The Current Status of BCG

What is the present status of BCG therapy for the treatment of leukemia? It is my understanding that commercially available BCG contains large amounts of soluble antigen and is unsuitable for use in immunotherapy and that the Trudeau Institute at Saranac Lake, New York, is about to release a suitable form of BCG for selective use in research. Is this correct? Furthermore, because of reports from England that the use of BCG has resulted in a significant reduction in the incidence of leukemia in children, some physicians in this country are interested in its application. Does evidence support this conclusion?

M.D. Trenton, New Jersey

Several independent trials have developed highly suggestive evidence that BCG will prolong and improve the quality of chemotherapeutically induced remissions of adult myelogenous leukemia. There is no evidence that it is curative, and trials in acute lymphatic leukemia have, to date, been negative.

While it is true that commercially available BCG contains dead organisms and soluble antigenic material, essentially all immunotherapeutic investigational studies have used or are using this type of BCG. The Trudeau Institute is developing a new form of BCG which is not yet approved for human use and which will require extensively controlled trials before it can be released. The National Cancer Institute has targeted immunotherapy, including BCG, as a major area for funding investigational and developmental work. Therefore, it is hoped that some questions about BCG will be resolved in as short a time as possible.

Reports on BCG vaccination in childhood as immunoprophylaxis are contradictory. The major positive report has come from studies of a large group of children immunized in Chicago over the last 25 years, but there are a number of epidemiologic problems about the methodologies used in that study. The National Cancer Institute is re-evaluating this data.

For additional information, you may wish to refer to an article by Bast, R.C.; Zbar, B.; Borsos, T., and Rapp, H.J., entitled BCG and Cancer which appeared in The New England Journal of Medicine, volume 290 on pages 1413-1420 and 1458-1469.

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Biopsy of Oral Cancer

A persistent tumor is suspected in a patient who has just completed a radical course of irradiation for primary carcinoma of the oral cavity. When should the suspicious lesion be rebiopsied and how reliable is such a biopsy in determining whether viable tumor is still present?

M.D., Columbus, Ohio

Following a course of radiation therapy, it is not uncommon for residual ulceration or induration to be present at the primary tumor site. If during the following weeks, progressive improvement is noted, with healing of the ulceration and softening of the underlying tissues, the tumor has been controlled.

While biopsy is indispensable and mandatory prior to initial treatment of an oral or pharyngeal tumor, it is far less useful and has certain disadvantages and limitations following radiation therapy. First, a biopsy site in recently irradiated tissues may persist as a superficially infected ulceration complicating and delaying healing. Second, a negative biopsy in irradiated tissue may give a false sense of security. Radiation often destroys tumor cells in the surface mucosa while extensions in deeper tissues less accessible to biopsy remain viable. Cytological smears of irradiated oral or pharyngeal lesions may also be misleading. Although malignant cells may be found in cytologic preparations, these cells may be irreversibly damaged and the tumor will ultimately be controlled.

Periodic examination is the most successful method for determining whether a lesion has been controlled by radiation therapy. The patient should be examined at weekly intervals following treatment by the same team of radiation therapist and surgeon. Gradual change over a period of four to six weeks can then be noted for evidence of healing or progressive induration. This brief period of delay is not harmful and we prefer to allow radiation reactions to subside before surgical treatment of persistent cancer. I have not seen persistent cancer grow out of control in this period.

Thus early biopsy is infrequently indicated. Only rarely, when the experienced observer remains in doubt after repeated examinations, is biopsy undertaken.

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Meningeal Sarcoma

A craniotomy was performed on a four-year-old girl for a large sphenoid ridge meningioma which subsequently proved to be a meningeal sarcoma. Although removal was total, tumor seeding could have possibly remained along the attachment at the sphenoid ridge. Can any therapy be recommended to prevent recurrence?

M.D., Des Moines, Iowa

Assuming the child has no signs of spread, I would advise a brain scan and CSF cytology to detect occult metastatic deposits. If none are found, I recommend a full course of megavoltage irradiation, covering the tumor's dural attachment and adjacent brain with generous margins. Although these tumors are not highly radiosensitive, the potential benefit of local radiotherapy clearly outweighs its acceptably small risk. I would not advise chemotherapy, either as an alternative or concurrently, since the risks are very real and the chemotherapeutic responsiveness of meningeal sarcomas is unknown.

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5-Fu and Colon Cancer

Is 5-Fu generally useful in patients with colon carcinoma and lymph node involvement following resection? Are weekly doses sufficiently effective to be used prophylactically, and if so, how long should the program be carried out?

