(C) MANAGEMENT OF BRAIN TUMOURS

1) SURGERY: Surgery is generally the initial and sometimes only treatment required. The aim is to remove as much of the tumour as is safely possible. Before the operation the neurosurgeon carefully studies the CT/MRI scans. The route and type of operation is then decided after discussing the risks and benefits of this operation with the patient. Hair is completely shaved before the operation. The operation is performed after giving anesthesia to the patient. While it is desirable to remove the tumour completely, this is not always possible if the tumour is very deep-seated or is in a very critical area. Therefore a tumour may be either completely or partially removed or only a biopsy may be taken. High-powered operating microscopes make it easier to see and remove tumours while sparing the normal brain. The operation may take many hours. The patient usually wakes up as soon as the effect of the anaesthesia wears off, but is kept in the ICU for some time to allow close observation and care.

The department performs routine microneurosurgical procedures at TMH. In addition regular ORs are conducted at ACTREC where patients enrolled on clinical trials are provided surgical care. The surgical department has state-of-the-art equipment including operating microscope (Zeiss OPMI Pentero), pneumatic drills, stereotactic frames, intraoperative ultrasound and Neuro-endoscope.

The department performs all major neurosurgical procedures for tumors including craniotomy (supra-and infratentorial), CSF diversion, stereotactic biopsy, transsphenoidal surgery, spinal laminectomy and laminoplasty for intradural and intramedullary tumors. Additionally, in collaboration with the Head-Neck services, we offer complex craniofacial and skull base surgeries including conventional anterior / anterolateral craniofacial resections, temporal bone surgery and transtemporal procedures, endoscopic as well as endoscopic-assisted craniofacial resections.

Image guided surgery: intraoperative ultrasound is routinely utilized during tumor surgery to facilitate accurate localization and maximal safe resection. The department is in the process of acquiring advanced ultrasound based navigation as well as intraoperative optical imaging for tumors. ***Stereotactic surgery:*** the department is equipped with a Leksell stereotactic frame each at TMH and ACTREC and provides stereotactic biopsies, as well as stereotactically guided therapeutic procedures. ***Minimally invasive neurosurgery***: the neurosurgical service is equipped with neuro-endoscope for endoscopic surgery as well as endoscopic assisted microneurosurgical procedures. In addition, in conjunction with the head-neck surgical services, we provide fully-endoscopic and endoscopically-assisted craniofacial

resections. ***Pediatric neuro-oncology***: the department provides surgical care for pediatric brain and spinal tumors and performs surgeries for all types of pediatric brain and spinal tumors. Along with the pediatric oncology group, comprehensive care for all such patients is provided. ***Skull base surgery and craniofacial resections:*** A joint multidisciplinary Skull Base Clinic is conducted every week (4 pm, every Thursday, Room 37, Main building, TMH). Along with our head-neck and reconstructive colleagues complex craniofacial resections (conventional as well as endoscopic assisted) are performed routinely.

In addition, the department maintains a prospective database of all patients to document the clinicoepidemiological, radiological, and pathological features of these tumors

Education and training: The service provides training for specialist registrars in neurosurgical oncology as well as craniofacial and skull base surgery. This involves regular bedside teaching, didactic lectures, as well as interactive joint clinic decision making sessions, besides supervision during operative procedures. Additionally, training of nursing and paramedical staff is also provided.

2) RADIOTHERAPY: Radiotherapy is an integral component of the multimodality management of primary brain tumours with potential impact upon local control, symptom improvement, and progression free survival for low-grade and benign neoplasm and also overall survival for malignant brain tumours. Following maximal safe resection, adjuvant radiotherapy is indicated for all high-grade primary brain tumours in the postoperative setting. For completely excised benign tumours, such as pituitary adenomas and benign meningiomas, currently there is no role of upfront adjuvant radiotherapy. For low grade gliomas too, with no residual tumour on neuroimaging, surveillance alone is a reasonable option. However radiotherapy is recommended in such tumours either if a macroscopic residual tumour is evident on postoperative imaging or if tumour progression is documented on serial imaging. For tumours in the eloquent cortex where only a partial excision or biopsy if possible, radical radiotherapy is needed to improve outcome.

Conventional radiotherapy: includes planning on the Varian simulator (Ximavision) with treatment delivery on 4 Telecobalt machines and 3 Linear accelerators.

Three-dimensional (3D) conformal radiotherapy (3DCRT): with the help of 3-D planning systems and Eclipse. Treatment is delivered on Trilogy, Varian 2100 CD and Varian 6 Ex linear accelerators with standard leaf multileaf collimators. Quality assurance (QA) includes verification with digitally reconstructed radiographs (DRR) and electronic portal imaging. Stereotactic Radiosurgery (SRS) and Radiotherapy (SCRT) using the BrainLab microMultileaf Collimator system(M3). ***Intensity modulated radiotherapy (IMRT):*** using Helios software of Cadplan and Eclipse with treatment delivered with dynamic MLC (DMLC) technique. ***Stereotactic conformal radiotherapy (SCRT) and Stereotactic radiosurgery (SRS):*** using Brain lab software and microleaf collimeters (micro MLC). ***TOMOTHERAPY:*** state of the art tomotherapy technique is also available at our centre and we are the only setup to possess this facility in the entire country which guarantees extremely precise treatment delivery with high accuracy.

