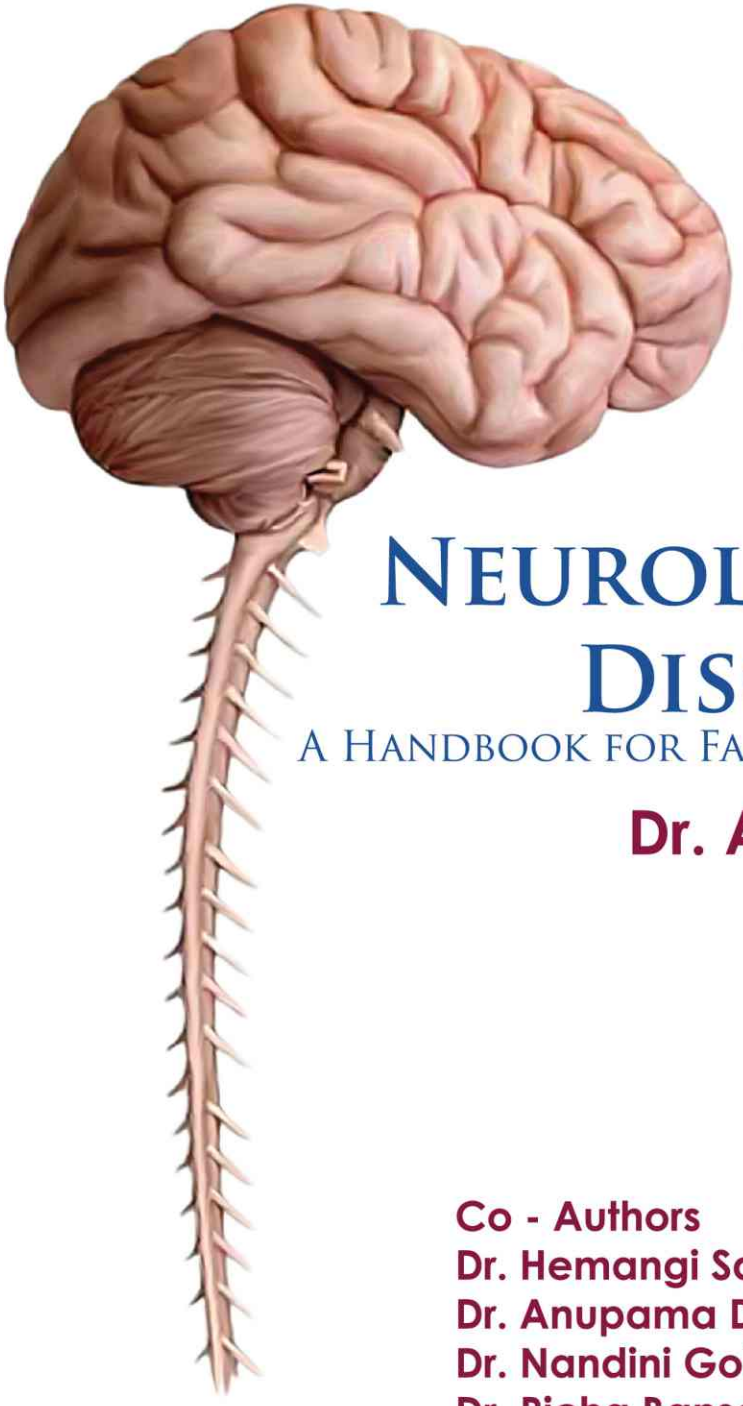

Neurological Disorders

A Handbook for Family Physicians

Dr. Alok Sharma
M.S., M.Ch.

Co - Authors
Dr. Hemangi Sane, M.D. (USA)
Dr. Anupama Desai, M.D.
Dr. Nandini Gokulchandran, M.D.
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A *NeuroGen* Publications


NeuroGen Brain & Spine Institute

NeuroGen Brain & Spine Institute is an International centre of excellence for Neurological disorders. Founded by Dr. Alok Sharma it is India's first dedicated Hospital for Stem Cell Therapy and Comprehensive Neurorehabilitation . Located adjacent to the Arabian sea on the scenic palm beach road in Navi Mumbai, this centre has a multidisciplinary team of expert and experienced medical professionals that provide holistic care using the latest technological advances in the world. It has treated over 5000 patients from 50 different countries. The care offered here is very professional yet very caring. A separate pediatric neurorehabilitation facility and other play areas makes it very child friendly. The institute is very scientific and academic in its approach and to date has published 69 scientific papers in international and national journals. 14 books have also been published and chapters contributed to several international textbooks. NeuroGen also has many International tie ups with leading organizations from America and other countries for research and treatment collaborations. The Institute is very quality conscious and has several certifications Including the ISO 9001:2008. Despite all the international partnerships and treatments offered to patients from all over the world the institute is very socially conscious and through the Stemcare foundation financially supports patients from the lower socioeconomic strata to be able to avail of the treatments that are needed. Its a policy of the institute that no patient should be deprived of any treatment due to financial reasons. NeuroGen doctors conduct free medical camps all over the country. Conferences, workshops and CME's are regularly conducted to impart knowledge to doctors, therapists as well as patient families. Cutting edge research, pioneering new treatments, the best medical professionals, comprehensive treatment facilities all under one roof and a caring holistic approach make NeuroGen Brain and Spine Institute a unique and special facility for patients with Neurological problems.




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Preface

When we were children, the word 'Doctor' meant only one thing - our "Local family doctor." He was called family doctor because he in many ways was a part of the family. He was a comforting figure who took care of our fevers, coughs, rashes, diarrheas, pains and anything else we may have from bronchial asthma to chicken pox. If there was any medical emergency at home he was the first person to be called. One was always sure that he would give us relief, whatever the reason and whatever it was that we were suffering from. His mere presence was comforting. He knew all about our family and kept track of all our health related issues. However, in the recent past the community of family physicians is diminishing and losing its relevance in the overall scheme of medical practice. Specialization, super-specialization, fancy hospitals and access to medical information on the internet has resulted in patient's directly reaching specialists and therefore bypassing the family physician who in earlier years was the link between the family and the all aspects of medical care. This has its disadvantages since the family physicians looked at the patient's as a whole and in context to the rest of the family and therefore, recommended medical advice in a more holistic fashion.

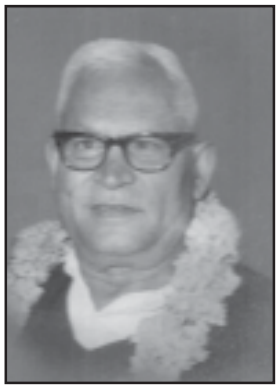
This book has therefore, been written for family physicians to update them on what is happening in the field of neurological disorders. Most serious neurological conditions have early warning signs and it is important, that family physicians pick up these signs so that early diagnosis through relevant investigations and correct treatments through appropriate referrals can be made. These can be life saving in many neurological conditions. Therefore this book starts with a sections on symptoms and elaborates on what these symptoms can be due to. There have been many rapid advances in the pharmacological treatments of neurological problems and a whole lot of new investigations are now available. Therefore, separate sections on these two important aspects have been included in the book. This will help family physicians make better informed prescriptions and ask for more focused investigations. There is a section on how to manage emergencies in the clinic as well as a separate section on some of the important neurological conditions such as stroke, brain tumors etc. The recent few years have also seen many new developments in treatments of neurological conditions that were earlier considered incurable. The availability of safer and more effective surgical techniques such as Microneurosurgery and Minimally invasive neurosurgery along with the recent evolution of revolutionary technologies such as Stem Cell Therapy have completely changed the overall methods of management as well as prognosis in the management of neurological disorders. We have therefore, included a section on recent advances so that family physicians can guide their patient's as to what are the best available treatments for their ailments. Wishing all our family physician friends and colleagues - 'A Happy and Informative Reading'!

Dr. Alok Sharma
(9820046663 / alok276@gmail.com)

Dedication

Dedicated to two outstanding human beings
(who also happened to be my grandfathers)

Dr. Gian Chand Sharma (New Delhi)
(1903 - 1972)



A Family Physician, General Practitioner from Karol Bagh, New Delhi who became my role model as to how a doctor should be.

From whom I learnt what is caring, compassion, healing and selfless service

Whose words to me I still remember : *"Never look at a patient as a source of 5 rupees. Patients come to a doctor in pain and suffering. Ease this suffering and god will look after your needs"*

Shri Sai Das Sharma, (Itarsi Madhya Pradesh)
(1887 -1966)

A Police Officer from Itarsi, Madhya Pradesh whose last wish inspired me to take up medicine as a career.

From the story of whose life I learnt the meaning of the words integrity, character, honesty, devotion and commitment.

Whose suffering and death from a late diagnosed malignancy taught me of the important role that a family physician could make in the life's of ordinary people by making early diagnosis of serious conditions.

– Professor Alok Sharma

Scientific Publications on Stem Cell Therapy In Neurological Disorders by the Authors

A) AUTISM

1. Alok Sharma, NandiniGokulchandran, Hemangi Sane, Anjana Nagrajan, Amruta Paranjape, Pooja Kulkarni, Akshata Shetty, Priti Mishra, Mrudula Kali, Hema Biju, Prerna Badhe. Autologous bone marrow mononuclear cell therapy for autism - an open label proof of concept study. Stem cell international. 2013 (2013), Article ID 623875, 13 pages.
2. Alok Sharma, NandiniGokulchandran, PrernaBadhe, PoojaKulkarni, Priti Mishra, Akshata Shetty and Hemangi Sane. An Improved Case of Autism as Revealed by PET CT Scan in Patient Transplanted with Autologous Bone Marrow Derived Mononuclear Cells. J Stem Cell Res Ther 2013, 3:2
3. Alok Sharma, Nandini Gokulchandran, Akshata Shetty, Hemangi Sane, Pooja Kulkarni and Prerna Badhe. Autologous Bone Marrow Mononuclear Cells may be Explored as a Novel. Potential Therapeutic Option for Autism. J Clin Case Rep 2013, 3:7
4. Alok Sharma, Nandini Gokulchandran, Hemangi Sane, Pooja Kulkarni, Nancy Thomas, Amruta Paranjape, Prerna Badhe. Intrathecal autologous bone marrow mononuclear cell transplantation in a case of adult autism. Autism open access. 2013, 3:2
5. Alok Sharma, Nandini Gokulchandran, Hemangi Sane, Pradnya Bhovad, Hema Biju,Akshata Shetty, Mrudula Kali and Prerna Badhe, Cell therapy effects portrayed on positron emission tomography computerized tomography scan of the brain serve as a new dimension for autism: A case report. Journal of Paediatric Neurology, (2014) (In Press).
6. Sharma A, Gokulchandran N, Shetty A, Kulkarni P, Sane H, Badhe P. Neuropsychiatric Disorder Tackled by Innovative Cell Therapy - A Case Report in Autism. The Journal Stem Cell Research and Transplantation. 2014 July (In Press)

B) CEREBRAL PALSY

1. Alok Sharma, Hemangi Sane, Nandini Gokulchandran, Prerna Badhe, Pooja Kulkarni and Amruta Paranjape. Stem Cell Therapy for Cerebral Palsy - A Novel Option. Cerebral Palsy. Challenges for the future. 2014: 217-242.
2. Alok Sharma, Hemangi Sane, Amruta Paranjape, Nandini Gokulchandran, Pooja Kulkarni and Anjana Nagrajan, Prerna Badhe. Positron Emission Tomography - Computer Tomography scan used as a monitoring tool following cellular therapy in Cerebral Palsy and Mental Retardation - A Case Report. Case Reports in Neurological Medicine. Volume 2013, Article ID 141983, 6 pages

3. Dr. Alok Sharma, Ms. Pooja Kulkarni, Dr. Hemangi Sane, Dr. Nandini Gokulchandran, Dr. Prerna Badhe, Dr. Mamta Lohia, Dr. Priti Mishra. Positron Emission Tomography - Computed Tomography scan captures the effects of cellular therapy in a case of cerebral palsy. Journal of clinical case reports. 2012 J Clin Case Rep 2:195.
4. Alok Sharma, Hemangi Sane, Pooja Kulkarni, Myola D'sa, Nandini Gokulchandran, Prerna Badhe. Improved Quality of Life in a Case of Cerebral Palsy after bone marrow mononuclear cell transplantation. Cell Journal. 2015; 17(2) (In Press)
5. Alok Sharma, Hemangi Sane, Nandini Gokulchandran, Pooja Kulkarni, Sushant Gandhi, Jyothi Sundaram, Amruta Paranjape, Akshata Shetty, Khushboo Bhagawanani, Hema Biju and Prerna Badhe. A clinical study of autologous bone marrow mononuclear cells for cerebral palsy patients: a new frontier," Stem Cells International, Jan 2015 (in press)

C) MUSCULAR DYSTROPHY

1. Dr. A. Sharma, Ms. P. Kulkarni, Dr. G. Chopra, Dr. N. Gokulchandran, Dr. M. Lohia, Dr. P. Badhe. Autologous Bone Marrow Derived Mononuclear Cell Transplantation In Duchenne Muscular Dystrophy-A Case Report. Indian journal of Clinical Practice 2012; 23 (3): 169-72
2. Dr. Suvarna Badhe, Ms. Pooja Kulkarni, Dr. Guneet Chopra, Dr. Nandini Gokulchandran, Dr. Alok Sharma Dystrophin Deletion mutation pattern and Cardiac involvement in 46 cases of Dystrophinopathies. Asian journal of clinical cardiology. Asian Journal of Clinical Cardiology, Vol. 15, No. 6, October 2012: 211-214
3. Alok Sharma, Hemangi Sane, PrernaBadhe, Nandini Gokulchandran, Pooja Kulkarni, Mamta Lohiya, Hema Biju, V.C.Jacob. A Clinical Study Shows Safety and Efficacy of Autologous Bone Marrow Mononuclear Cell Therapy to Improve Quality of Life in Muscular Dystrophy Patients. Cell Transplantation. 2013; Vol. 22, Supplement 1, pp. S139-S146.
4. Alok Sharma, Amruta Paranjape, Hemangi Sane, Khushboo Bhagawanani, Nandini Gokulchandran, and Prerna Badhe. Cellular Transplantation Alters the Disease Progression in Becker's Muscular Dystrophy. Case Reports in Transplantation. Volume 2013, Article ID 909328, 7 pages
5. Sharma A., Sane, H., Paranjape, A., Badhe, P., Gokulchandran, N., & Jacob V. Effect of Cellular Therapy seen on Musculoskeletal Magnetic Resonance Imaging in a Case of Becker's Muscular Dystrophy.Journal of Case Reports, 2013 3(2), 440-447.
6. Alok Sharma, Hemangi Sane, Amruta Paranjape, Khushboo Bhagwanani, Nandini Gokulchandran, Prerna Badhe. Autologous bone marrow mononuclear cell transplantation in Duchenne muscular dystrophy - a case report. American journal of case reports. 2013 (Ahead of Print)

D) SPINAL CORD INJURY

1. Alok Sharma, Prerna Badhe, Pooja Kulkarni, Nandini Gokulchandran, Guneet Chopra, Mamta Lohia, V.C.Jacob. Autologous Bone marrow Derived mononuclear cells for the treatment of Spinal Cord Injury. The Journal of Orthopaedics. 2011; 1(1): 33-36
2. Sharma A, Gokulchandran N, Sane H, Badhe P, Kulkarni P, Lohia M, Nagrajan A, Thomas N. Detailed analysis of the clinical effects of cell therapy for thoracolumbar spinal cord injury: an original study. Journal of Neurorestoratology. 2013;1:13-22
3. Sharma A, Sane H, Gokulchandran N, Kulkarni P, Thomas N, et al. (2013) Role of Autologous Bone Marrow Mononuclear Cells in Chronic Cervical Spinal Cord Injury-A Longterm Follow Up Study. J NeurolDisord 1: 138.
4. Alok Sharma, Hemangi Sane, Dipti Khopkar, Nandini Gokulchandran, Hema Biju, V C Jacob, Prerna Badhe. Cellular therapy targeting Functional outcome in a case of Cervical Spinal Cord Injury. Advances in Stem Cells 2014 (In Press)
5. Alok Sharma, Hemangi Sane, DiptiKhopkar, NandiniGokulchandran, V. C. Jacob, Joji Joseph, PrernaBadhe. Functional recovery in chronic stage of spinal cord injury by Neurorestorative Approach. Case Reports in Surgery 2014 (In Press)

E) STROKE

1. Alok Sharma, Hemangi Sane, Anjana Nagrajan, et al. Autologous Bone Marrow Mononuclear Cells in Ischemic Cerebrovascular Accident Paves Way for Neurorestoration: A Case Report, Case Reports in Medicine, vol. 2014, Article ID 530239, 5 pages, 2014. doi:10.1155/2014/530239
2. Alok Sharma, Hemangi Sane, Nandini Gokulchandran, Dipti Khopkar, Amruta Paranjape, Jyothi Sundaram, Sushant Gandhi and Prerna Badhe Autologous Bone Marrow Mononuclear Cells Intrathecal Transplantation in Chronic Stroke. Stroke Research and Treatment, Volume 2014, pages 1-9
3. Dr. Alok Sharma, Dr. Hemangi Sane, Dr. Prerna Badhe, Ms. Pooja Kulkarni, Dr. Guneet Chopra, Dr. Mamta Lohia, Dr. Nandini Gokulchandran. Autologous Bone Marrow Stem Cell Therapy shows functional improvement in hemorrhagic stroke – a case study. Indian Journal of Clinical Practice, 2012:23(2):100-105

F) MISCELLANEOUS

1. A. Sharma, P. Kulkarni, N. Gokulchandran, P. Badhe, V. C. Jacob, M. Lohia, J. George Joseph, H. Biju, G. Chopra. Adult Stem Cells for Spinal Muscular Atrophy. Bangladesh Journal Of Neuroscience. 2009; 25(2): 104-107
2. Sharma A, Gokulchandran N, Kulkarni P, Chopra G. Application of autologous bone marrow stem cells in giant axonal neuropathy. Indian J Med Sci 2010; 64 : 41-4

3. Alok Sharma, Guneet Chopra, Nandini Gokulchandran, Mamta Lohia, Pooja Kulkarni. Autologous Bone Derived Mononuclear Transplantation in Rett Syndrome. Asian Journal of Paediatric Practice. 2011; 15 (1): 22-24

4. A. Sharma, P. Badhe, N. Gokulchandran, P. Kulkarni, V.C Jacob, M. Lohia, J. George Joseph, H. Biju, G. Chopra. Administration of Autologous bone marrow stem cells intrathecally in Multiple Sclerosis patients is safe and improves their quality of life. Indian Journal of clinical Practice. 2011:21(11):622-625

5. Alok Sharma, Prerna Badhe, Omshree Shetty, Pooja Vijaygopal, Nandini Gokulchandran, V.C. Jacob, Mamta Lohia, Hema Biju, Guneet Chopra. Autologous bone marrow derived stem cells for motor neuron disease with anterior horn cell involvement. Bombay hospital journal. 2011; 53(1): 71- 75

6. Alok Sharma, Nandini Gokulchandran, Guneet Chopra, Pooja Kulkarni, Mamta Lohia, Prerna Badhe, V .C. Jacob. Administration of autologous bone marrow derived mononuclear cells in children with incurable neurological disorders and injury is safe and improves their quality of life. Cell Transplantation, 2012; 21 Supp 1: S1-S12.

