philippines (Foundation), Inc. (SGOP), the Philippine Society for Cervical Pathology and Colposcopy (PSCPC), and the Philippine Society for the Study of Trophoblastic Disease (PSSTD). The entire event will be held at the Hotel Intercontinental in Makati City. A Welcome Reception at the Bahia Lounge on the evening of July 31 will start the affair. The Opening Ceremonies in the morning of August 1, 2008 will commence with a keynote address to be delivered by Professor Genara Manuel-Limson, MD. Dr. Limson, a beloved mentor to many Gynecologic Oncologists in the country, is a past President of both the SGOP and PSCPC.

The topics to be covered during the two full days of scientific sessions were selected on the basis of their applicability to common clinical situations encountered by physicians who attend to the health needs of women who are at risk for, suspected to have, or diagnosed with neoplastic reproductive tract conditions. To unwind after each day of lectures, there would be social events that are guaranteed to be fabulously entertaining for all, as the less serious, fun-loving side of the members are revealed.

Commercial exhibits will be on display, courtesy of friends and associates from the pharmaceutical industry, health-equipment providers, and other medically-related enterprises. Despite the challenges of the times, they have expressed full support for the three Societies by joining this activity. The Organizing Committee gratefully acknowledges their participation and expresses its deepest gratitude to all sponsors.

Reminders

PSCPC Annual Business Meeting and Election of 2009-2010 Officers- August 1, 2008 4:00 p.m. (Grand Ballroom)

SGOP Annual Business Meeting- August 1, 2008 4:30 p.m. (Grand Ballroom)

PSSTD Annual Business Meeting- August 2, 2008 (Dasmariñas Room) after the 4:30 p.m. Closing Ceremonies

G GONZALES

EDITORIAL: Living the life of the dying

"Death be not proud, though some have called thee
Mighty and dreadful, for thou art not so . . . . " (Donne)

One time a junior resident asked me, "when you tag a disease *persistent progressive*, do we need to include the patient in the SI (Seriously Ill) List? Do we ask the relatives to sign a DNR request? Or do we send her home and let her do whatever she wishes to do?". Frequently asked questions, but how do we venture on the answers? Despite the progress that science boasts of, a big percentage of cancer patients still succumb to the disease, and most often than not, confronting these "end-of-life" issues has always been difficult - equally difficult for both the patient and the doctor. Today advancement in modern medicine have somewhat affected the way most medical professionals approach the problem. Clinicians (especially the younger ones) are sometimes distracted by unnecessary tests and futile treatments that unfortunately, leave the patient destitute. In an article entitled *Psychology and Death*, the author, H. Feifel, gave a meaningful reminder to the clinician. He said that one should "infuse compassion and benevolence to technology and competence. Life, he further added, is not just a matter of length but of depth and quality as well".

There is another problem that confronts the clinician – how to break the bad news! This has never been an easy job. Some articles showed that doctors are aware of this and in fact there is a demand among them for competence in communication. Regrettably, the way doctors impart information, together with honesty and authenticity has been shown to effectively bridge difficulties and allow the patient and her family to refocus on broader issues. (*M Barbato, Caring for the Dying: the Doctor as Healer*).

Losing the battle with cancer can evoke different emotions among patients – chiefly anger and grief, but surprisingly, in some, a sense of resolution and a "feeling of being in control" of the situation. To quote a cancer patient, 'I felt a sense of relief because now I can plan for a good death and make important decisions". The same situation, on the other hand, can likewise trigger depression and trauma among clinicians. Some doctors have owned up to a "feeling of failure", others, a feeling of dejection on being perceived to be "giving up" on the patient. Some have even admitted to a need to understand their own emotions and prejudices.

In the past two decades, no less than 30,000 articles have been written, all dealing with "quality of life" issues. Topics like comfort, dignity, and early recognition of "end-of-life" care choices are believed to heavily influence the quality of life an individual experiences during the dying process (*S Eues MD, Univ. of Phoenix*). Caring for the dying however need not stop on palliative management. Doctors can still do so much in terms of care for the dying patient. The patient's recognition of the doctor's compassion and the patient's perception of the doctor's empathy are small treasures that can give zest to a dying life. Quoting from an old article from JAMA (2003), it was written that patients can be comforted when doctors try to: (1) Relate beliefs about death to the meaning people attach to life; (2) Reflect upon the way in which death structures life; (3) Critically evaluate how encounters with death affect perspective upon life and (4) Assess the quality of dying. Perhaps, somehow, a "*quality* relationship" between the doctor and the patient may finally develop at the end of the road. In the end, the patient need not live her final days alone!

