this procedure only after conservative measures of pain control have been completely exhausted. In addition, patients who are overweight should lose excess weight and participate in a spine muscle strengthening and flexibility program before being considered as candidates for a fusion procedure. In a certain number of well-motivated patients, dedicated efforts directed at weight control, muscle strengthening, and maintenance of proper spinal alignment and body mechanics can obviate the need for a large surgical procedure. In the right patients, however, a fusion procedure for mechanical instability of the lumbar spine can make the difference between disability and a meaningful life.

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Implantable Neurosurgical Drug Delivery Systems

IMPLANTABLE NEUROSURGICAL DEVICES provide an elegant and novel means of delivering drugs to the central nervous system. They have had increasing applications in the management of intractable pain, certain neurologic disorders, and malignant lesions and infections of the central nervous system.

The epidural, subarachnoid, or intraventricular administration of medication represents an effective approach to the delivery of drugs to a specific site within the central nervous system. This approach provides for a controlled, direct, and precise delivery of drugs. The identification of opiate receptors in the central nervous system stimulated the development of a method assuring the direct delivery of synthetic and semisynthetic opioids to the brain and spinal cord. By circumventing the blood-brain barrier, smaller dosages of medication are feasible and systemic side effects are minimized.

Implantable devices consisting of reservoirs and pumps are gaining increasing favor in neurosurgical practice. The surgical implantation of such devices is reasonably safe and easy. Catheters are placed in either the spinal epidural space or the subarachnoid space through a small skin incision or inside the cerebral ventricles through a small twist-drill hole. These catheters are then tunneled subcutaneously and connected to an infusion pump that is placed in a subcutaneous pocket, generally in the abdomen, flank, or chest. Such a closed system provides the advantages of long-term, controlled, sustained delivery of medication with minimal inconvenience and risk of infection.

Rapid technologic advances have provided sophisticated delivery systems. Large reservoirs filled percutaneously and placed remote from the delivery sites permit conveniently long intervals between drug refills, thereby minimizing the risk of infection, discomfort, and other complications. Remote programmable pumps permit changes in drug dosage by telemetry.

The use of such systems has seen increasing acceptance in the treatment of intractable cancer pain, otherwise difficult to control by oral or parenteral medication. Lumbar or cervical spinal catheter placement is used for the treatment of truncal pain. The intraventricular administration of opioids is effective for head and neck pain. The use of such opioid drug delivery systems for chronic pain of benign origin has been attempted in certain centers, but such application remains controversial. Furthermore, because these systems are expensive, they probably are not justified for short-term use.

Similar drug delivery systems have been used to good advantage in the treatment of malignant tumors and infections of the central nervous system. The intrathecal administration of baclofen for spasticity has received recent attention. Other neurologic disorders undoubtedly will be treated in a similar manner.

The long-term use of implantable drug delivery systems can result in a number of complications. Blocked or migrating catheters and pump failure are easily recognized and generally readily corrected. The development of drug tolerance is a more serious problem. Although this often represents a "pseudotolerance" resulting from a mechanical system failure, such tolerance to opioid medications may occur with long-term use. Generally drug tolerance develops more slowly with continuous spinal infusion than with bolus administration. The problem may be overcome initially by increasing the concentration or substituting another opioid. In intractable cases, however, narcotic detoxification may be necessary.

The direct delivery of medication to the central nervous system using implantable devices assures a controlled, sustained, convenient, and long-term administration of effective medication without compromising normal neurologic function and with minimal systemic side effects. This method should not be construed as a panacea. Proper patient selection is essential. Advancing technology offers an exciting prospect for benefiting future generations of patients through neurosurgical care.

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Interstitial Radiotherapy for Malignant Glioma

CURRENT THERAPY FOR MALIGNANT GLIOMA consisting of surgical resection, external-beam radiotherapy, and carmustine (BCNU) chemotherapy can prolong survival, but the overall prognosis remains poor. Most patients have significant tumor progression within the first two years after their initial treatment.

While the efficacy of external-beam radiotherapy in controlling residual tumor following surgical resection has been well established, increasing doses of radiation are associated with increasing toxicity to the surrounding brain. One strategy to deliver additional radiotherapy to the tumor has been to give a "boost" of radiation by implanting radioactive sources into the tumor bed. The theoretic advantages of such "seed implants" include a relatively high overall dose of radiation to the tumor with relatively low exposure to surrounding brain. Another possible advantage of tempo-

rary implants is the delivery of constant low-rate radiation that may enhance biologic effects on malignant cells.