7. Alok Sharma, Prerna Badhe, Nandini Gokulchandran, Pooja Kulkarni, Hemangi Sane, Mamta Lohia, VineetAvhad. Autologous bone marrow derived mononuclear cell therapy for vascular dementia – Case report. Journal of stem cell research and therapy. J Stem Cell Res Ther 2012. 2:129.

8. Alok Sharma, Hemangi Sane, Amruta Paranjape, Nandini Gokulchandran, Mansi Takle, Prerna Badhe, Seizures as an adverse event of cellular therapy in pediatric neurological disorders and its prevention. Journal of Neurological Disorders. 2014 2(164), 2.

9. Alok Sharma, Hemangi Sane, Pooja Kulkarni, Jayanti Yadav, Nandini Gokulchandran, Hema Biju, Prerna Badhe. Cell therapy attempted as a novel approach for chronic traumatic brain injury - a pilot study. SpringerPlus Jan 2015 (in press)

10. Alok K Sharma, Hemangi M Sane, Amruta A Paranjape, Nandini Gokulchandran, Anjana Nagrajan, Myola D'sa, Prerna B Badhe. The effect of autologous bone marrow mononuclear cell transplantation on the survival duration in Amyotrophic Lateral Sclerosis - a retrospective controlled study. Am J Stem Cells 2015;4(1) (In press)

Contents

Section A

Neurological Symptoms & Their Management by the family physicians

1. Headache

Headache is one of the most common presenting symptoms of neurological disorders. Whereas the majority of them are innocuous and need only symptomatic treatment, some can be a sign of serious underlying disorders and therefore headaches should always be taken seriously. A headache is a pain in the head radiating above the eyes or the ears, behind the head or in the back of the upper neck.

When treating a patient with headache the first question in our mind should be - is it a **Primary headache** or is it a **Secondary headache**?

Primary headaches are not associated with any underlying major disease. Examples of primary headaches are tension headaches, migraine and Cluster headches. Secondary headaches are caused due to some other underlying disease. These may be minor ones such as uncorrected ophthalmic refractory error, sinusitis, withdrawal from caffeine and discontinuation of analgesics. They may also be symptomatic of major illnesses such as brain tumors, strokes, meningitis, and subarachnoid hemorrhages.

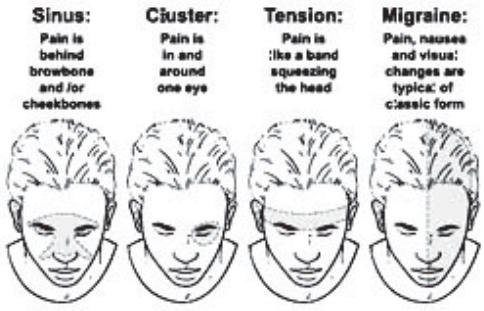


Fig. 1.1

Common types of Headaches:

1. Tension Headache:

It is the most common type of headache and occurs due to muscle tension producing ischemia of the scalp and facial muscles. It may have a band like discomfort and is not associated by any other symptom, patient is able to continue his/her normal activity. This type of headache builds slowly and may become severe.

These are generalized headaches of gradual onset and can be of mild to moderate severity. They are described by the patients as aching or pressure type of headache and are always non pulsatile. They last from one to two hours and occur during the later part of the day. They may be associated with grinding of the teeth, lack of sleep and difficulty in concentration. There is always some major underlying emotional or psychological cause which may be family or work related. Neurological examination does not reveal any abnormality.

Investigations: *None*

Treatment:

[1] Paracetamol 500mg 1 TDS for mild pain,

[2] Combination of Paracetamol & Codeine 1 TDS for mild to moderate pain,

[3] Paracetamol +Acelofenac 1BD for moderate pain

[4] Naproxen 1 BD for moderate to severe pain

[6] Amitriptyline 25 mg 1 QHS if difficulty to sleep

[7] Counseling / relaxation exercises / tranquilizers/ lifestyle changes may be helpful.

Referal:

Non responsive headaches to regular treatment or persistent severe progressive headache.

2. Migraine Headache

Migraine is an inflammatory disorder of the brain and its blood vessels, which results in hyper reactivity of the cerebral blood vessels. It is classified as a common migraine (migraine without aura), classical migraine (migraine with aura) and complex migraine.

Classical migraine headaches are throbbing in nature, mostly unilateral and often associated with flashes of light. Aura, nausea and vomiting, photo/phonophobia, scalp tenderness may be present in some of the cases. In the complicated migraine there are associated neurological signs and symptoms caused by vasoconstriction of intracranial vessels such as confusion, amnesia, transient monocular blindness, hemiparesis and limb paraesthesias. Migraine can be precipitated by red wine,menses,hunger,insomnia,perfumes, etc. A migraine typically lasts from 4 to 72 hours.

Investigations:

None for common or classical migraine. In complex migraine CT Scan/MRI scan may be done to rule out structural lesions if there is no relief.

Treatment:

Symptomatic relief (once attack starts). [1] Analgesics & NSAID's [2] Rest in a quiet,

dark room if possible, [3] Triptans-are prescribed for acute attack in the early stage. They should not be given in complicated migraine. (Sumatriptan 25mg, Zolmitriptan 5mg, Rizatriptan 5mg [4] Ergotamines (Dihydro ergotamine preferred in status migraine), [5] Isometheptene [6] Sedatives, [7]Antiemetics

(Practical management for acute attack:- :[1] Rizatriptan 10 mg stat followed by Naproxen and Tab Pantoprazole for 1-2 days)

Prevention:

[1] Identify and avoid trigger factors such as exposure to sunlight, delayed meals, delayed sleep, foods such as caffeine, cheese, chocolates, chinese food etc

[2] Prophylactic medications-Those patients who have more than one migraine per week should be put on prophylactic medications such as B-blockers, calcium channel blockers, tricyclic antidepressants, SSRI's ,anticonvulsants.

Practical management for migraine prophalaxis: Propranolol slow release 40 mg one tablet in the morning for 3 months + Amitryptline 10mg 1 hs or Flunarizine 10 mg HS

Referal:

Persistent migraine not responding to medications and migraine with associated other signs.

3. Headache due to uncorrected refractory error

The headache comes as after watching TV, reading for long. Is dull, aching, bilateral and may be bifrontal or generalized.

Investigations: *None*

Treatment: *Analgesics*

Referal:

Ophthalmologist or an optician for correction.

4. Headache due to Sinusitis

These are bifrontal headaches which are gradual in onset, moderate in severity, dull and boring in nature and associated with pain or pressure in the face. There is history of frequent cold with nasal discharge. Presence of tenderness on the sinuses (frontal,maxillary), sides of the nose is noticed on examination.

Investigations:

[1] Plain X-ray of Paranasal sinuses (PNS), [2] CT Scan PNS

Treatment:

[1] Analgesics, [2]Antihistaminic, [3] Antibiotics – All For seven days.

Practical management:-a combination of diclofenac tds, sulfamethoxazole + trimethoprim or amoxicillin and clavulanate – bd, fexofenadine (allegra) or pheniramine (avil) –qhs is a good combination.

Referal:

If there is no improvement even after seven days of the above treatment then refer to ENT surgeon for evaluation.

5. Headaches due to Hypertension

One of the early signs of Hypertension are Headaches. The classical feature of Hypertension headaches is that they occur early in the morning. They may present as pressure just behind the eyes or as headaches at the back of the head. They are sometimes associated by dizziness and palpitations . The headache may be mild or severe and occur more commonly in women than men. Any patient over 50 presenting with morning headaches should always have their blood pressure checked.

Investigations:

Regular monitoring of BP.

ECG, 2 D Echo , Stress test , Lipid Profile and Other cardiac investigations may be indicated in some cases.

Treatment :-

No analgesics

Medications for hypertension

Counseling for Lifestyle changes to reduce stress levels

Referral

If despite the above the BP remains high and headaches persist then the patient should be refereed to a cardiologist for further management.

It is important to note that Hypertension headaches are one type of headaches for which painkillers should not be given since they suppress only the symptoms and do not take care of the serious issue of hypertension. The treatment of hypertension headaches is control of hypertension and it has been noted that once the blood pressure is lower, the headache get relieved.

6) Cluster headache

These are episodic pain attacks at periorbital region it is usually excrutiating and deep and pulsatile in nature,pain is unilateral and lasts for 30 minutes to 2 hours.there are associated symptoms like lacrimation,redness of eye,nasal stuffiness,ptosis,and nausea.Alcohol provokes the attack.

Treatment:

Acute attack- [1] 100% oxygen for 10-15 mins, [2] Sumatriptan 6mg subcutaneous injection stat.

Prevention:

Prednisone 40mg/day for 5 days tapered over 3 weeks. [2] Indomethacin 75 mg/ day [3] others-lithium and ergotamine.

6) Trigeminal Neuralgia

Unilateral severe lancinating pain around the face, lips, gums. It is aggravated by a tickle or touch, pain burst happen over seconds to minutes with a refractory period afterwards. There may be associated flushing, salivation or lacrimation.

Investigation:

MRI/ CT scan must be done to rule out CP angle tumor.

Treatment:

[1] carbamazepine 100 mg BD [2] gabapentin 100 mg TDS [3] Others- Antidepressants- Ametreptonin, fluoxetine, clonazepam. [4] Avoid stimulation of trigger zone by air, heat or cold [5] In some cases surgical intervention may be required- nerve block, surgical decompression.

Referral:

Should be referred to neurophysician or neurosurgeon.

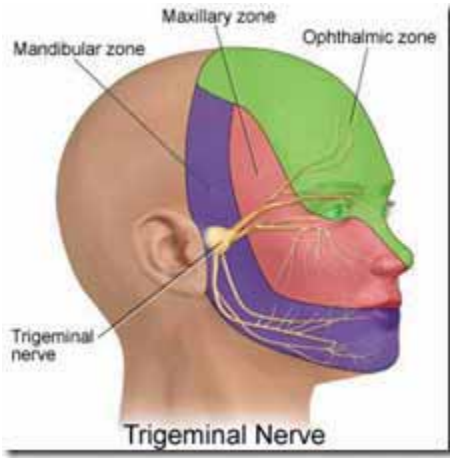


Fig. 1.2

Headaches due to serious underlying conditions:

Conditions causing secondary headaches are brain stroke, subarachnoid intracranial hemorrhage , brain tumors, meningitis, severe high blood pressure. These can cause

serious brain damage or even death. Thus, timely and accurate diagnosis of secondary headaches is crucial. Special blood tests, brain scans, and lumbar puncture (spinal tap) are necessary to establish these diagnoses. One should rely upon information obtained from the initial patient history and physical examination.

Common causes of serious headache:

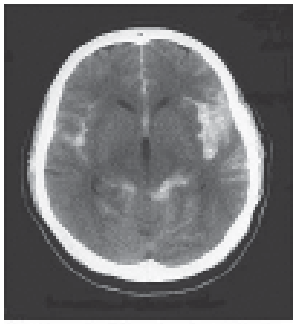
1) Sentinel headache due to subarachnoid haemorrhage

Sentinel headache (SH) is characterized as sudden (thunderclap headache), intense, and persistent headache, preceding spontaneous subarachnoid hemorrhage (SAH) by days or weeks. It is often described as the "worst headache of my life". It is the most common symptom to manifest 10-20 days before rupture of an aneurysm. In addition to headaches, sentinel leaks may produce nausea, vomiting, photophobia, malaise, or neck pain. These symptoms can easily be ignored by a physician. Therefore, a high index of suspicion is necessary to diagnose this type of headache due to subarachnoid haemorrhage.

The diagnosis of SAH should be based upon the following seven characteristics:

- Aged >=40 years
- Witnessed loss of consciousness
- Complaint of neck pain or stiffness
- Onset of manifestations with exertion
- Arrival by ambulance
- Vomiting
- Diastolic blood pressure ≥ 100 mm Hg or systolic blood pressure ≥ 160 mm Hg

The possibility of SAH should be suspected if any one or more of these is present along with acute nontraumatic headache which reaches maximum intensity within one hour, and the patient be referred to a neurophysician and hospitalized immediately.



Misdiagnosis of a subarachnoid brain hemorrhage, like the one shown on the right side of this CT scan, can lead to severe disability or death.

Fig. 1.3

2) Meningitis

Acute severe type of headache with neck stiffness and fever suggests meningitis. Meningitis may be mistaken as migraine sometimes due to the chief symptoms like pounding headache, photophobia, nausea, vomiting, etc. This requires hospitalisation and so patient should be referered to neurology department.

3) Tumours

Profound pounding dull, aching, or throbbing headache of medium intensity which worsens with exertion and change of position and may be associated with nausea or vomiting may suggest an intracranial tumour. The headaches may become more frequent, increasing in severity, and not easily relieved. Patient gets disturbed from sleep. They can also be worsened by coughing or sneezing and persistently occur on the same side often. Vomiting that precedes headache is a characteristic of posterior fossa tumours. This type of headache should be immediately investigated and brought to the concern of a neurophysician or neurosurgeon.

4) Stroke

Headache with symptoms such as acute weakness and numbness in the limbs and/or face, nausea, vomiting, an altered level of consciousness, may indicate increased intracranial pressure and are more common with hemorrhagic strokes and large ischemic strokes.

A detailed medical history of patient for identifying following risk factors of stroke should be acquired to suspect a stroke:

- Hypertension
- Diabetes mellitus
- Tobacco use
- High cholesterol
- History of coronary artery disease, coronary artery bypass, or atrial fibrillation
- Recent trauma
- Coagulopathies
- Illicit drug use (especially cocaine)
- Migraines
- Oral contraceptive use

In the presence of these risk factors and clinical presentation, the patient should be immediately hospitalized to prevent stroke and its life threatening effects.

5) Temporal arteritis

It is an inflammatory condition of arteries which involves the extracranial carotid circulation. Temporal arteritis presents with classical symptoms - headache, jaw

claudication, scalp tenderness, and visual disturbances. Fever, myalgia, anorexia, weight loss, anemia, and malaise may also occur as systemic inflammatory response. Temoral arteritis should be distinguished from systemic infections, connective tissue diseases, and compressive intracranial malignancies, etc by further clinical examination, blood and CSF testing, and neuroimaging. Temporal arteritis usually occurs in older people and is extremely rare in individuals younger than 50 years of age, and present with visual changes. If not treated, patient may develop partial or complete blindness due to involvement of ophthalmic artery or its branches. Therefore, immediate hospitalisation and referral is a must in this case.