SGOP Hymn / Anthem CONTEST

The Society of Gynecologic Oncologists of the Philippines will be celebrating its 25th Anniversary in 2009.This will be highlighted by the FOUNDATION DAY celebration in April. In line with this affair, the Organizing Committee is launching a SGOP HYMN/ ANTHEM Contest. The committee is now accepting entries for the said contest.

Some rules and guidelines for the contest are as follows: the composition must be original and relevant; it can be written in English or Tagalog. The contest is open even to non-members, as long as the entries are coursed through an SGOP member. The lyrics and notes should be submitted, along with a CD, to the secretary of SGOP or directly thru Dr. Aris Dungo, Chair of the SGOP Foundation Day Committee. Deadline is on January 31, 2009. A big cash prize awaits the winner and the song will be one of the highlights of the SGOP 25th Foundation Day Celebration.

A DUNGO

Interesting Case and Research Paper Contests:

The SGOP Committee on Research chaired by Dr. Rafael Tomacruz is still accepting papers for the 7th Interesting Case and Research Paper Contests. Due to unforeseen circumstances the contest has been moved to September 17, 2008, at 1 o'clock PM at the Bayanihan Hall of the UNILAB in Mandaluyong City. Cash prizes await the winners.

Deadline for submission of entries is on July 24, 2008, at 5 o'clock PM. Papers may be submitted through the SGOP Office or through the Chair, Committee on Research. For inquiries, please get in touch with Miss Marivic Mendoza at the SGOP Office, tel no. 526-4787 or any member of the Committee on Research.

The President's Notes

Our newsletter is a good venue to inform our members of the activities of our society. I am very happy to inform the members of our society for the many developments that has happened since the last issue.

Our midyear convention last April 12, 2008 at Taal Vista Hotel was a great success. Dr. Christine Palma and her members deserve to be congratulated. The presentation on the proposed revisions of the treatment guidelines was well attended, with everyone actively participating in the discussion. The revised guidelines are expected to be made available to our members during our annual convention. Everyone enjoyed a lot during the fellowship night. I give thanks to our benevolent sponsor, GSK, for their continued support. They already agreed to support our Midyear convention next year.

I hope SGOP members have received the forms to be filled up for our Gynecologic Cancer Registry. I strongly encourage all our members and all our fellows-in-training to actively participate in this project. The data that we generate from the registry will be of great help to us and will also be of benefits to our patients. The formal launching of the Cervicare Program is held in abeyance in the meantime. However, its activities are being undertaken. We will update the membership for any developments on this project soon.

Our society was founded in 1984. We will then be celebrating our Silver Jubilee next year, 2009. I have formed a committee, chaired by Dr. Aris Dungo, to plan for our celebration of our 25th founding anniversary. I hope everyone will also actively participate in this celebration to give honor and recognition to the founders of our society.

Dr. Gil Gonzalez and the members of the Organizing Committee of our Annual Convention 2008 deserved to be congratulated for the very beautiful program and activities they have prepared for us. They really exerted all efforts to make our annual convention this year a very good venue for us to update our knowledge and at the same time enjoy the camaraderie of our friends and colleagues. For the 2nd year, we are conducting this convention with the Philippine Society of Cervical Pathology and Colposcopy (PSCPC) and the Philippine Society for the Study of Trophoblastic Disease (PSSTD). However, we are at a new venue, at the Intercontinental Hotel in Makati City. I enjoin every to participate and enjoy in this year's convention.

The SGOP Clinical Practice GUIDELINES Revisited

On April 12, 2008 , SGOP members very carefully went through each recommendation in the latest revision of the SGOP Clinical Practice Guidelines. for Gynecologic Oncology. The latest guidelines were revised under the direction of the Ad Hoc Committee for the 2008 CPG headed by Dr Efren Domingo. The members of this committee are listed in Table 1, along with other individuals who contributed to the development of the guidelines.

The guidelines were first reviewed and revised by each subcommittee based on the best available evidence taking into consideration local data and Philippine clinical practice setting. The draft for each part of the CPG were presented to the Committee Chair , Dr. Domingo, the Advisers of the project namely Dr. Genara M. Limson and Dr. Augusto Manalo and the rest of the committee members , the faculty of the UP-PGH Section of Gynecologic Oncology for comments and inputs all Fridays of February and March .

