Plan Pregnancy by Age and Stage

Melanoma *from page 1*

There is an accumulation of recent data showing a lack of effect of pregnancy on melanoma survival, when studies control for Breslow depth of invasion (Cancer 1985;55:1340-4; Lancet 1991;337:1164-5).

► **How long must a woman who has been treated for melanoma wait before becoming pregnant?** "My answer is always that it depends on the stage of your disease plus your age," she said. The risk of death associated with cutaneous melanoma is greatest with high-risk lesions greater than 3 mm in depth, although most melanomas that dermatologists treat are 1 mm or less.

A study reporting that 83% of patients with metastatic disease present within 2 years of initial diagnosis recommended a 2-year interval between melanoma surgery and pregnancy (Lancet 1991;337:653-5). Opinions differ about the waiting period, with some physicians, including Dr. Bolognia, opting for a 3-year delay in a young patient with a high-risk lesion.

"The scenario that I see fairly frequently is the woman who is 40 years of age, has waited to have children, and has an in situ lesion," she said. "I tell them they can go ahead and try to get pregnant now and that we don't have to wait the 2 years. The way I think, the older the patient and the thinner the lesion, the more I am going to decrease the time they have to wait."

► **Does the prognosis differ if the cutaneous melanoma is diagnosed when the patient is pregnant?** For early-stage disease (American Joint Committee on Cancer stages I and II), there is no difference in prognosis, Dr. Bolognia said. Some retrospective series have suggested a worse prognosis, but at least nine controlled studies have shown no effect on survival with pregnancy-associated cutaneous melanoma, when controlled for Breslow depth.

► **What can dermatologists do to minimize the depth of melanomas identified in pregnant women?** Lower the threshold for performing a biopsy of suspicious pigmented lesions in pregnant women. "If you have a lesion that is worrisome to you, do a biopsy; don't say you'll wait until after the baby is born," she said.

Of multiple studies, three have shown increased tumor thickness for melanomas diagnosed during pregnancy, but this observation could be due to a variety of reasons, including a delayed diagnosis resulting from the belief that moles change during pregnancy; relative immunosuppression; and the effects of hormones or growth factors, Dr. Bolognia explained.

Her approach is to perform a complete history plus skin and lymph node examination, to excise the lesion with the recommended margins, and to discuss sentinel lymph node (SLN) biopsy if there are no palpable nodes or if the Breslow depth is 1-4 mm.

If signs or symptoms of metastatic disease are present, or if it is a high-risk lesion, then ultrasound or MRI is recommended. Use of MRI is accepted in the second and third trimesters, but dermatologists may encounter resistance from some radiologists to its use in the first trimester because of theoretical concerns about the potential for heat induction to have an effect on the fetus, said Dr. Bolognia, who reported no conflicts of interest.

A combination of radioactive technetium-99m sulfur colloid (Tc-99m SC) plus isosulfan blue dye is used to increase the sensitivity of SLN mapping and biopsy. However, a recent article recommended the use of only Tc-99m SC in pregnant women because of the risk of allergic reactions (up to 2%) and life-threatening anaphylaxis (0.7%-1.1%) associated with the blue dye (Cancer 2003;97:2130-3).

Women should be advised of this potential risk, but reassured that the radiation exposure with Tc-99m SC is in a very safe range, Dr. Bolognia said. The fetal dose is less than 5 mGy with the 1-3 mCi of Tc-99m SC injected for lymphatic mapping, which falls far short of the 5-10-cGy recommended safe limit for imaging studies during pregnancy.

► **If a pregnant woman has metastatic melanoma, what is the chance that the child will also develop melanoma?** If the placenta is involved, the chance of fetal metastasis is 20%-35%, with the majority of these babies not doing well, Dr. Bolognia said. Melanoma is the tumor that most frequently metastasizes either to the placenta or the fetus, and accounts for at least half of tumors with fetal involvement.

"The task for us as dermatologists is to remind the pathologists that the placenta doesn't need just a quick look, but a very detailed sectioning," she said. ■

Sensor Hones Into Odor Emitting Cancer Sites

BY DAMIAN McNAMARA
Miami Bureau

Imagine detecting skin cancer at a very early stage merely by using a sensor with an alarm that sounds when it detects abnormal variations in volatile chemical odors in the patient's skin.

Although still in the prototype stage, researchers proved the technology works with basal cell carcinoma, and plan to soon assess efficacy for early detection of melanoma and squamous cell cancers as well.

"It's very promising. There are volatiles present that are indicative of cancer. They are present in normal and cancerous skin, but levels change in a quantitative manner," said George Preti, Ph.D.