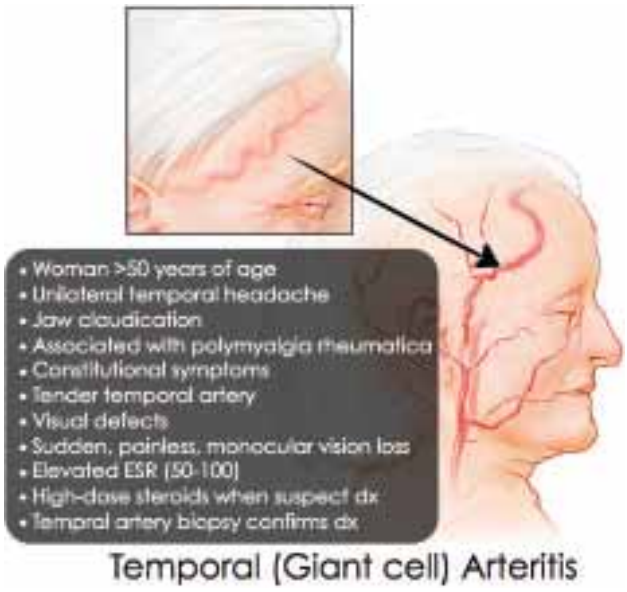


Fig. 1.4

Information that should be taken by the doctor includes:

1. The mode of onset of the headache: For example, patients with a subarachnoid hemorrhage typically report having a sudden onset of severe headache ("the worst headache ever").
2. The location of the headache: (on one side or both sides of the head). Headaches that persistently occur on the same side often are secondary headaches associated with one sided lesions such as brain tumors.
3. Associated fever and neck stiffness: Bacterial meningitis is a rapidly progressive and life-threatening disease with fever, headaches, stiff neck, and deterioration in mental function.
4. Associated mental deterioration, seizures, or weakness of the extremities or face, which can be symptoms of brain tumors.
5. Associated temporary weakness of the extremities or facial muscles, which can be symptoms of transient ischemic attacks.
6. Recent head injury: Headaches soon after injury to the head may be caused by subdural or epidural hematomas.
7. The age of the patient: Temporal arteritis typically occurs in older people and is extremely rare in individuals younger than 50.

Headaches those are different in severity and intensity need urgent attention,

investigations and reference.

Investigations:

[1] CT scan of the head. Should be done whenever the headache sis different in severity and character and also for late onset headches. CT scan of the head is useful for detecting accumulation of blood such as subdural hematomas and subarachnoid hemorrhages. It is moderately useful in detecting brain tumors and strokes not due to hemorrhage.[2] MRI scan of the head. An MRI scan of the head can detect infections of the brain, strokes and tumors. It is not so useful for acute hemorrhage. [3] Lumbar puncture. In some patients with subarachnoid hemorrhage, CT scans are normal, and lumbar punctures are necessary to demonstrate blood from the hemorrhage that has spread throughout the cerebro-spinal fluid(CSF). CSF is also useful for diagnosis of meningitis, it shows decreased sugar levels, increased proteins and increased cells (if major are polymorphs then it suggests Bacterial meningitis and if there are lymphocytes then it suggests Tubercular meningitis).

Treatment:

Specific treatment of the cause of the headache.

Referal:

Refer to Neurophysician or Neurosurgeon.

Drugs useful in symptomatic treatment of headache:

(A) General

[1] Paracetamol, [2] Paracetamol+ codeine, [3]Paracetamol +Acelofenac [4] Naproxen [5] Diclofenac (Brufen is not useful in headaches, except those due to sinusitits, and can in fact make some headaches worse)

(B) Specific

[1]Anti Migraine therapy, [2] Steroids, [3] Muscle relaxants, [4] Tricyclic anti depressants, [5] Anticonvulsants

Warning signs

1) Headache with fever with neck stiffness.
2) Sudden serious acute headache associated with vomiting and neck stiffness.
3) Headache after lumbar puncture which is relieved by lying down this type of headache is called spinal headache which is relieved by analgesics and plenty of fluids
4) Headache with projectile vomiting suspect for increased intracranial pressure this type of headache may be worst on lying down.

5) Headache which is localised and aggravated on chewing temporal arteritis.

6) Headache with neurodeficit.

7) Headache with high BP. More than 160/100

Summary

1] Sometimes a headache is a warning sign of something serious like stroke, brain tumors etc. so it should not be taken lightly. One should act promptly in diagnosing as well as treating the underlying cause. [2] Any patients whose headaches do not get relieved or worsen within 3 days of initial management should have a CT Scan done and should be referred to a Neurosurgeon or Neurophysician. [3] Sudden onset severe headaches are a sign of a possibly serious underlying disorder and must be investigated with a scan or referred to a Neuro consultant immediately. [4] for mild headaches the investigations to be done are (a) ESR, (b) Xrays PNS, (c) Check up by optician / opthalmologist for refractory error, [5] for severe headaches a CT Scan brain (plain & contrast) should be done.

Sample Prescription

Tension Headache

Rx

Tb Paracetamol 500mg 1—1—1 x 1 week (for mild headache) or

Tb Paracetamol (500mg) + Codeine (8mg) 1—1—1 x 1 week (for moderate) or

Tb Paracetamol(500mg) + Aceclofenac(100mg) 1—0—1 x 1 week(for severe) or

Tb Naproxen (500mg) 1—0—1 x 1 week (for severe headache)

Tb Amitriptyline 25 mg 0—0—1 x 1 week (if difficulty in sleeping)

Tb Pantoprazole 40 mg 1—0—1 x 1 week

Migraine headache

Rx

Acute attack

Tb Rizatriptan 10mg 1 tablet stat followed by Tb Naproxen 250mg 8 hourly with

Tb Pantoprazole 40 mg 1—0—1

Migraine prophylaxis

Tb Propranolol 40 mg(slow release) 1—0—0 x 3 months with

Tb Amitriptyline 10 mg 0—0—1 x 1 month or Tb Flunarizine 10 mg 0—0—1 x till relief is obtained

Tb Pantoprazole 40 mg 1—0—1 x 1 week

Cluster Headache

Rx

Tb Prednisone 40 mg 1—0—0 x 5 days (tapered over 3 weeks)

Tb Pantoprazole 40 mg 1—0—1 x 1 month

Refer to the neurologist.

2. Giddiness

Giddiness or lightheadedness, a very common symptom seen in practise, is a term used to describe a sensation of altered orientation in space usually described by the patient as "chakar". Giddiness, lightheadedness, disequilibrium and syncope are often mistaken for one another; most often caused by relative decrease in sensorium and are caused by different conditions.

The important enquires to be made are (a) whether there is a sense of the external environment rotating or spinning, (b) whether there is an associated loss of consciousness and (c) whether there are any preexisting medical, cardiac or neurological disorders.

A) Vertigo/ Dizziness is hallucination of movements which results in sensation of external environment spinning and rotating and is mostly caused by an otological disorder and sometimes by CNS disorders.

B) Disequilibrium is a sense of imbalance observed while walking due to cerebellar or spinal disorders effecting sensory proprioception.

C) Syncope which is loss of consciousness occurs secondary to inadequate cerebral profusion, a common cause of which is postural hypertension and cardiogenic factors.

Fig. 2.1

Examination

1) Physician should check the blood pressure in all positions to see postural hypotension.
2) Neurological examination to rule out any neurological deficit and to rule out secondary cause
3) ENT for otitis media or labyranthitis
4) Eye examination-to look for nystagmus,refractive error any visual deficit
5) ECG to rule arrhythmias and other causes.
6) See on what medications patient is on,medications as many of the drugs itself can cause dizziness.

Causes of Vertigo:

The three systems that are involved are the brain, the cervical spine and the inner ear.

1. Inner ear or vestibular dysfunction:

a. BPPV (Benign paroxysmal positional vertigo):

It is caused by displacement of otoconia into the posterior semi circular canal and it manifests as a rotational dizziness. The patient complains that the surroundings seem to rotate.

The key distinguishing feature is that it is positional. There is severe vertigo only in same positions of the head (i.e. right or left). In addition to vertigo, symptoms of BPPV may include dizziness (lightheadedness), imbalance, difficulty concentrating, and nausea.

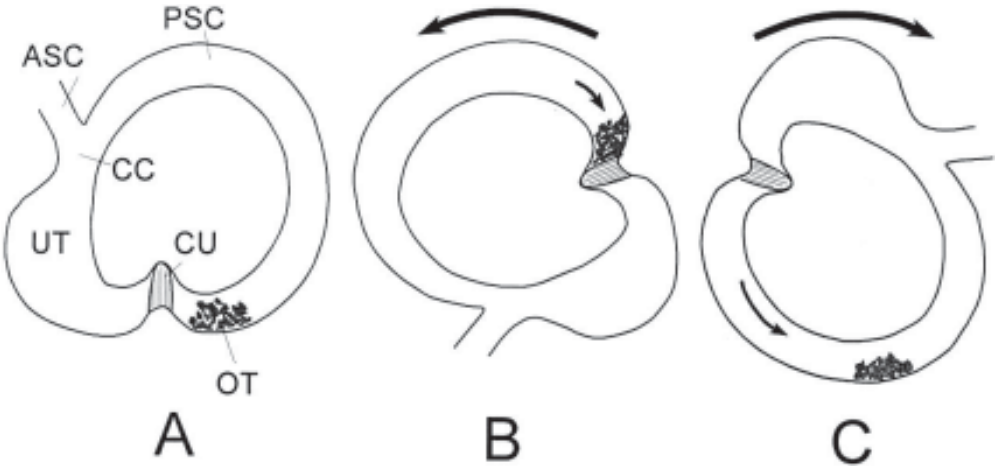


Fig. 2.2

Provocative factors: Vertigo symptoms are precipitated by changing the head's position with respect to gravity like looking up, rolling over or getting out of bed.

Causes of BPPV in young adults include head injury, and age-related degeneration of the otolithic membrane in older adults, surgical trauma, etc. It may also develop after long periods of inactivity.

Diagnosis: BPPV is diagnosed based on medical history, physical examination, vestibular and auditory tests. If vertigo does not respond to standard medicine or there are other associated neurological signs, then workup needs to be done to rule out other diagnoses.

1. Vestibular tests which include the Dix-Hallpike maneuver and the Supine Roll test, observe the nystagmus elicited in response to a change in head position. The semicircular canal involved in vertigo can be identified by these tests.
2. Audiogram: if it shows sensory neural deafness then get the following

a. SISI: if positive suggests a cochlear problem.

b. TDT testing: positive suggests a retrocochlear problem

3. An MRI scan will be needed to rule out other problems such as a stroke or brain tumour. MRI brain with gadolinium contrast can be ordered to evaluate for C P angle tumor.
4. Blood tests: CBC and serum electrolytes

Treatment:

[1] Tb Meclizine 25 to 50 mg orally every 4 to 6 hours

[2] Perform Epley's maneuver:

Start with patient sitting on couch. Turn patient's head (45 degrees) toward affected side. Pause in this position for 30 seconds. Lie patient flat, support the head throughout. Head remains turned to affected side and is hanging off end of couch. Pause in this position for 30 seconds. Turn the patient's head (90 degrees) towards the good ear. Pause in this position for 30 seconds. Keeping head looking in same direction, ask patient to gently move to lie on shoulder of good side, looking at floor, with chin close to shoulder. Pause in this position for 30 seconds. Gently bring patient to sitting position. Ensure head position does not change relative to trunk. Pause for 30 seconds. Finally, turn head to centre and flex neck to put chin on chest in one movement. Pause for 30 seconds

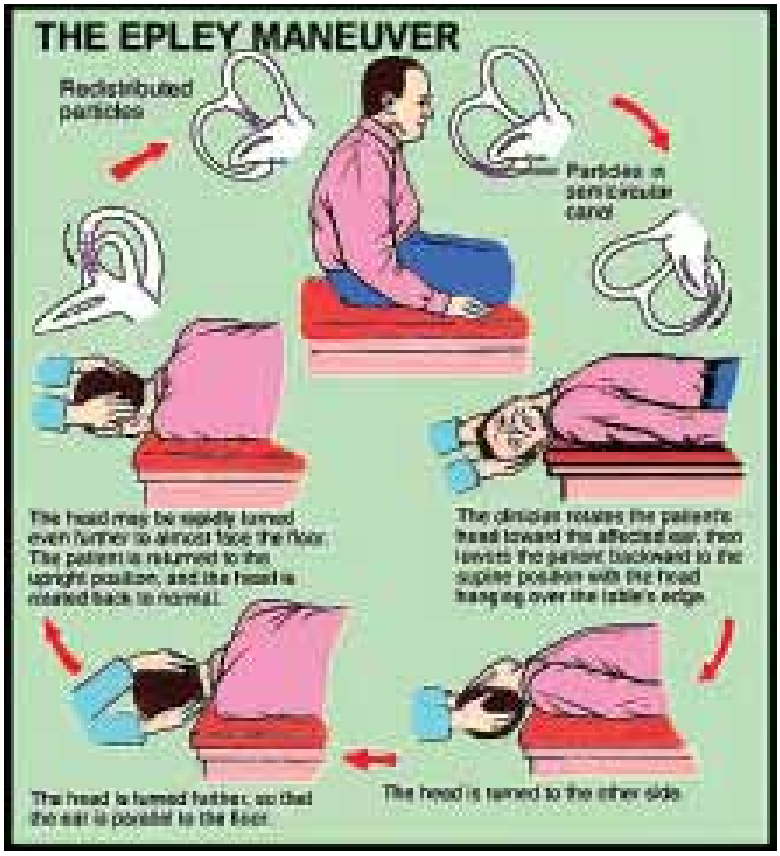


Fig. 2.3

[3] Vestibular rehabilitation

Precautions: The patient should be asked to sleep in an elevated position with two or more pillows and not on the side of the treated ear. A cervical collar should be given to avoid quick movements like looking up or down or head rotation.

Referal : Refer to ENT consultant.

b. Meniere's disease:

It is caused by collection of fluid in the inner ear. Presents with a combination of severe vertigo, tinnitus and nausea.

Causes

Cause is unknown, recent theory is intracranial compression of balance nerve by blood vessel

Signs & symptoms

- Hearing loss
- Vertigo

- Ear fullness
- During severe attack there may be pallor, sweating, nausea, vomiting and falling.

Investigations: Audiogram

Treatment: [1] Vertin TDS x 7 days. [2] Salt restriction (less than 1 to 2 gms sodium/ day) [3] Others- diuretics (most commonly hydrochlorothiazide/triamterene) Intratympanic dexamethasone or gentamicin,[4] In severe cases endolymphatic sac surgery

Referal: if no relief then refer to ENT consultant.

c. Labrinthitis:

Inflammation of the vestibular labyrinth(a system of intercommunicating cavities & canals in the inner ears). Clinically, patient experiences disturbances of balance and hearing to varying degrees and may affect 1 or both ears.

Causes

- **Physiological-**mismatch of vestibular,visual and somatosensory systems triggered by an external stimulus,such as a stop after whirling turns,heights,motion sickness
- **Pathological-**imbalance in vestibular system caused by a lesion within vestibular pathways
- **Infections-**especially viral, mumps
- **Others**-Tumors,Vasculitis,Infarction,Ototoxic drugs,Head injury

Investigations : CBC,LFT,blood sugar,creatinine etc

Treatment

[1] Tb Meclizine 25 to 50 mg orally every 4 to 6 hours

[2] Tb Domperidone tds

[3] In some cases, antibiotic or antiviral may be given

Referal: refer to ENT consultant.

d. Vestibular neuritis

Vestibular neuritis is acute, sustained dysfunction of the peripheral vestibular system which presents as nausea, vomiting, and vertigo, and normal hearing. Vestibular neuritis is generally distinguished from labyrinthitis by preserved auditory function.

Treatment

Methylprednisolone initially 100 mg orally daily then tapered to 10 mg orally daily over 3 weeks

e. Migrainous vertigo:

Vertigo associated with migraine headache.

Treatment

[1] Tb Meclizine 25 to 50 mg orally every 4 to 6 hours

[2] Migraine prophylaxis with serotonin reuptake inhibitor 5-HT1 receptor agonists(triptans)

2. Cervical Spine

a. Cervical spondylosis:

In the older age group the most common cause of giddiness is cervical spondylosis. (this is the most commonly missed problem in routine practise). It is associated with pain in the back of the neck radiating to head, one of the shoulders and upper limbs along with tingling and numbness of both hands. In advanced stages wasting and weakness of the hands may occur.