The final draft was then presented for final approval to the Officers, Board of Directors and General Membership of the SGOP. Affiliate members from other oncology specialties also attended and gave valuable inputs. The guidelines, which were previously distributed in booklet form to the SGO membership, are being reprinted for distribution to the the SGOP members.

In developing the SGOP clinical practice guidelines, no attempt was made to be all-inclusive or to cover all aspects of the discipline of gynecologic oncology. The outline chosen by the committee was followed for each organ site neoplasm and prepared in a comprehensive manner with appropriate references based on well designed trials.

The information in the 2008 SGOP clinical practice guidelines should not be viewed as a body of rigid rules. The guidelines are general and intended to be adapted to many different situations, taking into account the needs and resources particular to the locality, the institution, or the type of practice. Variations and innovations that improve the quality of patient care are to be encouraged rather than restricted. The purpose of these guidelines will be well served if they provide a firm basis on which local norms may be built. It is anticipated that these practice guidelines will be revised and updated frequently by the SGOP as progress is made in the field of gynecologic cancer.

Watch out for the final publication of the SGOP Clinical Practice Guidelines on cervical, endometrial, ovarian, fallopian tube, vulvar , vaginal cancer and uterine sarcomas.

J GERMAR

AD HOC COMMITTEE FOR THE SGOP 2008
CLINICAL PRACTICE GUIDELINES

CHAIR
Efren J. Domingo, MD, PhD

ADVISERS
Luciano S.J. Sotto, MD
Augusto M. Manalo, MD
Genara A. Manuel-Limson, MD
Virgilio R. Oblepias, MD

COORDINATORS
Jericho Thaddeus P. Luna , MD
Maria Julieta V. Germar , MD

CERVICAL CANCER
Ma. Lilibeth L. Sia Su, MD
Maria Julieta V. Germar , MD
Carolyn R. Zalameda-Castro, MD
Rosalyn C. Balacuit, MD

ENDOMETRIAL CANCER & UTERINE SARCOMAS
Efren J. Domingo, MD, PhD
Jean Anne B. Toral, MD
Christine Joy G. Garcia, MD
Ana Victoria V. Dy Echo, MD

OVARIAN & FALLOPIAN TUBE CANCERS
Filomena S. San Juan, MD, PhD
Jericho Thaddeus P. Luna , MD
Mary Evangeline A. Villa-Mercado, MD
Helen N. Retuta-Amorin, MD

VULVAR & VAGINAL CANCERS
Glenn B. Benitez, MD
Doris R. Benavides, MD
Renee Vina G. Sicam, MD
Edelyn A. Badilla, MD

PAIN
Ma. Lourdes Josefina K. Cabaluna, MD
Maura G. Catabijan, MD

PREVENTION & TREATMENT OF COMPLICATIONS
Elizabeth E. Espino-Estrebel, MD
Carol Marjorie H. Pacioles-Flavier, MD
Victorino C. Garcia, MD
Mary Lilia Bernadette V. Tinio, MD

From the

Philippine Board of Gynecologic Oncology (PBGO)

New SGOP Diplomates and Fellows to be inducted

Three new candidates for Diplomate status will be inducted into the SGOP on August 1, 2008 during the Annual Business Meeting. They passed the written and oral examinations conducted by the Philippine Board of Gynecologic Oncology last July 4 & 11, 2008 at the UP-PGH Cancer Institute. The successful examinees are: Elizabeth Espino-Strebel, M.D. (UP-PGH), Carol Pacioles-Flavier, M.D. (UP-PGH), and Sherryl Pua, M.D. (JRRMH). The 2008 PBGO is composed of Gil S. Gonzalez, M.D. (Chair), Cecilia Ladines-Llave, M.D., and Virgilio R. Oblepias, M.D.

Likewise six diplomates will be inducted as Fellows of SGOP on the same date. They are Ronald Augustine O. Campos, M.D., Ruth Judith Gay V. Cristobal, M.D., Rommel Z. Dueñas, M.D., Pherdes E. Galbo, M.D., Esther Rhadamanthine V. Ganzon, Jr., M.D. and Victoria M. Sy-Fernando, M.D.

