Bronchoscopic phototherapy is available now for 2 distinct categories of tracheobronchial cancer: roentgenographically occult superficial squamous cell carcinoma and advanced malignancy causing significant airway obstruction. Laboratory and clinical experience show that the photodynamic effect of hematoporphyrin derivative phototherapy (HpD-PT) may be useful for treating superficial cancers that penetrate less than 5 mm into bronchial mucosa. The larger, obstructing cancers are better managed by high-power laser sources, such as the YAG laser, which are effective by hyperthermal photocoagulation, thermal necrosis, and tissue vaporization.

Bronchoscopic phototherapy of cancer involving the tracheobronchial tree is currently available for treatment of two distinct kinds of lesion: roentgenographically occult superficial squamous cell carcinoma and advanced malignancy causing significant airway obstruction.

Detection and Treatment of Early Lung Cancer

Roentgenographically occult lung cancer principally affects male smokers between the ages of 45 and 76 years. The predominant cell type is squamous cell carcinoma. Extensive pathologic investigation of roentgenographically occult squamous cell bronchogenic carcinoma suggests that these cancers evolve from in situ to progressively more invasive stages. The tempo of progression cannot be determined precisely, but it is generally accepted that in situ cancers tend to be indolent, slowly growing tumors. Aggressive detection and localization of occult lung cancer, therefore, would provide opportunity for treatment at an early stage. In studies of roentgenographically occult lung cancer, the number of lesions still in situ has ranged from 13% to 35%. Multicentric carcinomas are common in these cases. Up to 15% of the patients have simultaneous occult lung cancers at the time of detection. More important, new metachronous primary lung cancer has developed in these patients at a rate of 5% per year of observation.

Most patients with occult lung cancers are heavy smokers and have an increased operative mortality due to postoperative complications from associated lung and heart diseases. Moreover, surgical management of occult lung cancer may significantly reduce pulmonary reserve, because the cancer involvement may require pulmonary resection, such as pneumonectomy or bilobectomy. And, in many cases, pulmonary reserve will be compromised further by surgical treatment of a subsequent primary lung cancer.

Clearly an alternative method of treatment is desirable to conserve pulmonary parenchyma in these patients. A new method of local bronchoscopic phototherapy for lung cancer has been introduced recently, which, if effective, will spare lung parenchyma. However, this treatment affects only the superficial portion of the cancer and does not penetrate more than 4-5 mm into the bronchial wall. Consequently, the major problem is to determine whether the lesion is limited to the bronchial wall. Potentially suitable for this treatment are all carcinomas still in situ or with microinvasion to a depth less than full thickness of the bronchial wall. Bronchoscopic experience with these cancers indicates that the endoscopic appearance of the tumor at the time of localization correlates with the postsurgical TNM classification. In our experience, if the lung cancer was not endoscopically visible at the time of localization, no evidence of extrabronchial invasion or metastatic involvement of lymph nodes has been found. It seems reasonable, therefore, to consider local bronchoscopic management for patients with roentgenographically occult squamous cell carcinoma that is not visible on bronchoscopic examination.

These tumors, although best suited for local treatment, are the most difficult to localize. However, there is available an endobronchial tumor marker capable of labeling cancer cells. This is a hematoporphyrin derivative (HpD). HpD is specifically concentrated by cancer cells, and after irradiation with light of appropriate wavelength, it produces a characteristic fluorescence that allows accurate localization of the tumor.

Unfortunately, because of the low intensity of the HpD fluorescence and the optical losses in the fiber bundles of the flexible fiberbronchoscope, one cannot observe fluorescence and perform bronchoscopic examination with standard white-light illumination at the same time. In the search for early bronchogenic carcinoma, white light is important. It permits detailed inspection of the endobronchial anatomy and allows visualization of the subtle changes in mucosal color and texture indicative of early cancer. Bronchoscopic fluorescence detection systems have been developed that overcome these technical problems. One system employs an image intensifier to enhance the fluorescence. The other system involves a photoelectric fluorescence detector, which converts the fluorescence signal into an audio signal, allow-
ing the physician to perform a normal bronchoscopy with white light.35
With use of HpD and any detection device, it is possible to localize squamous cell carcinomas before they become bronchoscopically visible. It should be emphasized, however, that the presence of HpD fluorescence is not specific for carcinoma. Areas of moderate and marked squamous cellular atypia also concentrate HpD, although the levels of fluorescence seem to be somewhat lower than those noted in frank carcinoma. The only acceptable proof of cancer remains pathologic confirmation based on examination of biopsy specimens and bronchial brushings.

In our current clinical practice, indications for use of an HpD fluorescence bronchoscopic detection system begin with squamous carcinoma cells in the sputum. Two situations qualify: (1) squamous carcinoma cells in the sputum with a chest roentgenogram negative for cancer, normal laryngologic findings, and routine bronchoscopic results not disclosing the cancer's location; and (2) squamous carcinoma cells in the sputum with a localized peripheral abnormality on the chest roentgenogram. In the latter situation, one should consider the possibility of a simultaneous occult squamous cell carcinoma.