Investigations:

1. Lateral and AP x-rays of cervical spine.
2. MRI cervical spine to be done if degenerative changes seen on the x-rays.

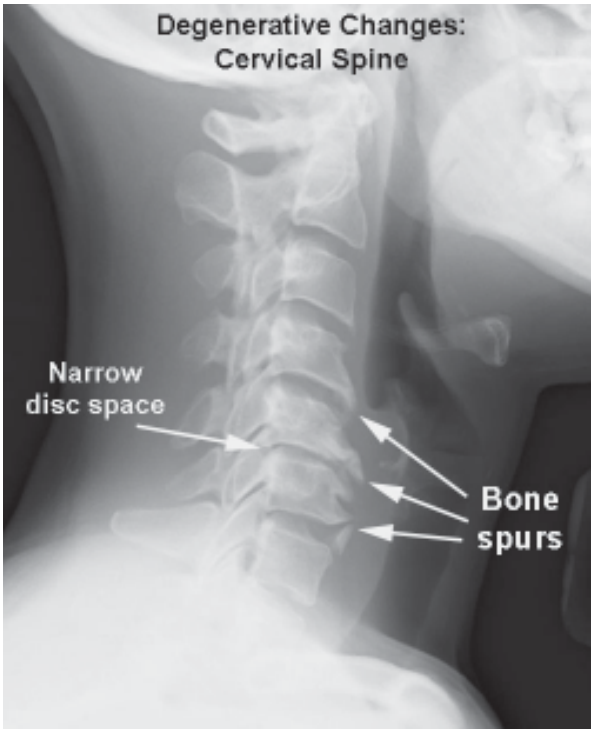


Fig. 2.4

Treatment:

1. Analgesics and Anti inflammatory combinations. (Brufen + paracetamol or diclofenec sodium)
2. Muscle relaxants (a)Methocarbamol 1 tab TDS (b)Chlorozoxanone 1 tab TDS (c) baclofen 10 mg TDS
3. Physiotherapy. (short wave diathermy, traction, neck exercises)
4. Soft cervical collar (till relief)

b. Other causes may include:

Cranio-vertebral junction anomalies**,** Atlanto-axial dislocation, Cervical spinal tuberculosis /tumors

3. Brain:

a. Vertebrobasilar insufficiency:

This results from decreased blood supply to brain from its posterior vascular supply .There is a sudden onset of dizziness with imbalance while walking along with nausea and vomiting. In advanced stages loss of consciousness may occur.

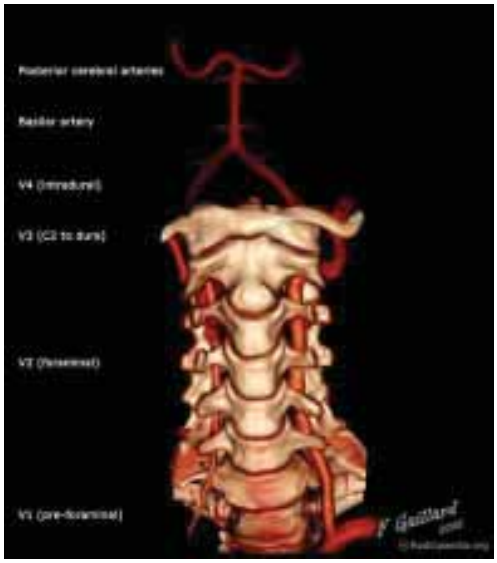


Fig. 2.5

Investigations: MRI brain with angiography.

Referal: Refer to neurosurgeon or neurophysician.

b. Other causes may include:

Cerebellar infarct**,** Brain stem infarct**,** C P angle tumor**,** Cerebellar hemorrhage**,** Basilar migraine**,** Seizure

4. Other causes of vertigo:

1. Orthostatic hypotension
2. Cardiac arrhythmias/ other cardiac problems
3. Hypoglycemia / other manifestations of Diabetes
4. Alcohol intoxication
5. Hyperventilation syndrome
6. Panic related
7. Drug toxicity(anticonvulsants,salicylates)
8. Medical conditions like Uremia.

Treatment

[1] Orthostatic hypotension

[2] Midodrine (promatine)titrated up to 10 mg orally 3 times a day

[3] Fludrocortisone initially 0.1 mg orally daily,titrated up weekly until peripheral edema develops or to a maximal dosages

Hyperventilation syndrome

Breathing control exercises, rebreathing into small paper bag, beta blockers,antianxiety agents eg serotonin reuptake inhibitors or short term benzodiazepines.

Management of Cardiovascular Disease

Management is beyond the scope of this book-refer to cardiologist

(B) Disequilibrium

Treatment of underlying cause is described in Section C.

(C) Syncope and pre syncope:

When loss of consciousness is temporary and there is spontaneous recovery it is called syncope. It may be preceded by symptoms like dizziness or faintness or "the presyncope". This occurs due to reduction of blood flow to the brain.

Presyncope symptoms vary in duration and may increase in severity until loss of consciousness. Symptoms may include light headedness, sweating, pale skin, blurred vision, nausea, vomiting, etc. These are usually brought about by hypotension with reduction of cerebral blood flow. Three-fourths of the systemic blood flow is contained in the venous bed and any interference in venous return may result in reduction in cardiac output.

Syncope must be differentiated from vertigo, coma, drop attacks, dizziness, sudden cardiac death, and seizures.

Neurological causes of syncope and pre syncope:

This condition is also known as 'neurally mediated hypotension', 'the fainting reflex', 'vasodepressor syncope', 'vasovagal syncope', or 'autonomic dysfunction'. The brainstem structures are supplied by vertebrobasilar arteries, which is responsible to maintain consciousness and which may cause syncope due to vascular disease.

Those who experience syncope may also have symptoms of focal neurologic ischemia such as arm and leg weakness, diplopia, ataxia, dysarthria, etc. Neurological causes should be suspected if headache or dizziness occurs during recovery from syncopal episodes.

In middle age, neurocardiogenic syncope remains the most frequent cause of syncope.

Common causes of syncope in elderly persons include orthostatic hypotension, postprandial hypotension, medications, carotid sinus hypersensitivity.

Other forms of neurocardiogenic syncope (so-called situational syncope) related to deglutition, micturition, defecation, and cough are more common in the middle-aged or elderly patients than in young patients

Neurocardiogenic syncope may occur in the following situations:

- after prolonged periods of standing
- after being in a hot summer weather, a hot crowded room, or a hot shower
- immediately after exercise
- after emotionally stressful situations
- after having food (since blood flow shifts to the intestinal circulation during the process of digestion)

How to diagnose

The Physician should look for emergency care in cases of massive internal haemorrhage. The position of the patient is also important. If a patient has syncope in supine position it may be due to seizure.

Key clinical features of neurocardiogenic syncope

- It tends to be situational.
- It is often recurrent
- It is often preceded by at least a few seconds of prodromal symptoms.
- It occurs when the patient is in the upright position, and is resolved and can be aborted by assuming the supine position.
- After recovery, patients with neurocardiogenic syncope often complain of a "washed out" and tired feeling.

Examination

- Check the blood pressure in supine, sitting and lying down position

- Check the heart rate in supine, sitting and lying down position
- Cardiac and neurological examination

Investigations:

Tests involve serum electrolytes, glucose and haematocrit, creatinine, etc.

ECG and Echocardiogram to rule out cardiac causes

Management

Non Pharmacological

Patients with frequent episodes of syncope should take extra precaution while climbing stairs, swimming alone, operating heavy machines, driving. Patients who have lost consciousness should be placed in recovery position which will help to improve cerebral flow. Clothing that fits tight around the neck or waist should be loosened.

Patients experiencing neurocardiogenic syncope should avoid situations that predispose to syncope (e.g., dehydration, stress, alcohol consumption, prolonged standing, and extremely warm environments). Anxiety management and coping skills should be taught. It is important to reassure the patient that this is a benign condition.

Pharmacological

Drug therapy is necessary in vasovagal syncope when the episodes are frequent with associated risks. Metoprolol 25 to 50mg bid, atenolol 25 to 50 qd.

Serotonin reuptake inhibitors like paroxetine 20 to 40 mg qd, or sertraline 25 to 50 mg qd in some patients is helpful.

Management for Neurological cause

Seizure-see chapter number 4

Stroke-see chapter number 20

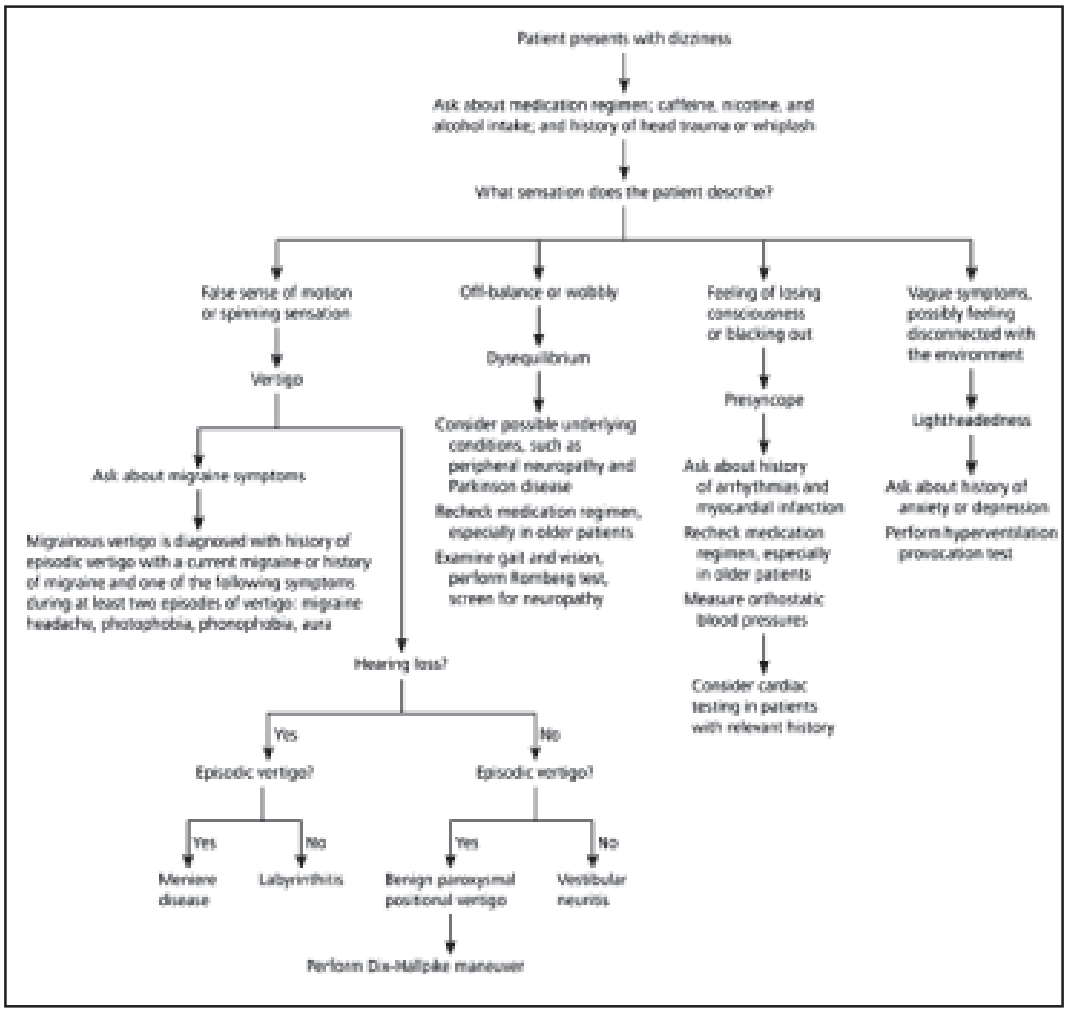

Patient presents with dizziness
Ask about medication regimen; caffeine, nicotine, and alcohol intake; and history of head trauma or whiplash
What sensation does the patient describe?
False sense of motion or spinning sensation
Off-balance or wobbly
Feeling of losing consciousness or blacking out
Vague symptoms, possibly feeling disconnected with the environment
Vertigo
Dysequilibrium
Presyncope
Lightheadedness
Ask about migraine symptoms
Consider possible underlying conditions, such as peripheral neuropathy and Parkinson disease
Recheck medication regimen, especially in older patients
Examine gait and vision, perform Romberg test, screen for neuropathy
Ask about history of arrhythmias and myocardial infarction
Recheck medication regimen, especially in older patients
Measure orthostatic blood pressures
Consider cardiac testing in patients with relevant history
Ask about history of anxiety or depression
Perform hyperventilation provocation test
Migrainous vertigo is diagnosed with history of episodic vertigo with a current migraine or history of migraine and one of the following symptoms during at least two episodes of vertigo: migraine headache, photophobia, phonophobia, aura
Hearing loss?
Yes
No
Episodic vertigo?
Episodic vertigo?
Yes
No
Yes
No
Meniere disease
Labyrinthitis
Benign paroxysmal positional vertigo
Vestibular neuritis
Perform Dix-Hallpike maneuver

Fig. 2.6

Summary:

Giddiness can be the presenting symptom of potentially life threatening conditions. If in doubt get urgent CT scan or MRI and advise admission with reference to the concerned consultant.

It is very important to differentiate whether the patient has dizziness/ vertigo or syncope because the causes & treatment will vary accordingly. Syncope is a more serious symptom & therefore has to be evaluated by a specialist Doctor & patient workup needs to be done immediately.

Vertigo is a common symptom encountered by a family physician. It is most commonly caused by inner ear disturbances. Therefore, a thorough ENT checkup is required if the symptoms do not resolve by standard medicines or are recurrent.

Sample Prescription For Vertigo

Rx

Tb Meclizine 25 mg to 50 mg 4 to 6 hourly

Tb Domperidone 10 mg 1 – 0 – 1

Vestibular rehabilitation

3. Memory Problems

Memory problems include inability to recall past experiences and are divided into long term and short term memory loss. Loss of recent memory is an important indication of age related cerebral degeneration and most often goes undiagnosed. It is important to note that this is a symptom that patient would never complain himself unless asked. It is the relatives who will confirm on questioning that the patient forgets immediate past events. Since the patients have very vivid recollection of the long term events they believe their memory is good, therefore the distinction between long term and short term memory is very important.

Therefore loss of recent memory is a symptom that all family physicians must ask their patients (>60) and their relatives. A distinction should be made between long term memory and short term memory, when obtaining the history of memory loss.

Causes

1. Senile dementia
2. Normal pressure hydrocephalus
3. Multiple lacunar Infarcts
4. Alzheimer disease
5. Multiple sclerosis
6. Other rare degenerative disorders

Mechanism of recent loss of memory

Ccerebral atrophy and degeneration of medial temporal lobe result in gradual decline of memory function. A common triad of symptoms i.e. loss of recent memory, urinary incontinence and ataxia definitely suggest cerebral atrophy with increase in cerebral size resulting in a condition referring to normal pressure hydrocephalus (NPH). Interestingly patients never tell about these symptoms, however when asked they will answer in affirmation. Hence, it is very important to enquire about these three symptoms whenever any patient above sixty years presents with any neurological symptoms.

Investigations

1. MRI Brain - It would pick up small ischemic areas and other degenerative neurological conditions if present.
2. CT scan Brain
3. Serum B12, folate, TSH , CBC and electrolytes

Chronic Memory Loss:

1. Senile dementia:

This is a clinical diagnosis and is made after excluding normal pressure hydrocephalus which may coexist. The most important symptom in these patients is loss of recent memory.

Treatment:

Donepezil – is available in 5 mg / 10 mg given TDS. Patients report an instant improvement within 48 hrs of starting the medication. Should be taken for 6 wks and may be continued for longer depending on the response. There are no major side effects, though it is important to follow up once every 15 days while on Donepezil.

2. Normal pressure hydrocephalus: (Refer Fig. 3.1)

Clinical diagnosis is by presence of triad of loss of recent memory, urinary incontinence and ataxia. It coexists with dementia and is confirmed by a CT scan or an MRI scan.

Treatment

This condition is correctable by surgery. The operation done is Ventriculo–peritoneal (VP) shunt.

3. Multiple lacunar infarcts/ Vascular dementia : (Refer Fig. 3.2)

These patients have multiple small infarcts, none of which are big enough to cause neurological defects. However there is cerebral atrophy.

Treatment:

Treatment is similar to cerebral ischemia.