During the past decade, the development of image-directed stereotactic systems has resulted in the ability to treat tumor volumes with radioactive sources (iodine 125 or iridium 192) with a high degree of accuracy and safety. Results from early trials of interstitial radiotherapy in selected patients have been encouraging, with quality survival as long as five years in a number of patients. Many neurosurgical centers are currently using this approach to treat malignant brain tumors (primary as well as metastatic) in conjunction with external-beam radiotherapy. Several groups have reported benefits of such treatment when compared with historical controls, but such effects in controlled studies remain to be quantified. Complication rates, both short and long term, also need to be better defined. Preliminary data suggest that short-term morbidity is less than 5%, but a number of patients require subsequent operations for recurrent masses. Posttreatment masses may include large volumes of necrotic tissue thought to result from the radiation implants. Because this is a relatively new form of treatment, long-term efficacy and complication rates also require further definition.

To summarize, interstitial radiotherapy is a logical adjuvant therapy in the management of malignant brain tumors. Initial data suggest efficacy in selected patients. Whether such therapy will become the standard of care will depend on the results of ongoing phase III investigations such as those of the Brain Tumor Cooperative Group. Randomized, controlled studies such as those of the Brain Tumor Cooperative Group hold the promise that the indications for and efficacy of interstitial radiotherapy will be determined.

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Management of Prolactin-Secreting Pituitary Adenomas

PROLACTIN-SECRETING ADENOMAS are the most common functioning pituitary tumors that present to clinicians. The successful integration of medical and surgical therapy provides an extremely high potential for the effective treatment of such tumors in terms of resolving endocrine symptoms and intracranial mass effects.

The medical treatment of prolactin-secreting pituitary tumors is based on the physiology of prolactin release—prolactin being the only hormone of the anterior pituitary to be regulated exclusively by a mechanism of tonic inhibition effected by neurotransmitter release from the hypothalamus. The neurotransmitter regulating the release of prolactin has dopaminergic characteristics, but whether it is dopamine is unknown. Bromocriptine, an ergot derivative with dopaminergic characteristics, effectively suppresses prolactin secretion and restores prolactin levels to normal in greater than 95% of patients with prolactin-secreting adenomas. It also significantly reduces the size of large prolactin-secreting tumors in at least 50% of patients and usually precludes further tumor growth once therapy is instituted. Bromocriptine therapy represents an acceptable alternative to surgical therapy, but the drug is not curative and not all patients tolerate its use. Furthermore, cessation of the drug results in a rapid return of hyperprolactinemia and the tumor reverts to at least its original size. Therefore, bromocriptine therapy is required for the lifetime of a patient when used alone.

Approaches to treatment involve a consideration of the stage of the tumor. Stage I lesions (less than 1 cm in diameter and confined to the intradural sella) are most amenable to surgical cure. The main indication for the treatment of such small lesions is patients' desire for pregnancy. The possible genesis of premature osteoporosis in women who are amenorrheic and hypoestrogenemic as a consequence of systemic hyperprolactinemia is a hypothetical concern that awaits clinical confirmation. In our experience, surgical resection of stage I lesions has an 84% chemical cure rate a year after resection, with morbidity less than 1% and mortality 0%. Serum prolactin levels measured six weeks postoperatively are used to determine whether further intervention is necessary. Bromocriptine therapy, on the other hand, restores normal serum prolactin levels in virtually 100% of patients who tolerate the drug, thus allowing normal pregnancy. Care must be taken with this approach, however, because tumor regrowth may necessitate reinstituting bromocriptine therapy during pregnancy. For stage I lesions, therefore, either surgical resection or bromocriptine therapy can effectively maximize the potential for pregnancy. The choice of therapy should depend on the patient's preference, taking into account the need for long-term medical management should an operation be deferred.

Stage II tumors (greater than 1 cm in size, with or without supraseller extension but without invasion of the dura or bone of the sella turcica) present similar treatment options, although the chemical cure rate of surgical treatment is only 50%, compared with 90% with bromocriptine use. Some stage II tumors, such as those that are cystic or of low density on a computed tomographic scan, generally do not shrink with bromocriptine therapy. This underlines the advantage of surgical resection in such cases—the reduction of tumor size.

Stage III tumors (local invasion of dura and sella) and stage IV tumors (diffuse sellar invasion with or without extension into the anterior, middle, or posterior fossa) defy cure by any single means. Surgical therapy alone achieves only a 25% physiologic cure of stage III lesions, and the physiologic cure of stage IV lesions approaches 0%. On the other hand, high doses of bromocriptine, with resulting increases in side effects, are required to have an effect on such large tumors. Therefore, we use combined therapy in stage III and IV tumors. The patient is initially placed on a regimen of increasing bromocriptine doses until a serum prolactin level of less than 20 ng per ml is established. If, after six weeks of normal prolactin levels, no reduction in tumor mass is observed on serial imaging studies, surgical resection is attempted. Imaging studies are done at three and nine months postoperatively and yearly thereafter. If postoperative imaging fails to show tumor progression and the prolactin level remains normal, no radiation therapy is given. Should the tumor progress despite bromocriptine therapy, radiation therapy is usually given. One indication for more urgent surgical intervention is progressive visual compromise despite bromocriptine therapy. Should significant reductions in tumor size be achieved with bromocriptine use, continued medical management becomes an op-