G Gonzales

Chemotherapy. . . *(From page 6)*

OVARIAN SUPPRESSION

There have been isolated reports on spontaneous ovulation and pregnancies in women taking estrogen and, interestingly, OCPs. Exogenous estrogen could act by sensitizing the granulosa cells to the effect of FSH leading to ovulation and conception. Similarly, OCPs may act by down-regulating the LH and FSHRH. However, the interventional studies using OCPs for gonadotropin suppression in POF failed to show resumption of follicular activity. In some cases, it is possible to foresee premature menopause among women undergoing anticancer treatment with chemotherapy. Because dividing cells are more sensitive to the cytotoxic effects of these drugs, it has been hypothesized that inhibition of the pituitary-gonadal axis using GnRHa would render the germinal epithelium less susceptible to the cytotoxic effects of chemotherapy

Ovarian suppression with the use of GNRH agonist or antagonist treatment during chemotherapy is highly controversial as a method to maintain fertility. A small study evaluating 54 patients compared with retrospective controls suggested a benefit in preserving menstrual function from ovarian suppression with GnRH analogs in women undergoing chemotherapy for Hodgkin's and non-Hodgkin's lymphoma. However, a small prospective study of 18 women receiving chemotherapy for Hodgkin's lymphoma, did not show any benefit at this approach. Large randomized clinical trials of ovarian suppression should be performed with fertility preservation and not just menstruation as the outcome measure.

Because GnRH analogs are available, this strategy has been employed without clear evidence of its efficacy or full understanding of its potential risks and benefits especially in women with hormonally-sensitive tumors. At this time, since there is insufficient evidence regarding the safety and effectiveness of GnRH analogs and other means of ovarian suppression on female infertility preservation, women interested in ovarian suppression are encouraged to participate in clinical trials.

CONCLUSION

Most anti-cancer drugs affect dividing cells and are therefore expected to affect the granulosa and theca cells of the ovary more than the non-dividing oocytes. The ovaries of women who receive chemotherapy typically have normal to mildly decreased numbers of larger maturing follicles. Many of the post menarcheal women are amenorrheic during chemotherapy, often with high serum gonadotrophin concentrations, but menstrual function and fertility often return several months to years after cessation of treatment.

Alkylating agents such as Cyclophosphamide and Procarbazine are the best documented and most potent anti-cancer drugs capable of inducing ovarian dysfunction. These drugs are alter base-pairs, leading to DNA cross-links, introducing single-strand DNAs and as a result, affect both resting cells such as the oocytes and dividing cells such as the granulosa cells and theca cells. There is limited data to make any general comment regarding the effects of Doxorubicin, Cisplatin and Taxanes.

In the same manner that we discuss the potential complications of cancer treatment, we have a responsibility, as oncologists to inform our patients and/or their mothers, of the possible risks that chemotherapy may impair ovarian function and fertility. Premature menopause is a great possibility which women should keep in mind when contemplating postponement of pregnancy to allow completion of graduate education or career advancement. Management of infertility should be done by specialists and controversial means of management with no clear evidence of efficacy be performed under the setting of clinical trials.

CHEMOTHERAPY-INDUCED OVARIAN DYSFUNCTION/FAILURE

Ma. Patricia P. Luna-Sun, M.D.

Several environmental elements and toxins can cause hypogonadism – cigarette smoke, chemicals, viruses and radioactivity. Some causes are life saving such as anti-cancer chemotherapy and radiotherapy. In fact, one of the greater concerns of women and mothers of young girls undergoing treatment for cancer is the effect such treatment will have on the ovaries and future fertility.

There is no established definition of chemotherapy-induced ovarian failure but Molina et al (2005) suggest using "irreversible amenorrhea lasting for several months following chemotherapy and an FSH level of $\geq$ 30 MIU/ml. In this condition, there is cessation of any physiological activity in the ovaries. Ovarian reserve is partially defined by the FSH concentration on the 3rd day of the menstrual cycle. Normally, FSH from the pituitary signals the development of follicles in the ovaries. In turn, the ovaries produce estradiol that causes feedback inhibition in the pituitary so that FSH concentration remains at $\leq$ 10 MIU/ml. In ovarian failure or menopause, depletion of ovarian follicles results in FSH levels of >40 MIU/ml on Day 3 of the cycle because of the absence of feedback inhibition in the pituitary. Chemotherapy can cause fibrosis of the ovary with destruction of the follicles resulting in failure of ovulation, amenorrhea and sterility. With temporary ovarian failure, the normal menstrual cycle may not resume for 6 to 12 months after treatment is completed. Ovarian function may be erratic and may include months of amenorrhea interspersed with normal menstrual periods.