1. Aspirin
2. Clopidogrel
3. Pentoxyphyline
4. Neuroprotective drugs – Piracetum, Citicholine
5. Memory enhancers – Donepezil
6. Supportive therapy – Neuroprotective vitamins (folic acid, methylcobalamine, Biotin)

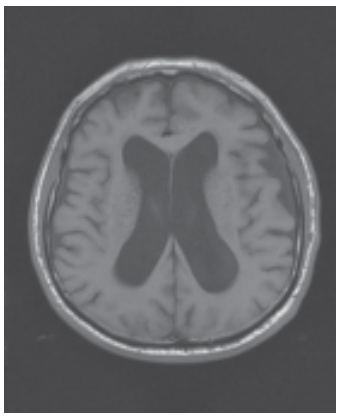


Fig. 3.1

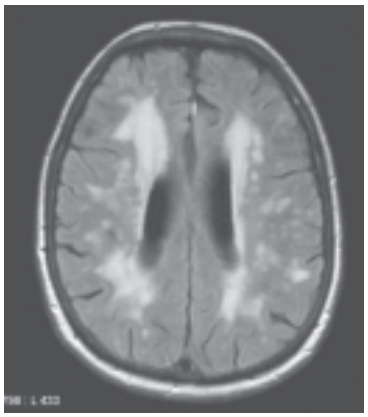


Fig. 3.2

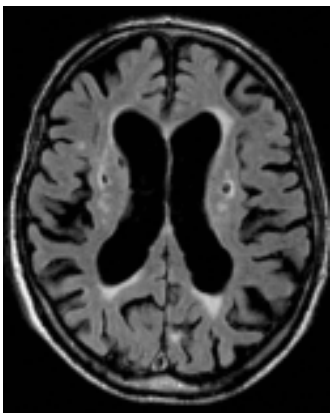


Fig. 3.3

Practical management:-In the authors experience the best combination of drugs for the above are Donepezil 10 mg -TDS + Citicholine – 1 BD + neuroprotective vitiamins

Referral:

Patient with senile dementia can be managed by the family physician and need not be referred, however if the CT /MRI shows NPH then refer to a neurosurgeon. Patients with vascular infarcts should be referred to a neurophysician.

Memory clinics:

In the last 1-2 yrs many memory clinics have come up in the metros.

4. Alzheimer's: (Refer Fig. 3.3)

It is characterized by progressive deterioration of higher mental functioning with impaired short term and long term memory, impaired judgement and abstract thinking, personality changes, sleep disturbances, mood disturbances and affected speech. The rate of progression may be variable.

Management

1) Basic principle

i. Ensure that dehydration, infections, metabolic disturbances, pain are treated effectively.

ii. Correct hearing or visual loss

iii. Avoid anticholinergic agents

iv. Reduce the psychoactive medications with possible cognitive side effects to the fewest at the lowest effective doses.

A) Pharmacologic therapy

i. Degenerative dementia

Donepezil, Rivastigmine, Vitamin E are to be used

ii. Other alternative medications like Ginkgo biloba, Hydergine are also been used nowadays.

iii. For behavioral symptoms like depression, selective serotonin reuptake inhibitor is to be used.

iv. For anxiety, bupropion to be used

v. For delusion, hallucinations, agitation medicines like donepezil, rivastigmine, tacrine, respiridone, carbamazepine, valproic acid are to be prescribed.

3) Non Pharmacologic therapy

i. Many of irreversible dementia needs multidisciplinary team which includes:

A neurologist, psychologist, physiotherapist, occupational therapist, speech therapist

ii. A physician should take charge in treating dementia patients and should coordinate with other doctors of the team with regular follow ups.

iii. Psychological therapy- Behavior modification technique

iv. Rehabilitation: Research has shown that physical activity has slowed down the progression of cognitive defects. Physiotherapy and occupational therapy are few of the helpful therapies.

v. Environment changes : Modify the response, modify tasks

vi. Care for the caregivers : Counseling of the caretaker is very important as it is stressful to handle dementia patients. Psychologists can give tips to the care givers about handling the patient.

Pharmacology & supplements

1) Cholinesterase inhibitors

   i. Tablet Donepezil to give 1 tablet of 5 mg at bedtime may increase to 10 mg in 4 to 6 weeks for mild to moderate disease

   ii. Tablet Galantamine extended release start 8 mg every morning with food may increase 16 mg after 4 weeks

   iii. Tablet Rivastigmine 1.5 mg twice a day may increase to 3 mg twice a day after 2 weeks

2) NMDA receptor antagonist

   Memantine start with tablet 5mg daily at weekly intervals to maximum 20 mg/day doses greater than 5 mg should be divided in bid. Extended release tablet start 7 mg per day, increase at weekly intervals to target dose of 28mg/day, for renal impairment reduce to 14mg/day

3) Neuroprotective drugs

i. Tablet CO Q or Tablet Ubiactiv also tablet vitamin c, vitamin e, multivitamin especially B complex including B12 & folic acid.

ii. Other alternative medicines like gingkoba bibola are also being used.

Contraindications

i. Antipsycotics (haloperidol, risperidone) - severe depression, Parkinson's disease, hypo-hypertension

ii. Tricyclic antidepressants (nor tryptiline, desipramine) - acute recovery phase following myocardial infarction

iii. Acute liver disease, peptic ulcers

Sun-downing, aggressive behavior

i. Antipsychotic drugs such as haloperidol or respiridone 0.5-1.0 mg a day

Sleep disturbance

i. Tablet zolpidem Tb Restyl 0.2 mg, alprazolam 0.5mg

ii. Tb Temazepam 15 mg 0—0—1 at bedtime to be given

Acute memory loss

Warning signs

1) Acute onset of memory problem

2) Rapidly progressing memory problem

3) Dementia associated with other acute symptoms

If the patient has the above warning signs one should order the following investigations

- CBC, LFT, Creatinine, electrolyte levels, ESR
- T3,T4, TSH, Vit B 12, Folic acid
- VDRL or Fluorescent treponemal antibody absorption test
- Toxin screening: heavy metal

Differntial diagnosis of acute memory problem

- Delirium
- Dementia
- Electrolyte imbalance
- Heat stroke
- Schizophrenia
- Depression
- Alcoholism
- Normal pressure hydrocephalus

Special investigations to be ordered to differentiate between various above causes

1) CT Head (preferably with & without contrast) to rule out tumours or focal neurological deficit
2) MRI Brain –more sensitive than CT to diagnose brain soft tissue pathology
3) PET CT Brain-will show hypometabolism in various areas of brain depending upon the cause.
4) CSF testing

   (Findings are described in dementia chapter)

Reversible memory problem	**Irreversible memory problem**
Hypothyroidism	Vascular dementia
Vit B12 & folate deficiency	Alzheimers
Hepatic encephalopathy	Fronto temporal dementia
Uremic encephalopathy	Dementia with lewy body
Infections - Meningitis - Encephalitis - Brain abscess - Syphilis	Parkinson's
Resectable tumours like small meningioma	Neurodegenerative disorders
Medicines -side effect of drug can cause memory loss Eg-Anticholinergic	Non resectable tumors
Toxins - Heavy metal - Elicit drugs	Progressive multifocal leukoencephalopathy
Hypertension - hypertension encephalopathy - subdural hematoma - normal pressure hydrpcephalus	HIV
Depression	Prion disease -Crentzfeldt-Jakob disease -Endocrine
	Neuronal storage disorders
	Leukodystrophy

Below are the screening questions to differentiate various types of dementia:

1) Onset - sudden or gradual
2) Progression - rapid or slow
3) Severity - mild, moderate or severe
4) Any associated symptoms
   a) Focal neurological deficit
   b) Infections - any history of fever, weight loss, gait impairment

Depending upon the associated symptoms, causes differ

1) In the presence of atypical course such as rapidly progressive, waxing &waning, or series of abrupt changes in clinical course, consider causes like vascular, infectious, inflammatory/autoimmune, toxic/metabolic processes, multiple sclerosis, Dementia with Lewy bodies, Frontotemporal dementia, vascular dementia, Creutzfeldt–Jakob disease.
2) If there is presence of systemic symptoms such as headache, fever, dry eyes/ mouth, arthralgia, weight loss, or skin lesions then consider infectious, inflammatory/autoimmune, neoplastic, paraneoplastic processes.
3) If there is presence of sleep disorder, such as excessive day time sleepiness, loud snoring, restlessness, insomnia, leg jerks while sleeping then the patient may have obstructive sleep apnoea, central sleep apnoea, restless leg syndrome, periodic limb movement disorder.
4) Presence of neuropsychiatric symptoms such as behavior or personality change, apathy, visual hallucinations, delusions, agitation may be due to toxic or metabolic processes, infectious or inflammatory conditions or DLB, FTD
5) If there is presence of neurological symtoms or signs like diplopia, dysphagia, face &limb weakness or numbness, gait unsteadiness, then consider brain tumor or abscess.
6) In the presence of Parkinson's signs such as masked facies, abnormal gait, stooped posture, tremors, ridigity, suspect Parkinson's disease, DLB, NPH.

Examination

1) Check blood pressure, heart rate
2) Check for any signs of trauma (head injury)
3) Also look for nuchal rigidity, papilledema, focal facial or limb weakness, abnormal deep tendon reflexes, Parkinsonism, gait impairment, fasciculations.
4) Mini mental status examination

Treatment

Treat the underlying cause.

SUMMARY

Memory problems are very common in elderly population. Normal aging beyond 65 years may be associated with memory loss called senile dementia. It is very important to differentiate abnormal memory loss, for eg. Alzheimer's dementia, etc. from normal aging as the prognosis will differ. Early identification and treatment can help to preserve and slow down the progression of dementia. Lifestyle modifications, environmental modifications and rehabilitative techniques play a key role in the management of dementia. MRI and PET scan are used as diagnostic and monitoring tools. Anticholinesterase drugs (donepezil), neuroprotective agents are used for pharmacotherapy.

In patients with acute memory loss, underlying causes need to be identified, investigated and treated appropriately and immediately.

Sample Prescription

Rx

1) Cognitive impairment
   Tb Donezepil 5mg 1-0-0 or
   Tb Rivastigmine 1.5mg 1-0-1
   Or Tb Galantamine 4mg 1-0-1
2) Sleep disturbance
   Tb Temazepam 15 mg 0-0-1 or
   Tb Zolpidem 5 mg 0-0-1
3) Depression
   Tb Nortriptyline 25 mg tds
4) Neuroprotection
   Tb CoQ10 300 mg bd or Tb Ubiquinol 100 mg bd
   Tb Vit C 1-0-0, Cap Vit E 400 mg 1-0-0
   Cap Mecobalamin 0-1-0, Tb folic acid 1-0-0, Tb Omega3 fatty acids 1-0-0

4. Convulsions

These are the involuntary movements associated with loss of consciousness. They may exist by themselves or present as an underlying neurological disorder.

There are **three phases** of a seizure:

Aura – This is the unusual sensation of a start of a seizure. The person will remain conscious but experience unusual feelings or sensations. The person may experience sudden and unexplainable feelings of joy, anger, sadness, or nausea. He or she also may hear, smell, taste, see, or feel things that are not real.

Ictus – Meaning the attack.

Postictal – Meaning after the attack and postictal refers to the after effects of the seizure like loss of consciousness.

Causes of convulsions:

- Brain malformations or metabolic disorders.
- Lack of oxygen (hypoxic brain injury) or intracranial haemorrhage during birth.
- Low levels of blood sugar, blood calcium, blood magnesium or other electrolyte disturbances.
- Fever
- Congenital conditions (Down's syndrome; Angelman's syndrome; tuberous sclerosis and neurofibromatosis) and other genetic factors
- Head trauma
- Alcohol or drugs
- Brain tumours- Supratentorialtumours
- Drug withdrawal
- Medications, Maternal use of drugs.
- Infection that could be viral, bacterial or parasitic
- Stroke
- Alzheimer's disease

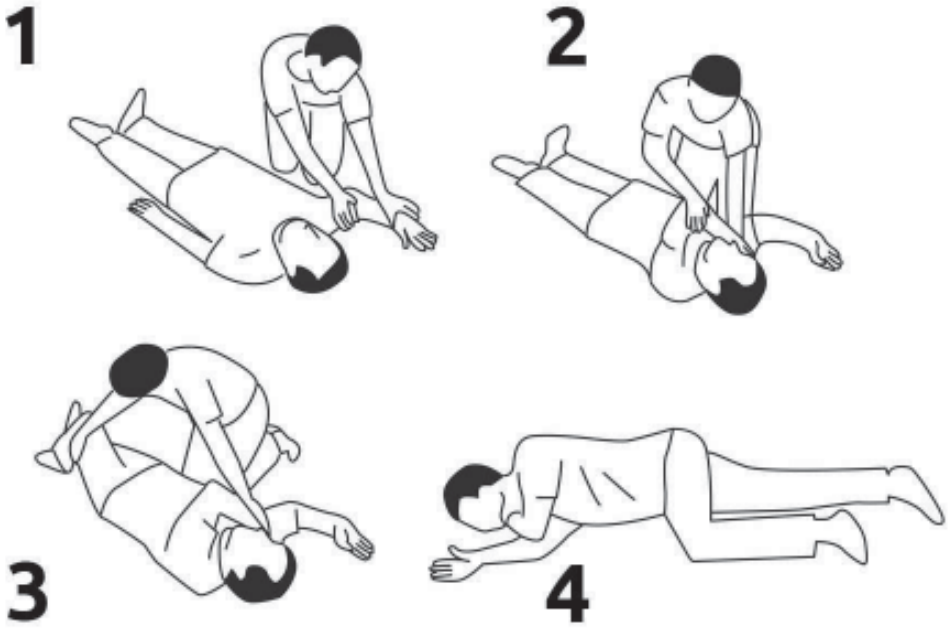


Fig. 4.1

Investigations:

1. EEG
2. CT Brain /MRI
3. Blood Investigations- CBC, Electrolytes, LFT, Creatinine, Blood sugar, Calcium, Magnesium.

Referal:

Should be made to a neurophysician or a pediatrician incase of children.

Treatment:

1. Treat the seizure episode with anticonvulsant as given below according to the type.
2. Treat the underlying cause with medications for medical conditions and surgery for operable cases.
3. Monitor and follow up regularly for repeat episodes. Ask the patient to maintain record of seizure episode e.g. frequency of seizures, severity of seizures, precipitating factors, etc. Adjust the current dose or add another anticonvulsant if not under control.

Types

A. Febrile:

Most commonly seen in children of 6 months – 6 years age group. It presents as generalized convulsions with febrile episodes. Sometimes also seen with administration of vaccines.

Treatment:

Single episode no treatment required. Repeated episodes with EEG changes anticonvulsants should be started as advised by the pediatrician. Valparin, Gardinal, Levitiracetam.

B. Generalized Tonic – ClonicSeziures:

Most commonly seen in adults and are associated with loss of consciousness. There is sustained contraction followed by rhythmic contractions of all four extremities. Tonic clonic movements (stiffening of limb along with jerking movements) last for a few seconds to a few minutes. They invariably have post convulsive period of drowsiness or stupor, lasting from a few minutes to a few hours.

Treatment:

1. Anti convulsants – any of the following
   a. Phenytoin
   b. Levitiracetam
   c. Sodium valproate
   d. Phenobarbitone (Gardinal)
   e. Carbamezapine
   f. Clonazepam

C. Absence Seizure:

These consist of a brief lapse of awareness, it may occur in children as well as adults. These are divided into simple absence seizure (there is no limb involvement and post icteric phase) and complex absence seizure (loss of muscle tone).

Treatment:

Not all anticonvulsants are effective in this type of seizures e.g. Carbamazepine is ineffective, whereas Phenytoin and Gardinal are not very effective.

Drugs used are: Sodium valproate, Ethosuximide, Lamotrigine, Acetazolamide, Clonazepam

D. Partial Seizure:

There are of two types of partial seizures: simple partial (associated with psychic phenomena known as Déjà vu, sense of unreality) which results in focal motor movements without loss of consciousness. Complex partial, there is alteration in consciousness, bizarre sensations such as dream like state, automatism or olfactory sensations. Partial seizures occur due to focal brain lesions such as tumors, infections, head injury and vascular malformations.

Treatment:

Any one of the following anticonvulsants can be given

1. Phenobarbitone
2. Phenytoin
3. Levitiracetam
4. Carbamazepine
5. Oxcarbazepine
6. Clonazepam

If not responding to the above then the following should be given

1. Topiramate
2. Lamotrigine

Surgery if unresponsive to above treatment

E. Myoclonic Seizures:

These are characterised by repetitive jerking of large muscle groups. They are clonic movements often confined to one limb, but may sometime involve the axial musculature. They occur due to diffuse cerebral condition such as infections, metabolic disorders such as uremia.