M. D., Lafayette, Indiana

5-Fu can be used as an adjuvant to surgery in colon cancer patients who have a high risk of local recurrence or distant metastases including those with entire invasion of the wall or where lymph nodes are involved and a so-called curative resection has been performed. In these two groups of patients with a mortality rate of 50-60 percent in five years, there has been a substantial improvement in survival rates. We have also employed 5-Fu when there is residual lymph node involvement or liver metastasis, but only an occasional patient has manifested complete disappearance of residual tumor. Our practice is to provide a loading dose of 5-Fu in good risk patients, administering four daily doses intravenously followed by weekly injections. However, many investigators believe that only weekly doses are adequate.

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Malignant Melanoma in Pregnancy

My patient, who is six months pregnant, recently had a malignant melanoma removed from the sacrum, hopefully in its entirety. Please advise on further treatment for her.

M. D., Southport, North Carolina

A few malignant melanomas appear to be aggravated by the hormonal changes which occur either during pregnancy or while on oral contraceptives. Such patients need to be followed extremely closely during pregnancy. Following pregnancy, I advise them not to become pregnant again and not to use oral contraceptives for a period of at least three years, as most recurrences with malignant melanoma occur during that period. There are no tests which can be performed at this time to demonstrate which melanomata are adversely affected by pregnancy, nor has abortion been proven effective in such patients. If this woman, who is six months pregnant, should have metastatic disease, chemotherapy or a combination of chemo-immunotherapy should immediately be started. At this stage of pregnancy, we have not found that such treatments are injurious to either patient or fetus.

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Papillary Adenocarcinoma of the Thyroid

A 29-year-old female presented with a nodule in the left lobe of the thyroid. It may be significant that five and a half years previously, she received 500 rads superficial type irradiation with the 100 KV X-ray, with one mm. aluminum filter to an area 1 1/2 x 1 cm. in diameter covering the keloid scar in the left earlobe. The surrounding tissues were shielded from any irradiation, and the radiologist believed the penetration to be sufficient to effect the posterior part of the scar.

Following excision, the pathologist reported that the nodule was benign. However, the surgeon was somewhat suspicious and performed total excision of the left lobe of the thyroid and the isthmus. The final pathologic diagnosis was "papillary adenocarcinoma, well differentiated, of the thyroid gland closely approaching adherent skeletal
muscle on the anterior surface. **Two months postoperatively, the patient now appears in excellent health, with no evidence of clinical recurrence. Is the surgery that has been performed adequate? Kindly outline proper follow-up for this patient.

M.D. Toledo, Ohio

Did the earlier irradiation cause the tumor? Radiation to the thyroid is a known contributing cause of thyroid cancer, especially in children who have been irradiated for thymic hypertrophy or for enlarged tonsils. However, well-shielded superficial irradiation to the earlobe is probably irrelevant to this patient’s subsequent development of thyroid cancer.

Should the patient be operated on again? Two separate issues must be considered: the need for a radical neck dissection and the adequacy of the thyroidectomy. As the surgeon was suspicious of the nodule at operation, it is presumed that he examined the regional lymph nodes carefully, and found no evidence of metastases. The question of radical neck dissection for papillary thyroid cancer without clinically involved lymph nodes was recently reviewed by Hutter, Frazell, and Foote. They concluded that dissection of the clinically uninvolved neck was of small benefit. Of 88 patients who were treated without neck dissection, 11 subsequently developed recurrent disease: the ultimate fate of most of these patients would not have been influenced by neck dissection at initial treatment. This agrees with the practice of most thyroid surgeons at the present time. Neck dissection should be performed only on involved nodes either at initial treatment or subsequent follow-up.

The common practice in papillary thyroid carcinoma is to perform a total lobectomy on the involved side and a subtotal lobectomy on the opposite side, because papillary thyroid carcinoma is multicentric in 10 to 20 percent of cases. In this case, the distinction between resection of the isthmus and subtotal contralateral lobectomy is in the eye of the surgeon; one man’s isthmus resection is another’s subtotal lobectomy. Evidently, the remainder of the right lobe appeared normal to the surgeon. To remove the right lobe could possibly be justified, but I would not re-operate on this patient.

From the data of Frazell et al. a tumor in a young patient carries an 89 percent 20-year survival rate, regardless of size. If the tumor is smaller than five cm. in diameter, a 96 percent 20-year survival would be expected. Although the prognosis is quite good, follow-up should be prolonged since papillary thyroid carcinoma is notoriously liable to recur long after excision. The right lobe and the cervical lymph nodes should be carefully examined yearly for at least 20 years.

It is standard practice to give thyroid replacement therapy following thyroidectomy for cancer. This prevents myxedema in the patient who has had subtotal thyroidectomy and suppresses the tumor if it is hormone dependent. Papillary tumors are far less common hormone dependent than are follicular carcinomas. Nonetheless, I would give sodium levothyroxine (Synthroid), 0.2 mg. per day, for life.

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