The first description of cytotoxic induced gonadal dysfunction was reported in 1948 and was caused by an alkylating agent, nitrogen mustard. The alkylating agent, cyclophosphamide is most frequently at the center of adjuvant regimen and appears to be the major cause of ovarian failure. There seemed to be a significant interaction between age at diagnosis and treatment with cyclophosphamide such that this drug was a significant risk factor only for the older age group. As the number of oocytes declines with advancing age, the ovaries of older women become more vulnerable to gonadal toxins compared with those of younger subjects. The risk of developing treatment-induced ovarian failure therefore, is dependent on the patient's age and the total cumulative dose of chemotherapy before developing amenorrhea and there is a greater likelihood of resumption of menses after treatment is discontinued.

In the realm of gynecologic oncology, Tangir, Jacob et al, did an original research on the effect of chemotherapy on ovarian function among young women and girls who underwent fertility-sparing surgery for malignant germ cell tumors of the ovaries. The primary regimens for the patients who attempted to conceive were VAC (Vincristine, Actinomycin, Cyclophasphamide), PVB (Cisplatin, Vinblastine, Bleomycin), and BEP (Bleomycin, Etoposide, Cisplatin). Although cyclophosphamide had already been implicated in previous studies as a risk factor for ovarian dysfunction among post-menarcheal girls treated for childhood cancers, this study added that the cumulative dose administered was also an important factor. This study revealed that cyclophosphamide did not have a significant impact on fertility of these patients even with use of Actinomycin D and Vincristine. The use of this effective combination did not decrease the chances of conception in those who had fertility- preserving surgery. In this study, more patients, on Cisplatin-based regimen developed menstrual irregularities compared to those who received alkylating agents. However, there was no difference in fertility outcomes between patients with VAC and cyclophosphamide and those treated with platinum-based combination. As of now, the paucity of studies involving premenopausal women receiving chemotherapy for gynecologic malignancies makes it impossible to establish the definitive role each of the more widely used agents play in inducing ovarian dysfunction and failure.

Thus far, conclusion on whether cyclophosphamide can bring about ovarian dysfunction or failure have not been consistent. At this point, we can state that the risk for ovarian dysfunction depends on the patient's age at the time of diagnosis with girls treated before puberty having a reduced risk of developing gonadal damage compared to those treated after menarche. Premenarcheal ovaries may be more resistant to the toxicity from chemotherapy because of the relatively large amount of oocytes in reserve. This information is extremely important to the parents of young girls and to the young women themselves diagnosed with the various malignancies requiring chemotherapy and who are concerned about the effects of such treatment on future hormonal and reproductive functions.

MANAGEMENT

Management of ovarian dysfunction needs to address 2 major medical issues – hormonal replacement and infertility. Important aspects of management include consideration of gonadal protection, germ cell storage and assisted fertilization.

HORMONAL REPLACEMENT

Long term HRT is needed for relief of menopausal symptoms and to prevent long-term sequelae of estrogen deficiency such as osteoporosis. It is continued up to the age of 50 when risk and benefit of continued treatment are reviewed. No data are available to evaluate the impact of treatment on the development of breast cancer or of cardiovascular events in young women with POF. Extrapolation from studies in older women may not always be applicable in this subset of women. The choice of estrogen is made and a separate consideration is given to progestin in women with intact uterus. Androgen replacement is useful in women who complain of persistent fatigue and loss of libido despite optimal estrogen replacement.

The general measures to improve muscle strength and prevent bone loss are advised such as increasing physical activity, ensuring an adequate diet, calcium and vitamin D supplementation and avoidance of behavior that promote bone loss such as smoking and alcohol abuse. Monitoring bone mineral density helps identify the women with osteoporosis who will benefit from specific therapeutic interventions such as bisphosphonates.

FERTILITY

Few randomized trials have failed to demonstrate any significant improvement in ovulation and pregnancy rates using various modalities. Options to preserve future fertility among patients who will undergo chemotherapy include IVF followed by cryopreservation of the embryo, cryopreservation of mature oocyte, cryopreservation of ovarian tissue and subsequent transplantation which should be performed in centers with the necessary expertise and under approved clinical protocols. Only IVF and embryo transfer using donor oocyte has demonstrated high success rate and is considered to be the fertility treatment of choice in patients with POF.

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