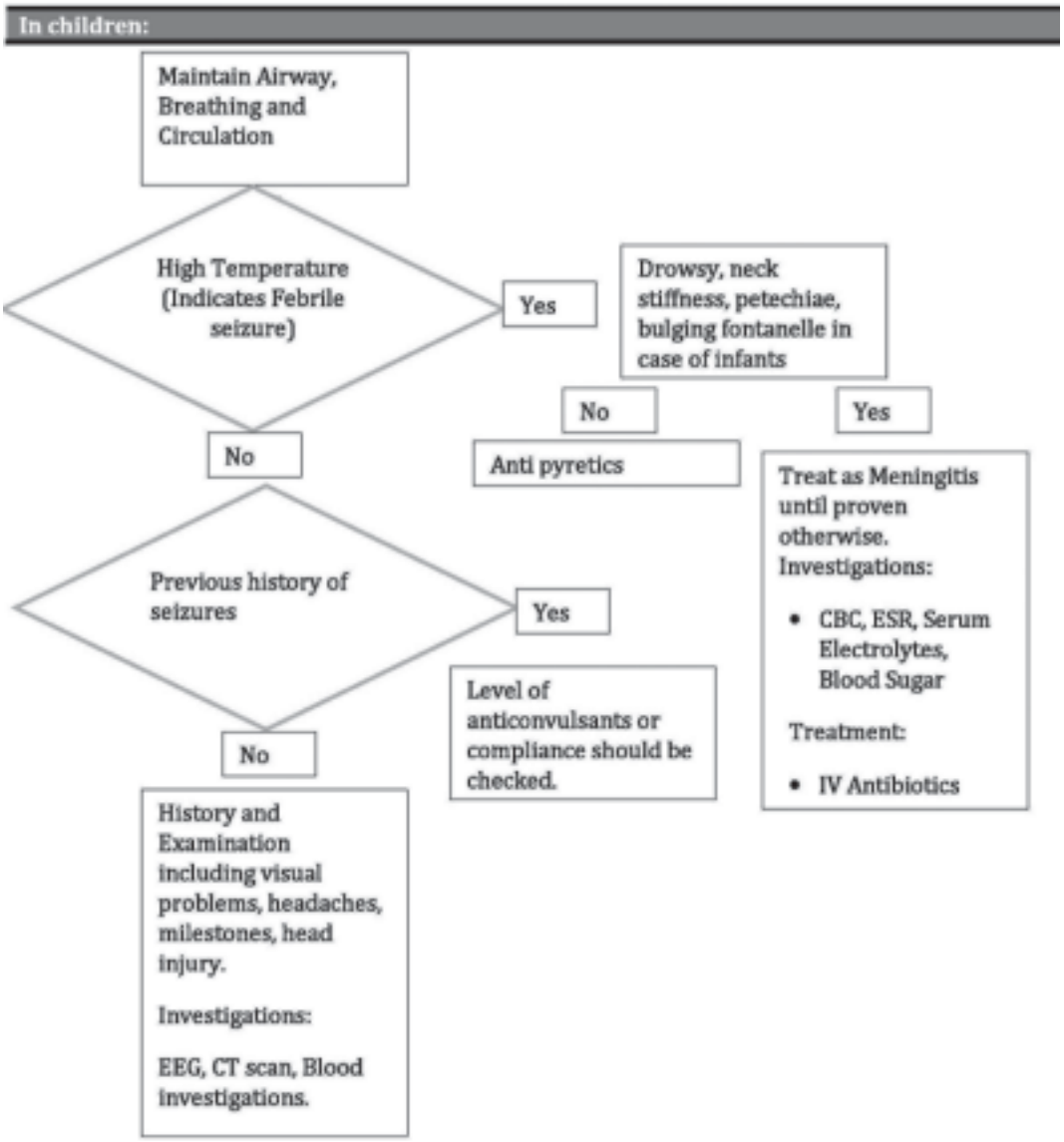
Treatment:

1. Sodium Valproate
2. Levitiracetam
3. Benzodiazepines (Diazepam)
4. Topiramate
5. Lamotrigine

Surgery if unresponsive to above treatment

a) Removal of seizure focus
b) Temporal lobectomy
c) Vagal nerve stimulation.

Management of Acute Seizures



	Management in Adults	
0-5 minutes	Airway Breathing and Circulation **(ABC)**	
	Monitor Vital signs	
	Establish IV access and send blood for investigations	
	Blood glucose to be checked	Treat Metabolic imbalances and hypoglycemia as quickly as possible
	Treatment: Lorazepam 0.1 mg/kg/dose upto 4mg maximum IV/IMover 2-4 minutes	
	OR Diazepam 0.5mg/kg/dose maximum upto 20mg/dose IM or rectally	
	IF SEIZURES PERSIST	
10-15 minutes	Repeat Lorazepam	
	Monitor for hypotension, tachycardia, bradycardia	
	Phenytoin 20mg/kg/dose	
	IF SEIZURES PERSIST	
15-20 minutes	Phenobarbital 20mg/kg/dose IV	
	Monitor for respiratory depression	
	IF SEIZURES PERSIST	
20-30 minutes	Repeat Phenytoin	

What questions should be asked by you?

- Age of onset?
- Precipitating factors?
- How often?
- What time of the day?
- Is its onset sudden? Or gradual?
- Was there loss of consciousness?
- Is it associated with sweating? Pallor? Mental disturbance? Involuntary micturition?
- Was there any associated vomiting? Projectile vomiting?

- Does any family member suffer from epilepsy?

Summary

TYPE OF CONVULSION	INVESTIGATIONS	REFER TO	TREATMENT
FEBRILE CONVULSION	IN A SINGLE EPISODE NO INVESTIGATIONS ARE REQUIRED. HOWEVER IF THERE ARE REPEATED EPISODES THEN EEG SHOULD BE DONE. IF FOCAL IN NATURE THEN CT/MRI MAY BE ADVISED.	PAEDIATRICIAN OR A NEUROLOGIST	FOR A SINGLE EPISODE NO TREATMENT IS REQUIRED. IN REPEATED EPISODES WITH EEG CHANGES ANTICONVULSANTS SHOULD BE STARTED AS ADVISED BY THE PEDIATRICIAN.
ABSENCE SEIZURE	EEG, CT BRAIN PLAIN AND CONTRAST, MRI	NEUROLOGIST	ETHOSUXIMIDE | LAMOTRIGINE | SODIUM VALPROATE | ACETAZOLAMIDE | CLONAZEPAM
ATONIC SEIZURES			PHENOBARBITAL | PHENYTOIN | PRIMIDONE | SODIUM VALPROATE
FOCAL SEIZURES	EEG, CT BRAIN PLAIN AND CONTRAST, MRI	NEUROLOGIST	CARBAMAZEPINE | CLONAZEPAM | LEVETIRACETAM | OXCARBAZEPINE | PERAMPANEL | PHENOBARBITAL | PHENYTOIN || SODIUM VALPROATE |
GENERALIZED SEIZURES	EEG; CT BRAIN PLAIN AND WITH CONTRAST; MRI SCAN	NEUROLOGIST OR GENERAL PHYSICIAN. NEURO SURGEON IN CASE OF OCCURRENCE AFTER HEAD INJURY.	SODIUM VALPROATE | CARBAMAZEPINE | CLONAZEPAM | PHENOBARBITAL | PHENYTOIN |
PSYCHOGENIC SEIZURES	EEG	PSYCHIATRIST	

5. Paralysis

Paralysis is the complete loss of muscle function for one or more muscle groups. It can be associated with sensory loss along with the motor loss. It can occur on one or both sides of the body. Paraplegia is the paralysis of lower half of the body whereas paralysis of all four limbs is called quadriplegia. Hemiplegia (sometimes called hemiparesis) is a condition that affects one side of the body.

What are the types?

Localised or generalized paralysis

Localized paralysis affect only a part of the body like facial paralysis – which is usually limited to one side of the face or paralysis of the hand.

Generalized paralysis affects a wider area like monoplegia – where one limb is paralysed; hemiplegia – where the arm and leg on one side of the body are paralysed; paraplegia – where both legs, or sometimes the pelvis and some of the lower body are paralyzed; quadriplegia where both the arms and legs are paralysed

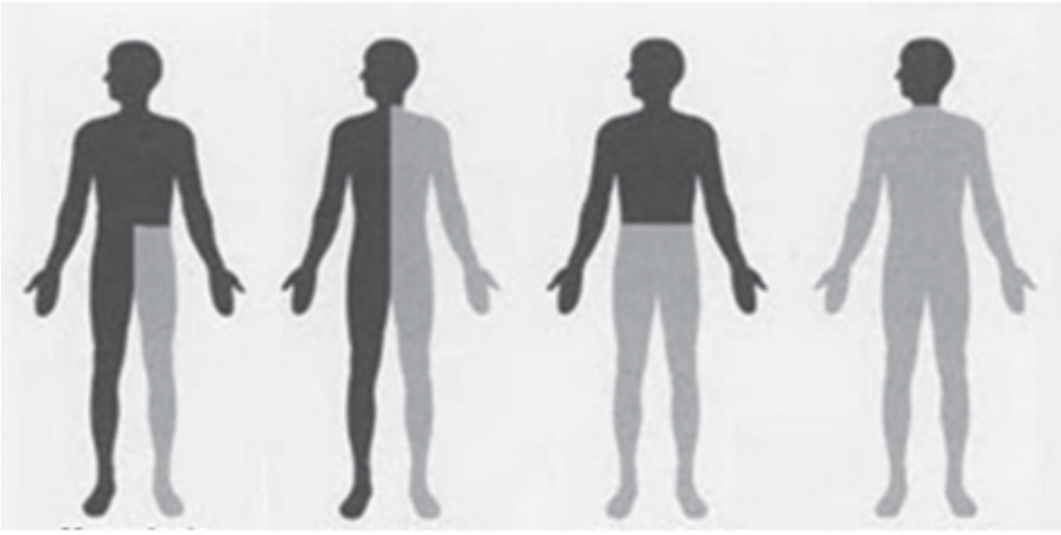


Fig. 5.1

Temporary and permanent paralysis

Paralysis can either be temporary or permanent. Bell's palsy is a relatively common type of temporary paralysis. Sometimes paralysis that occurs after a stroke can also be temporary.

Paralysis caused by serious injury, such as a complete spinal cord section, is usually permanent.

Partial or complete paralysis

Paralysis can be partial – where there is some muscle function and sensation; for example, if a person can move one leg but not the other, or feel sensations such as cold and heat.

It can be complete – where there is complete loss of muscle function and sensation in affected limbs.

Spastic or flaccid paralysis

Paralysis can be spastic – where muscles in affected limbs are unusually stiff or display spasms, and movements are not under the control of the individuals.

In flaccid paralysis, muscles in affected limbs are floppy and weak. Patients with flaccid paralysis often experience muscle weakness without spasms.

In some conditions, such as motor neuron disease or cerebral palsy, it is possible to experience episodes of spastic paralysis followed by flaccid paralysis, or the other way around.

Depending on the levels of spinal cord injury

Spinal cord injury between C1 and C7 is likely to result in quadriplegia.

The extent of the paralysis and subsequent loss of muscle function will depend on level of injury-C1 to C4 spinal cord injury will result in little or no movement in limbs and patient will also need a ventilator to assist breathing. C7 spinal cord injury patients will be able to extend their elbows and may have some movement in their fingers.

T2 to T12 spinal cord injury will result in little or no function in lower limbs.

L1 to L5 injury may result in limited movement in the lower limbs.

The most common types of paralysis are-

Stroke where the blood supply to the brain is suddenly stopped or there is haemorrhage in the surrounding brain tissue.

Spinal Cord Injury can cause damage to the nerves within the spinal canal due to mostly trauma to the vertebral column, affecting sensory, motor and autonomic function below the level of injury.

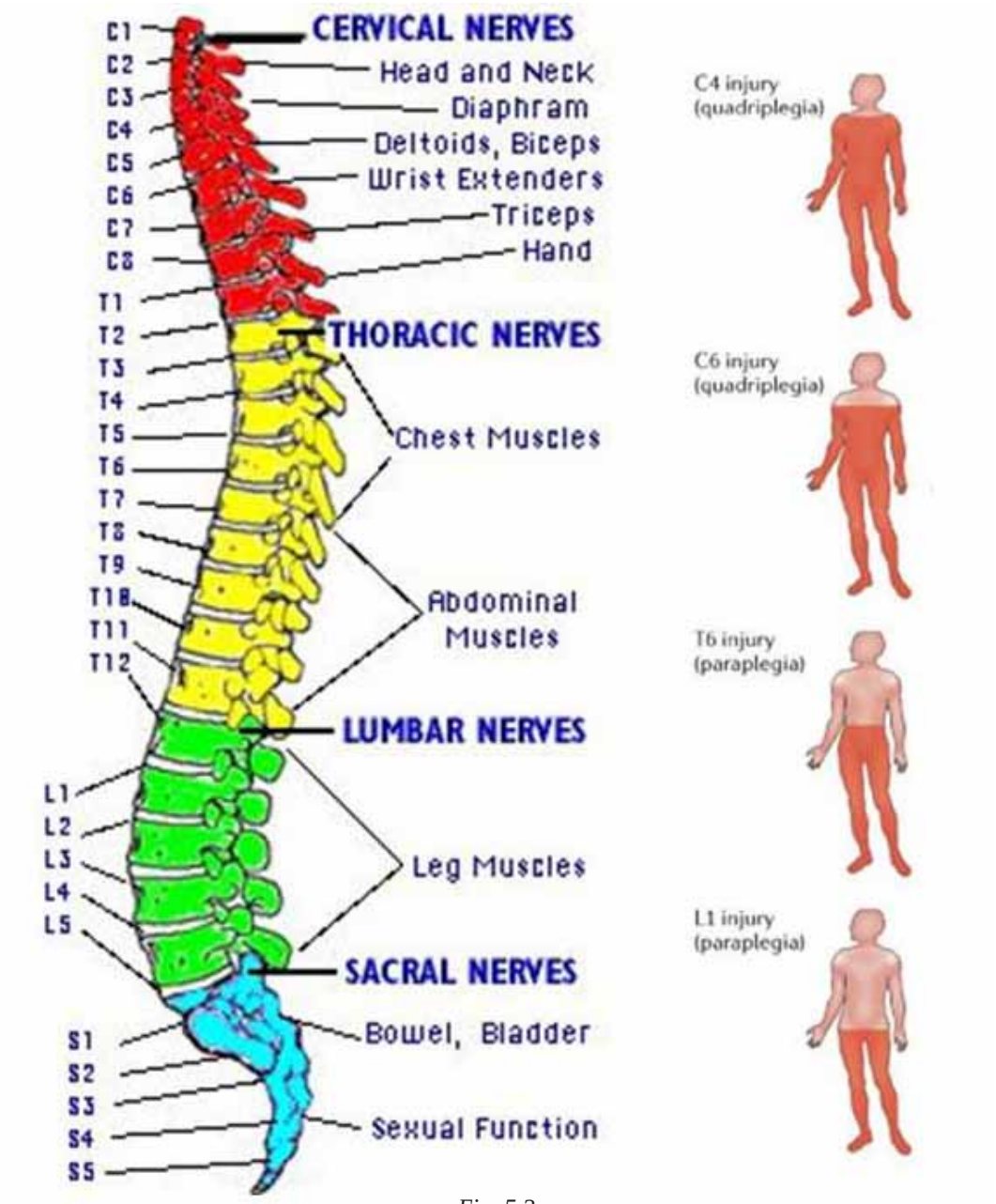


Fig. 5.2

Amyotrophic Lateral Sclerosis ALS, also called Lou Gehrig's disease, is a progressive neurological disease where the progressive degeneration of the motor neurons eventually leads to their death. When the motor neurons die, the ability of the brain to initiate and control muscle movement is lost. Patients in the later stages of the disease may become totally paralyzed.

Poliomyelitis (infantile paralysis) has been eradicated from almost every country in the world since the vaccines have been used. Paralytic polio occurs due to destruction of motor neurons within the spinal cord, brain stem, or motor cortex.

Spina Bifida is a type of neural tube defect leading to incomplete closure in the spinal column.

Multiple Sclerosis is a disorder of the brain and spinal cord involving decreased nerve function associated with scar formation on the covering of neurons.

Guillain-Barre Syndrome is a disorder in which the body's immune system attacks part of the peripheral nervous system.

Cerebral Palsy is a group of conditions that affect control of movement and posture.

Brachial plexus injury can be due to excessive stretching, tearing, or other trauma to a network of nerves from the spine to the shoulder, arm, and hand.

Muscular Dystrophy is a type of genetic diseases characterized by progressive weakness and degeneration of the skeletal muscles that control movement.

Syringomyelia/Tethered cord can include progressive deterioration of the spinal cord, progressive loss of sensation or strength, profuse sweating, spasticity, pain and autonomic dysreflexia.

Transverse Myelitis is a neurological disorder caused by inflammation across one segment of the spinal cord.

The most common paralysis one is likely see in a practice are-

Bell's palsy:

Localized paralysis occurs in Bell's palsy where one side of the face may be paralysed due to inflammation of the facial nerve i.e. the seventh cranial nerve, on that side. Patients present with following complaints:

1. Muscle weakness or paralysis
2. Forehead wrinkles disappear
3. Overall droopy appearance
4. Impossible or difficult to blink
5. Nose is constantly stuffed
6. Difficulty in speaking
7. Difficulty eating and drinking
8. Sensitivity to sound (hyperacusis)
9. Excess or reduced salivation
10. Facial swelling
11. Diminished or distorted taste
12. Pain in or near the ear

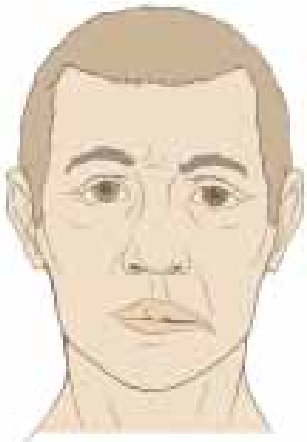


Fig 5.3 Bell's palsy - Drooping eye, drooping corner of mouth

13. Drooling
14. Eye closure difficult or impossible
15. Dry eyes due to lack of tears
16. Drooping of the eye brows
17. Lower eyelid droop
18. Sensitivity to light

Investigations:

After taking a history and carefully observing the symptoms, tests that may be ordered include various blood tests, MRI, or CT scan. These tests will either add conviction to a diagnosis of Bell's palsy, or provide the information needed to proceed in another direction.