Stereotactic Radiosurgery with Micro Multi Leaf Collimator [BrainLab]

3) CHEMOTHERAPY: Principles of chemotherapy and biological therapy

The role of chemotherapy and biological therapy in the multidisciplinary management of primary brain tumours continues to evolve rapidly. The goal of chemotherapy is to kill tumour cells directly by making them unable to replicate or to enhance normal process of cell death - apoptosis. Chemotherapy drugs may be cytotoxic or cytostatic. Some chemotherapy drugs act during specific parts of the cell cycle (cell-cycle specific drugs). Other drugs are effective at any time during the cell cycle and are referred to as non cell-cycle specific drugs. Combining non cross-resistant drugs to improve efficacy and reduce toxicity is the basis of contemporary multi-agent chemotherapy regimens.

- TEMOZOLOMIDE
- PCV (Procarbazine, CCNU, Vincristine)
- BEVACIZUMAB is a VEGF inhibitor used in recurrent high grade gliomas (most commonly in glioblastomas)

4) PAEDIATRIC BRAIN TUMOURS

Medulloblastoma: Medulloblastoma is the most common brain tumour in children accounting for approximately 7-8% of all intracranial tumours and 30% of pediatric brain tumours. It was originally described by Bailey and Cushing in 1925, and is now thought to arise from neural stem cell precursors in the granular cell layer of the cerebellum. It has a high propensity of spreading throughout the neuraxis via the cerebrospinal fluid (CSF). Extraneuraxial systemic metastases though well recognized are uncommon. The cornerstone of treatment is surgery in the form of maximal safe resection followed by adjuvant radiotherapy (craniospinal irradiation followed by tumour bed boost). Adjuvant chemotherapy is indicated in high-risk disease with standard dose CSI or in average risk disease whenever CSI is reduced. Apart from providing histologic confirmation, surgery also has the added benefit of restoring the natural CSF pathways in the brain

Adjuvant *chemotherapy* has become an integral part of treatment for medulloblastoma (MB). Several chemotherapeutic agents (especially alkylators and platinums) have been shown to be effective against medulloblastoma, and various chemotherapeutic strategies have been studied.

Primary CNS germ cell tumours: Germinomas: Germinomas are highly chemotherapy-sensitive tumours. Regimens that use cisplatin, carboplatin, or cyclophosphamide, along with vinblastine or vincristine, bleomycin, and etoposide, are capable of producing complete and partial response rates in as high as 90% in newly diagnosed patients. The current focus centers on the optimal balance of chemotherapy and radiation therapy.

Nongerminomatous germ cell tumours (NGGCT): The secreting intracranial NGGCT show an inferior prognosis compared to germinoma. In NGGCT, with standard chemotherapeutic regimens along with radiation, response rates exceeding 80% and survival rates of 48% to 80% have been seen. Relapse rates appear to be higher in the patients treated with involved field RT only. Therefore, craniospinal irradiation for all patients is advisable. At TMH, these patients receive 4 cycles of cisplatinum based chemotherapy (PEI, appendix) are applied, followed by a delayed tumour resection and craniospinal irradiation (30-35 Gy plus 20-24 Gy tumour boost).

5. ANTIEPILEPTICS AND STEROIDS

Antiepileptic prophylaxis: Management of seizures in patients with brain tumours is a very contentious issue. The incidence of seizures in patients with brain tumours varies from 20-75% depending on the age, location and type of tumour. The highest incidence is in young patients with low grade tumours of the temporal lobe. Moreover, a large proportion of patients who do not present with seizures initially ultimately develop seizures during the course of disease.

Management of patients who present with seizures: Following perioperative prophylaxis, these patients are continued on AEDs for at least 2 years. They are assumed to have an established epileptogenic focus secondary to tumour and need to be treated with antiepileptic drugs (AEDs) as any other patient with symptomatic epilepsy. The AEDs can be discontinued if they have been continuously seizure free for 2 years.

Choice of AEDs: Commonly used AEDs include phenytoin, phenobarbitone, carbamazepine, and valproic acid. The first three have a narrow therapeutic window. Moreover, they are enzyme inducers and may produce drug interactions with concurrent chemotherapy leading to subtherapeutic levels. They also may cause extensive (rare) skin reaction with RT. Phenytoin remains the most commonly prescribed AED. Serum levels should be monitored and potential drug interactions borne in mind. Newer drugs like oxycarbamazepine, topiramate (as first choice) and levetiracetam (as add on) are promising and need further evaluation in trials.