PHOTOTHERAPY OF EARLY LUNG CANCER

The main thrust for the development of bronchoscopic technique for local treatment of bronchogenic carcinoma is to offer an alternative to radiotherapy for residual local disease or an alternative to surgical therapy for in situ and early invasive squamous cell carcinoma. In this type of phototherapy (PT), again, HpD is at the center of recent research. The first reported instance of cancer response to hematoporphyrin derivative phototherapy (HpD-PT) was in a case of bladder carcinoma.39 Subsequently, pioneering work by Dougherty and associates36-38 has shown the potential for this technique in the treatment of a variety of malignant tumors involving the skin and subcutaneous tissues. Over the past four years approximately 150 patients with bronchogenic carcinoma have received HpD-PT on an experimental basis. The major groups involved in this research include the Tokyo Medical College Hospital, the University of Southern California School of Medicine, the Roswell Park Memorial Institute, and the Mayo Clinic. HpD-PT still is new, experimental, and unproved in the local treatment of lung cancer. However, the overall experience of the four groups indicates that it has the potential for becoming a successful modality in the treatment of in situ and early invasive bronchogenic carcinoma. It is clear that HpD-PT will not be successful in curing or even controlling a large obstructing tumor of the tracheobronchial tree, particularly if the tumor erodes through the bronchial wall. In this situation HpD-PT has caused bronchopleural fistula and significant hemorrhage from necrotic tumor. Furthermore, the edema and exudate produced during the treatment has worsened the bronchial obstruction. It seems, therefore, that this treatment is not suitable for urgent treatment of an obstructive major airway.

In our current practice HpD-PT is reserved for cancers that are within the reach of the flexible fiberoptic bronchoscope, are less than 2-3 cm in diameter, and give no evidence of eroding through the bronchial or tracheal wall.

The combination of HpD fluorescence bronchoscopy and HpD-PT now gives the clinician the ability to localize early, roentgenographically occult bronchogenic cancer and to proceed with local bronchoscopic treatment in those patients who are at high risk both for surgical resection and for the development of a subsequent primary lung cancer.

PHOTOTHERAPY OF CANCERS PRODUCING AIRWAY OBSTRUCTION

Treatment of recurring malignant tumors that obstruct the airways has been limited to surgical resection, radiotherapy, chemotherapy, and, on occasion, biopsy resection or cryotherapy via a rigid bronchoscope. The therapeutic possibilities have been expanded with introduction of the medical laser. Three medical laser systems are currently available for direct ablation of tissue. The carbon dioxide laser delivers radiation in the far infrared region, with a wavelength of 10,600 nm. This very long-wavelength radiation cannot be conducted by a quartz monofilament and is limited to rigid endoscopic systems. Also, this wavelength is absorbed by water and pulmonary secretions, so its effectiveness requires an absolutely dry field. And because its depth of penetration is less than 1 mm, a bronchoscopic session to remove tumor can be quite prolonged.23-24

The argon laser delivers blue-green light with a wavelength of 514 nm. This light can be conducted by a flexible quartz monofilament and, therefore, can be used with a fiberbronchoscope. The major drawback is that this wavelength is strongly absorbed by hemoglobin: poor tissue penetration limits its value.24

The neodymium-YAG laser (neodymium-yttrium-aluminum-garnet) delivers radiation in the near infrared, with a wavelength of 1,064 nm. It can be conducted by a quartz monofilament and is useful with the flexible fibroscope. Since only a little light of this wavelength is absorbed by hemoglobin and water, it can penetrate to several millimeters. Bleeding vessels encountered incidentally during thermal necrosis of the tumor can be photocoagulated, provided they are no more than a few millimeters in size. Therefore, the presence of a small amount of surface hemoglobin does not interfere with ablation of large amounts of tumor tissue.

This laser has been used successfully by several groups to open airways obstructed by various courses, including postintubation tracheal stenosis, tracheal involvement with esophageal carcinoma, cylindroma of the trachea, carcinoid tumor, and inoperable malignant tracheobronchial carcinoma.23-24

The major effect of this instrument is to produce thermal necrosis of tissue, which allows debulking of tumor, while photocoagulation helps control slight superficial bleeding during treatment. The actual heating of the tumor produces tumor shrinkage and a reduction in blood supply, so that large pieces of tumor can be removed with a biopsy forceps as the treatment progresses. The major complications include hemorrhage from tumor necrosis and hemorrhage from perforation of a large blood vessel. The potential for a bronchopleural fistula exists, but none has been reported so far. Careful anesthetic technique is required to reduce the risk of fire. It should be emphasized that in all cases this form of treatment has been for palliation of obstructive symptoms.
In our current clinical practice we apply the following criteria to select patients for this form of phototherapy: (1) the airway obstruction has been unresponsive to other reasonable therapy, (2) the lesion should be protruding into the bronchial wall without obvious extension beyond the cartilage, (3) the axial length of the endobronchial component of the tumor should be less than 4 cm, (4) the bronchoscopist should be able to see the bronchial lumen, and (5) there should be functioning lung tissue beyond the obstruction. If these criteria are not met, risk of complication is increased; the expected benefit to the patient should be weighed carefully before treatment is attempted.

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