Treatment:

1. Steroids (prednisone 80 mg once a day for three days, then 60 mg once a day for three days, then 40 mg once a day for three days, then 20 mg once a day for three days, then discontinue use.
2. Analgesics
3. Combination of steroids with antivirals
4. Vitamin B complex
5. Eye care
6. Surgery (decompression of the seventh nerve)
7. Physiotherapy

Referal:

Refer to a neurophysician or an ENT surgeon.

Stroke (cerebro vascular accidents):

Brain strokes either present as Transcient ischemic attack(TIA) or as full blown cerebro vascular accidents (CVA) causing hemiplegia (weakness on one side of the body) .Most paralyses caused by nervous system damage are permanent in nature. The paralysis of TIA is reversible whereas those of a CVA are irreversible. It is very important to remember that most CVAs are preceded by TIA. If these TIA are correctly diagnosed, investigated and treated, a full blown brain stroke can be easily prevented.

Since majority of patients present initially to their family physician, it is very important to be aware of this condition and treat it promptly. The role of the family physicians in the prevention of CVA is therefore vital and crucial.

Common causes for brain stroke and TIA that should be kept in mind by the physician are –

A – Anxiety
B – Body build
C – Cigarette Smoking
D – Diabetes/ Diet
E – Exercise lack
F – Family History
G – Gout
H – Hypertension

TIA's: Patients present with one sided loss of sensations with limb weakness along with blindness in one eye and difficulty in talking with giddiness. One, some or all of these may be present. These last for a few minutes and then restore by themselves.

Investigations:

1. CT scan or MRI of the brain with CT angiography or MR angiography
2. Carotid Doppler with 2D Echo
3. Lipid profile and diabetes screening.

Referal:

Urgent reference to a neurophysician or neurosurgeon.

Treatment:

1. Identification and control of risk factors:
   a. Control of hypertension with anti hypertensives
   b. Intake of tobacco and smoking should be stopped.
   c. Reduction of anxiety with help of meditation or counseling.
   d. Weight reduction
   e. Diet regulation or moderation.
   f. Diabetic control if present.

The patient should be made aware to take care of the following –

A – Anxiety
B – Body build
C – Cigarette Smoking
D – Diabetes/ Diet
E – Exercise lack
F – Family History
G – Gout

H – Hypertension

2. Identify if ischemia or hemorrhage with CT scan or MRI
3. In case of ischemia – Aspirin and clopidogrel should be started, along with neuroprotective drugs – Piracetam or citicholine, Methylcobalamin, Pyridoxine, Folic acid combinations.
4. Identification of the cause of ischemia- can be due to stenosis or occlusion of large vessels such as carotid artery or smaller vessels such as branches of middle and anterior cerebral artery.

Carotid stenosis:

If the stenosis is less than 50% then patient is treated medically. If 50% to 70% then stenting is required. For stenosis of more than 70% surgical removal of the atheroma is needed. The diagnosis of carotid stenosis can be made with a carotid Doppler study.

Small vessel ischemia:

These are mostly treated medically. However in a few selected cases stenting or the surgery of STA-MCA bypass are treatment options.

What is the management of chronic paralysis?

Bladder and bowel management:

Almost all types of spinal cord injury result in the loss of normal bowel and bladder function.

There are many methods that can be used to manage a paralysed bladder. It is important to ensure the bladder is emptied regularly because an overly full bladder can trigger a serious complication called autonomic dysreflexia in high spinal cord injuries.

There are two main types of catheter. They are:

- Intermittent catheter – the catheter is temporarily inserted into the bladder and removed once the bladder is empty. This leads to lesser complications then indwelling catheter.
- Indwelling catheter - remains in place for many days or weeks and is held in position by a water-filled balloon in the bladder like the Foleys catheter, silicon catheter. Indwelling catheters can be complicated by problems such as bladder spasm, infection, blockage and leakage around the catheter, urinary stones, etc.

There are options to help people with paralysis empty their bowel:

- Bowel retraining – The aim is to improve the consistency of stools and establish a regular time to empty bowel. Medications such as dulcolax suppository can be regularly used.

- Enemas – liquid is injected into bowel to help stimulate it to empty.

Referral:

An Urologist should be referred.

Neuropathic pain:

Neuropathic pain is pain caused by nerve damage. Neuropathic painrequires alternative medications such as amitriptyline or pregabalin, a gaba analogue as it does not usually respond to ordinary painkillers, such as paracetamol or ibuprofen.

Breathing difficulties:

Breathing assistance from a ventilator maybe required if the diaphragm is paralysed. A positive pressure ventilator can either be invasive –tracheostomy or non-invasive – bi-Pap or C-Pap

Swallowing difficulty:

Dietary advice would be helpful from a dietician, who can guide about consistency and type of food for a particular problem. Ryle's tube may be required for some patients with no gag reflexes. PEG tube is a long term option.

Spasticity and muscle spasms

Spasticity is a medical term that means abnormally stiff and rigid muscles. Many people with paralysis develop spasticity and involuntary muscle spasms (where muscles cramp and contract).

Treatment:

Muscle relaxants such as baclofen, tizanidine or dantrolene. If muscle relaxants are not effective, an injection of botulinum toxin (Botox) may be given for localised spasms. The effects of the injection usually last for up to three months.

Intrathecal baclofen therapy: surgically implanting a small pump on the outside of the body connected to the spinal cord delivers regular doses of baclofen directly to the spine.

Bed sore management:

Prevention: Special foam mattress or air mattress may be required for bed ridden patients. Keep the skin dry by applying powder. Turn the patient on sides every two hourly. Keep the perennial area clean and dry after urine or motion.

Treatment:

Daily dressing with betadine. Dermatology referral. Medication- calendula, permin gel, multivitamin and good nutrition will help in healing of bed sore.

6. Neuropathic Pain

Neuropathic pain generally results from damage to nerves or impairment in the central nervous system. It is diagnosed when pain is out of proportion to the injury. Pain generally presents itself in the form of burning or tingling.

Causes

Most common causes of neuropathic pain seen in practice are diabetes,herpes zoster (shingles),alcoholism, B 12 deficiency,trauma (nerve damage or spinal cord injury) ,degenerative disc disease(spondylosis).

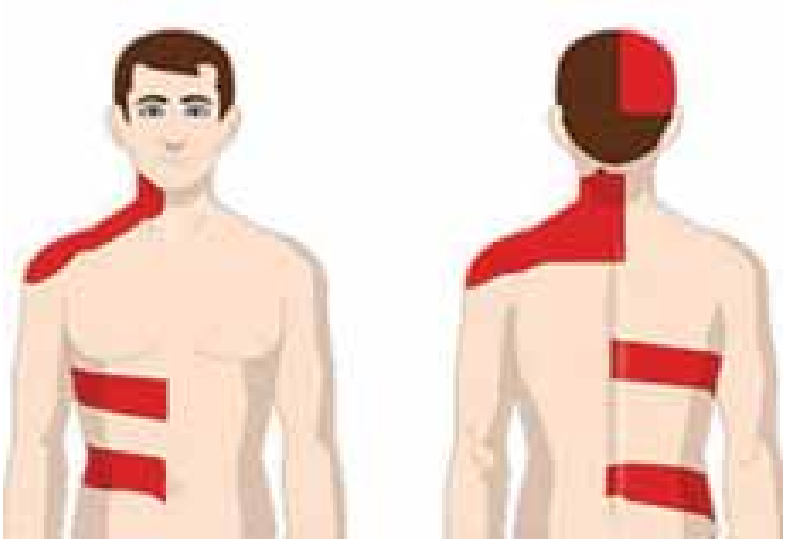


Fig.6.1

Other causes are trigeminal neuralgia,multiple sclerosis, HIV or AIDS,post chemotherapy and due to toxins.

It can also present itself after surgeries such as mastectomy or amputation (phantom limb).Phantom limb syndrome is a condition which occurs when patient still feels the pain from the missing limb as the nerve ending misfire and send abnormal signal to the brain.

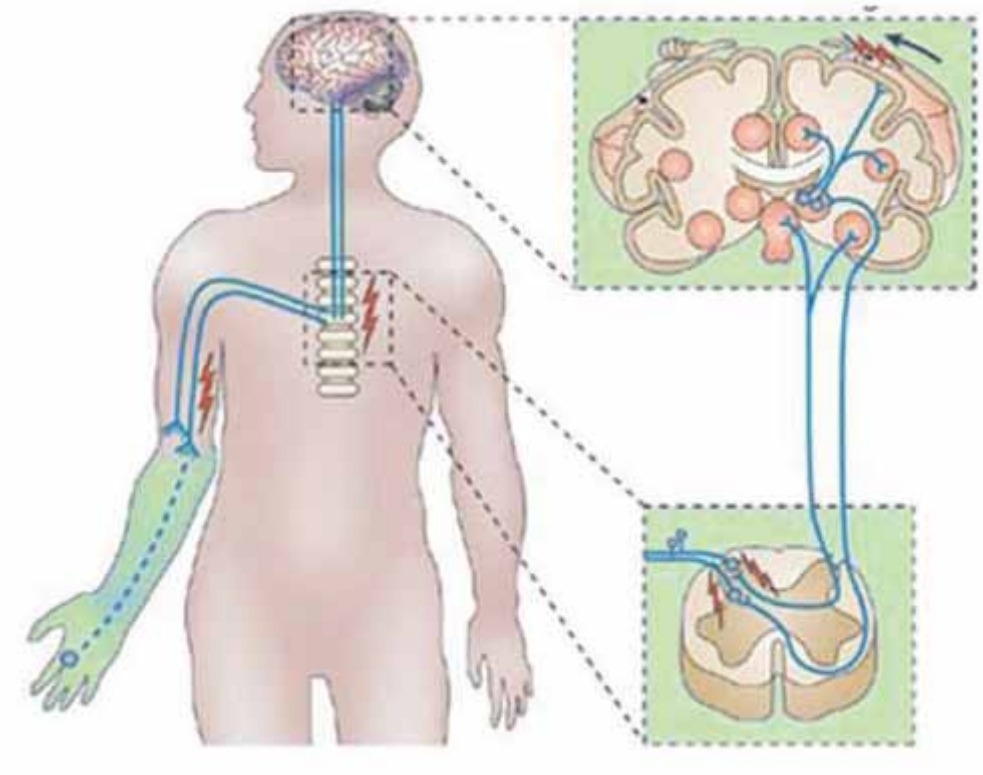


Fig.6.2

Pressure on nerves due to malignancy can also cause neuropathic pain.

Pain in movement disorders such as Parkinson's disease and dystonia, pain secondary to spasticity, pain in frozen shoulder secondary to stroke are all categorized as neuropathic pain.

Signs & Symptoms

Burning or shooting or piercingpain is typical of neuropathic pain, but in some cases it may also be deep and aching.The pain may be radiating along the damaged nerve.Tingling & numbness may be associated with the pain.

Increased sensitivity to touch and not alleviated by any of the normal pain killers. The pain is long-lasting, typically persisting after the cause has been removed.The pain is usually in the area of innervation of the damaged nerve, but the surrounding areas may also be involved.

Investigation

Neuropathic pain is diagnosed on the basis of symptoms. Blood sugar &B 12 level may be checked.Look for compression of nerve, rash (herpes zoster).

Treatment

For treatment antidepressants and anticonvulsants are most commonly used as regular analgesics do not work.

Diabetic neuropathy

Pregabalin75 mg bid & may increase to 150 mg bid & then maximum upto 300mg bid Or

Gabapentin 300mg on day 1, 300mg bid on day 2, 300 mg tds on day 3, & continue 300 tds for 1 week .If the pain is not getting controlled the dose can be increased upto 600 mg tds gradually.

Post herpetic neuralgia

Antidepressants such as amitriptyline (Tryptomer) 25-75mg per day is recommended.

Trigeminal neuralgia

Carbamazepine (Tegretol) start 100mg bid & can increase by 100mg each dose to a maximum of 400mg bid in case of neuralgiacaused by pressure.

Post-surgical patients -Tramadol 50mg bid/tds then can increase to 100 bid/tds maximum upto 200mg bid.

Localised pain

Local application of anaesthetic like xylocainegel or patch.

Surgical option may be required in non responding cases or severe cases.

Botox intradermal injections in case of focal pain can be used and is effective for around 14 weeks.

Surgery:

Epidural implantation of electrode in the spine for chronic leg pains has been tried.Intrathecal pumps have also been tried in some patients.Nerve ablation procedure in severe cases can be done.

Rehabilitation

Mobilization and physiotherapy are important to prevent disuse atrophy. Patient must be protected from depression and appropriate counseling should be provided.

Referal-pain management specialist, neurophysician or neurosurgeon.

7. Physical Disabilities in Children

A physical disability is any condition that permanently prevents normal body movement and/or control. There are many different types of physical disabilities.

Below are some questions to be asked when a child suffering from any kind of physical impairment or disability is brought to you:

1. Ask whether the illness or condition causing physical dysfunction is congenital (present since birth) or acquired.
2. Ask about the course of illness and disability - the onset, duration and progression; whether the disability, for e.g. weakness, is progressive or non progressive.
3. Ask whether the child has any associated intellectual impairment (delays in oral language development, self-help or self-care skills, developing social skills, deficits in memory and problem solving skills, etc), visual or hearing problems
4. Ask whether there is any delay in overall development of the child (delayed sitting, crawling, walking, speaking, interacting with parents, etc compared to normal typically developing child)
5. Ask the parents about a detailed birth history of the child, which includes - Prenatal history (mother suffered from infection, hypertension during pregnancy, on medications other than pregnancy related medicines, etc); Perinatal history (whether the baby was full term or pre term, delivery was normal or assisted - Caesarean section or took too long, whether the baby cried immediately after birth or not); Postnatal history (whether the baby suffered from fever, jaundice, etc)

Causes of physical disabilities

There are many different causes for physical disabilities. These include:

1. Perinatal hypoxia: Injury to the brain due to problems during gestation (prenatal), during childbirth (natal) or after birth (postnatal)
2. Serious infections affecting the brain, nerves or muscles, such as poliomyelitis
3. Inherited or genetic disorders, such as muscular dystrophy, leucodystrophy, glycogen storage disorders, etc.

4. Conditions present at birth (congenital birth defects), such as spina bifida, meninmgomyelocoele, etc.
5. Trauma: spinal cord injury and head injury

Some of the main ones include:

Cerebral palsy

Cerebral palsy is caused by damage to the parts of the brain which control movement during the early stages of development. In most cases, this damage occurs during pregnancy. However, damage can sometimes occur during birth and from brain injuries in early infancy (such as lack of oxygen from near drowning, meningitis, head injury or being shaken).

Children with cerebral palsy may have:

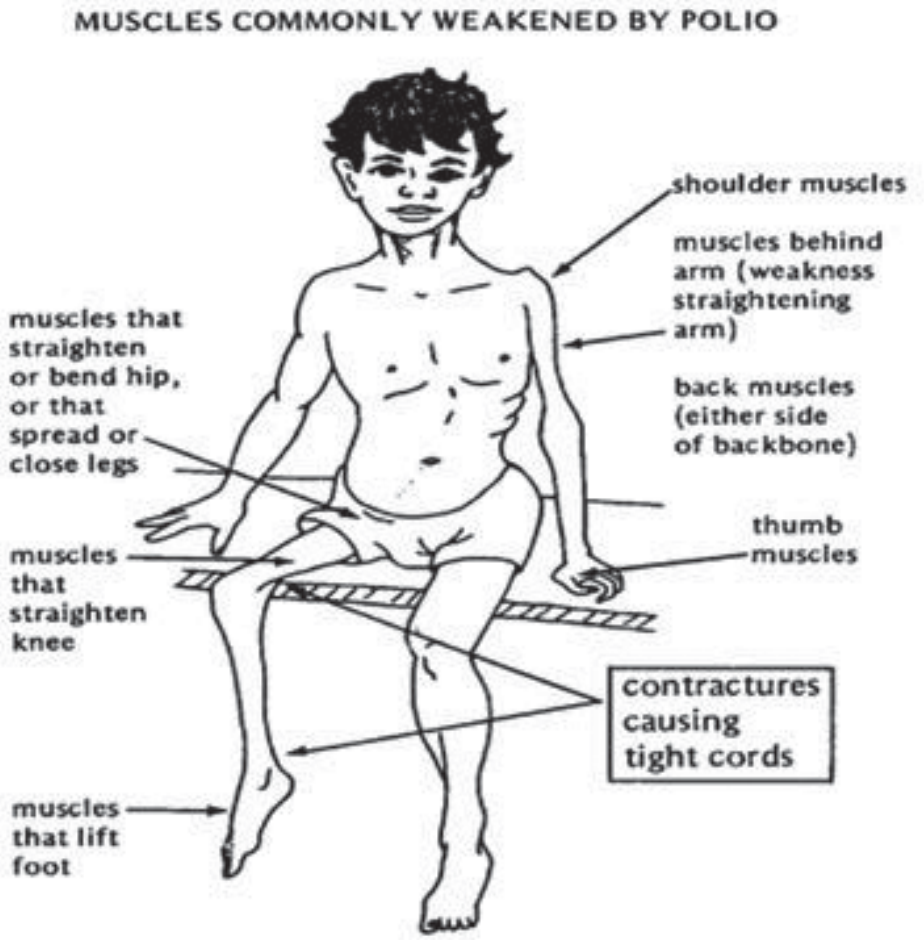
- delayed development
- abnormal posture (the ability to put the body in a chosen position and keep it there)
- difficulty in movement of body parts or the whole body
- muscle weakness or tightness
- involuntary muscle movements (spasms)
- imbalance and incoordination
- difficulty talking and eating.