Using gas chromatography and mass spectrometry, Dr. Preti and his associates demonstrated that basal cell carcinoma lesions in 11 people emitted different levels of volatile organic skin chemicals, compared with noncancerous skin, in 11 controls. They found many of the chemicals to be odorous. Coauthor Michelle Gallagher, Ph.D., presented their findings at the annual meeting of the American Chemical Society. Specific chemical identities have not been released.

The current study builds on previous research done by Dr. Gallagher and her associates. In a report, they identified nearly 100 different chemical compounds normally emitted by the forearm and upper back of 25 healthy volunteers (Brit. J. Derm. 2008 July 12; [doi: 10.1111/j.1365-2133.2008.08748.x]). The study included patients aged 19-79 years and found some changes in skin emissions with age.

Other reports are anecdotal or only evaluate skin odor differences at the underarm (J. Chem. Ecol. 2005;31:1607-19; Chem. Biodivers. 2004;1:2042-50). The researchers began assessing skin emissions after studies showed that dogs were able to identify people with early-stage cancers using their heightened sense of smell (Integr. Cancer. Ther. 2006;5:30-9; BMJ 2004;329:712).

This was a proof-of-principle study, said Dr. Preti, who estimated clinical availability could take 7-10 years. He and his colleagues used a volatile organic chemical sensor designed for industrial and other applications, and next plan to design a probe specific to human skin.

Dr. Preti is a member of the Monell Chemical Senses Center, a nonprofit institute in Philadelphia. Dr. Gallagher was a postdoctorate fellow in Dr. Preti's lab at the time of the study; she is now at Rohm and Haas in Spring House, Pa. The authors of the study had no relevant financial disclosures. ■

History of Melanoma Should Not Disqualify Patients From Transplant

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Having a history of melanoma should not preclude a patient from receiving an organ transplant, according to Dr. Daniel Berg.

Roughly half of the approximately 100,000 new cases of melanoma diagnosed in the United States each year are in situ melanomas, and there is no reason these patients should not proceed to organ transplantation, but "the transplant docs don't necessarily separate these out" from other melanomas, Dr. Berg said at the annual meeting of the Pacific Dermatologic Association.

Patients with a history of stage T1a melanoma probably can safely undergo organ transplantation if they have gone 2 years without a recurrence of the melanoma, he said. At least 5 years without recurrence should be required in patients with melanoma stage greater than T1a or with tumor stage b before considering organ transplantation, added Dr. Berg, director of dermatologic surgery at the University of Washington, Seattle. Transplantation should be avoided if there is a history of metastatic melanoma.

Should a new melanoma in a posttransplant patient be found, treatment is the same as for other melanoma patients, with a couple of exceptions. For more aggressive melanoma (with a tumor larger than 1 mm in diameter, or a positive sentinel node), consider reducing immunosuppressive therapy, Dr. Berg suggested. If a posttransplant patient develops metastatic melanoma, try to determine if the melanoma originated in the patient's own body or in the organ donor. Metastatic melanoma that came from transplant should prompt you to notify other recipients of organs from the same donor. Their risk for metastatic melanoma is very high.

One study of 20 recipients of organs from 11 donors who retrospectively were diagnosed with metastatic melanoma found that 17 recipients developed to stage IV, and most died. Ceasing immunosuppression produced complete remission in five organ recipients (Transplantation 1996;61:274-8).

If an organ recipient gets metastatic melanoma from a donor, consider withdrawing immunosuppression, an allograft explantation, or retransplantation to improve the chance of survival, Dr. Berg said. The medical literature recommends against using organs from donors with any history of melanoma, but this may be overkill, he suggested. A review of data on 140 transplant patients who unwittingly received organs in 2000-2005 from donors with a history of melanoma found that one organ recipient died of metastatic melanoma (Transplantation 2007;84:272-4).

The organ in the recipient who died came from a donor who had been diagnosed with melanoma 32 years earlier. Another 27% of donors were diagnosed with melanoma within 5 years of their deaths, but none of those recipients died of melanoma.

"So, what do you do with a patient who has a sister who's willing to give him a kidney, and that sister had an in situ melanoma?" Dr. Berg asked. "You should be prepared to be an advocate for them" to proceed with transplantation. ■

Waiting Period for Organ Transplant After Melanoma

Previous history of:	Okay to transplant?	Waiting period
In situ melanoma	Yes	None
Stage T1a (< 1 mm)	Yes	2 years
Stage > T1a or b	Yes	5 years
Metastatic melanoma	No	N/A

*Waiting period refers to recurrence-free time after melanoma treatment.
Source: Otley, C.C., et al., "Skin Disease in Organ Transplantation" (Cambridge: Cambridge University Press, 2008)