Children can have different types of cerebral palsy:

- Hemiplegic (involves muscle movements and weakness on one side of the body)
- Diplegic (involves muscle movements and weakness in the lower part of the body)
- Quadriplegic (involves muscle movements and weakness in both arms and both legs)
- Ataxic (involves problems with balance and coordination).
- Dystonic/choreoathetoid (involuntary movements of hands ,legs and head /neck/ face)

Poliomyelitis

Poliomyelitis is an infectious disease caused by polio virus. A very few cases of poliomyelitis develop a paralytic poliomyelitis. Paralytic poliomyelitis may be clinically suspected in children experiencing a) acute onset of flaccid paralysis in one or more



limbs with b) decreased or absent tendon reflexes in the affected limbs that cannot be attributed to another apparent cause, and c) without sensory or cognitive loss. Minor symptoms such as fever, headache, vomiting, diarrhea, neck stiffness and pain in the arms and legs may be present and last for few days. There are many causes of acute flaccid paralysis (AFP); polio virus infection is one of the main causes. Acute poliomyelitis affects the anterior horn motor neurons of the spinal cord and brain stem causing severe muscle pain and spasms, followed by flaccid asymmetric weakness and muscle atrophy. Paralysis is usually asymmetric, begins in proximal extremities, and progresses to distal muscle groups. Paralysis remains for days or weeks before slow recovery occurs over months or years. Physical activity and intramuscular injections during the acute paralysis period should be avoided since they are known to cause exacerbation of the symptoms. There is no cure for poliomyelitis, however, it can be prevented by regular immunization through vaccination as per schedule. Therefore, family practitioner plays a very important role in prevention of polio. One should emphasize compliance to vaccination schedule.

Congenital defects

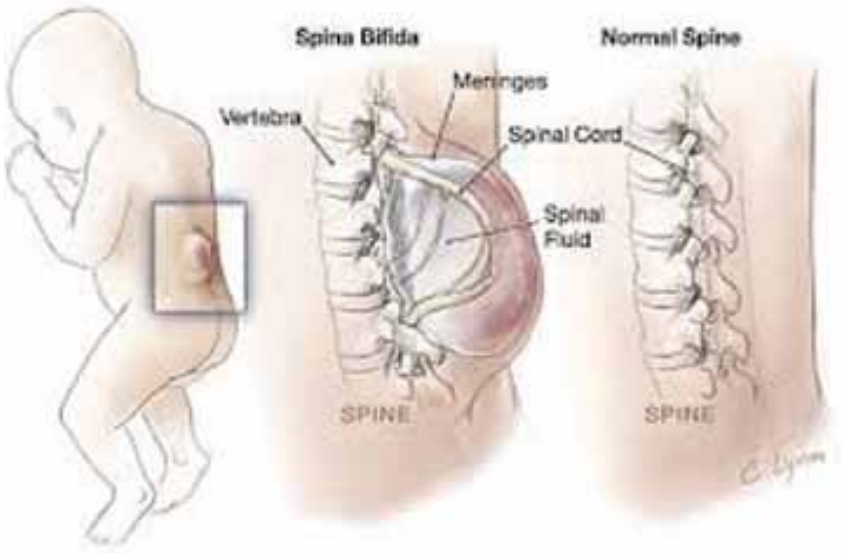
Spina bifida

Sometimes, a baby's spinal cord does not develop normally during pregnancy. When this happens, the child can have a physical disability called spina bifida. The type and amount of disability caused by spina bifida will depend upon the level of the abnormality of the spinal cord. Children with spina bifida may have:

- partial or full paralysis of the legs
- difficulties with bowel and bladder control.

They may also have:

- hydrocephalus (high pressure on the brain because of fluid not being drained away normally
- bone and joint deformities (they may not grow normally)
- curvature (bending) of the spine.

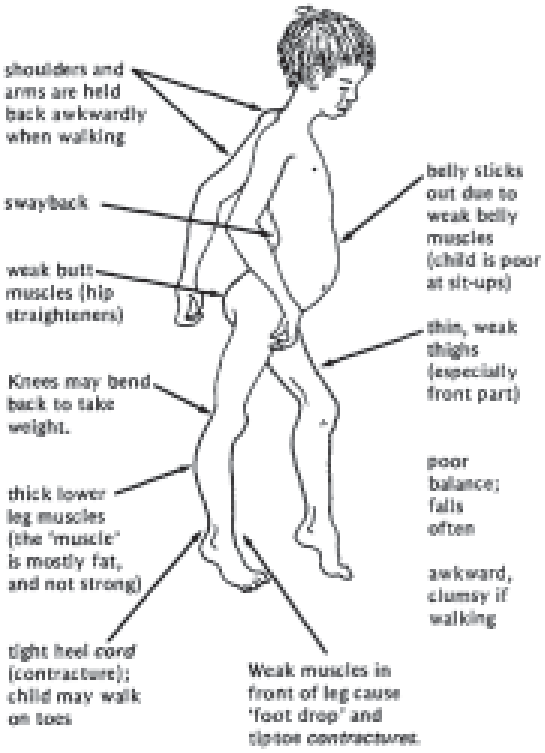


Muscular dystrophies

When a child has muscular dystrophy, the muscles show progressive weakness. The child may have difficulty running, walking, getting up from the floor, etc. Children can have different types of muscular dystrophy. The most common type is Duchenne Muscular Dystrophy which occurs only in boys. All types of muscular dystrophy are genetic even though other family members may not have the condition.

Multiple disabilities

Some children with physical disabilities will have other disabilities, such as intellectual, visual or hearing impairments. They may also have communication difficulties or



other medical conditions such as epilepsy or asthma. When a child has several different types of disability, professionals talk about multiple disabilities rather than listing separate conditions.

Acquired brain and spinal injuries

Physical disabilities may result from permanent injuries to the brain, spinal cord or limbs that prevent proper movement in parts of the body.

Investigations to be considered:

1. CT scan: A CT scan of the brain or spinal cord could be ordered as a screening tool to identify the underlying CNS pathology.
2. MRI scan: An MRI brain or spinal cord could be ordered in highly suspected cases of CNS disorders (encephalitis, epilepsy, etc). It is also helpful in detecting congenital malformations of the brain and spinal cord (meningomyelocele, spina bifida, etc)
3. Blood tests: Various blood tests to identify metabolic disorders (phenylketonuria, juvenile diabetes, etc), electrolyte imbalance and vitamin deficiencies (hypokalemia, Vit B12 deficiency, etc), hormonal disorders (hypothyroidism), etc could be ordered.
4. EEG: An EEG is ordered to identify any coexisting epileptic foci in the brain.

8. Intellectual Disability in Children

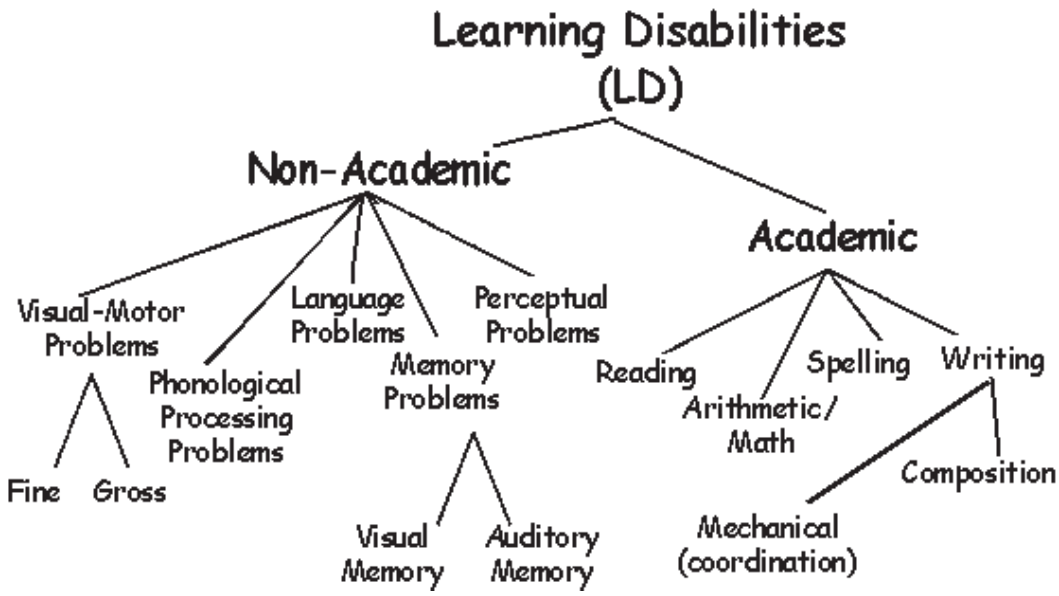
Intellectual disability (ID) is characterized by below-average intelligence or mental ability and a lack of skills necessary for day-to-day living. People with intellectual disabilities can and do learn new skills, but they learn them more slowly. The degrees of intellectual disability vary, from mild to profound.

Mental retardation is used as a blanket term for all patients with intellectual disabilities. However, this is not appropriate as all the children with IDs do not have low IQ. Therefore, we as doctors need to distinguish between MR and MR like conditions. We need to be sensitive and careful before labeling a child with MR as it may be very daunting for the parents and may affect the future of the child.

Intellectual disability can be divided into a) Mental retardation, b) Autism spectrum disorders and c) Learning disability

a) **Mental retardation:** In cases of mental retardation, intelligence level as determined by individual standard assessment is below 70, and the ability to adapt to the demands of normal life is impaired. Behavioral traits associated with MR may include aggression, dependency, impulsivity, passivity, self-injury, stubbornness, low self-esteem, and low frustration tolerance.

b) **Autism spectrum disorders:** Autistic children do not generally have diminished cognitive functioning. They have normal, even above normal intelligence. The issue with autistic children is their inability to function socially within the social



environment. They are unable to communicate with the outside world, using language. The classical triad of ASD shows: deficits in socialization, language and communication, stereotypical repetitive behavior.

c) **Learning disability:** A child who has learning disability may have difficulty reading, writing, spelling, reasoning, recalling and/or organizing information if left to figure things out by themselves or if taught in conventional ways. Common types of learning disabilities include: Dyscalculia, dysgraphia, dyslexia, language processing disorders, deficits in auditory processing, visual perceptual/ motor deficit, memory deficits, etc. A child suffering from ADHD may also present with LD. Children with learning disabilities are of average or above average intelligence. LDs should not be confused with learning problems which may be due to visual, hearing, or motor handicaps; mental retardation; emotional disturbance; and or environmental, cultural or economic disadvantages.

Someone with intellectual disability has limitations in two areas. These areas are:

- Intellectual functioning. Also known as IQ, this refers to a person's ability to learn, reason, make decisions, and solve problems.
- Adaptive behaviors. These are skills necessary for day-to-day life, such as being able to communicate effectively, interact with others, and take care of oneself.

IQ (intelligence quotient) is measured by an IQ test. The average IQ is 100. A person is considered intellectually disabled if he or she has an IQ of less than 70 to 75.

A child's adaptive behavior is analyzed by observing the child's skills and comparing them to other children of the same age. Things that may be observed include how well the child can feed or dress himself or herself; how well the child is able to communicate with and understand others; and how the child interacts with family,

friends, and other children of the same age.

Signs of intellectual disability in children

- Impaired comprehension or understanding
- Slow learning
- Delayed developmental milestones
- Delayed speech and language, and communication deficits
- Slow memory
- Abnormal behavior
- Affected ADLs
- Affected logical reasoning and problem solving ability

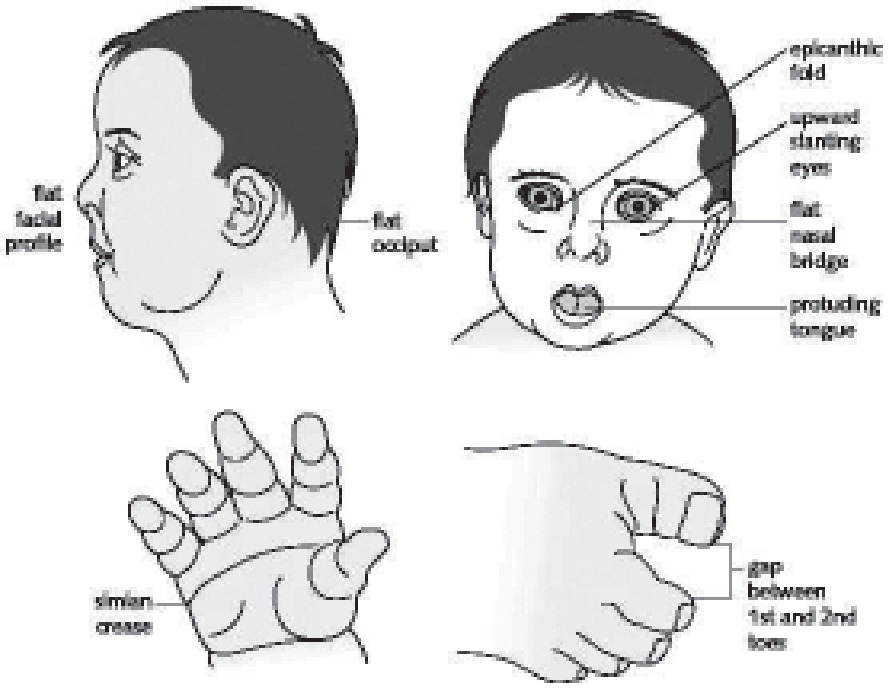
In children with severe or profound intellectual disability, there may be other health problems as well. These problems may include seizures, mental disorders, motor handicaps, vision problems, or hearing problems.

Causes:

ID could be a result of abnormal brain development or brain injury after birth or during childhood.

The most common causes of intellectual disability are:

- Genetic conditions: These include things like Down syndrome and fragile X syndrome.



- Problems during pregnancy: Things that can interfere with fetal brain development include alcohol or drug use, malnutrition, certain infections, or preeclampsia.
- Problems during childbirth: Intellectual disability may result if a baby is deprived of oxygen during childbirth or born extremely premature.
- Illness or injury: Infections like meningitis, whooping cough, or measles can lead to intellectual disability. Severe head injury, near-drowning, extreme malnutrition, exposure to toxic substances such as lead, and severe neglect or abuse can also be a cause.

Prevention:

Certain causes of intellectual disability are preventable. Nutritional causes and problems during birth are the most common causes in India. Getting proper prenatal care, taking a prenatal vitamin, and getting vaccinated against certain infectious diseases can also lower the risk that your child will be born with intellectual disabilities.

In families with a history of genetic disorders, genetic testing may be recommended before conception.

Certain tests, such as ultrasound and amniocentesis, can also be performed during pregnancy to look for problems associated with intellectual disability. Although these tests may identify problems before birth, they cannot correct them.

Diagnosis:

Intellectual disability may be suspected for many different reasons with a series of supportive investigations such as:

1. CT scan: A CT scan may help in identifying any structural abnormality or damage to the brain.
2. MRI scan: An MRI may help in diagnosing the disorder by helping visualize tissues of the brain and their integrity.
3. Blood tests: Blood tests may help identify metabolic disorders and nutritional deficits causing impaired mental function.
4. EEG: An EEG may help identify an underlying epileptic focus in the brain even before the symptoms arise.
5. Genetic testing: It is used to confirm the diagnosis by showing mutations in various genes which may be hereditary or acquired during gestation.

Section B

Neurological Investigations

(I) Neuroradiology

9. Computed Tomography (CT)

Neurological CT scans are used to view the brain and spine. They can detect bone and vascular irregularities, certain brain tumors and cysts, herniated discs, epilepsy, encephalitis, spinal stenosis, a blood clot or intracranial bleeding in patients with stroke, brain damage from head injury, and other disorders. It can also be used to guide biopsies.

Computed tomography, also known as a CT scan, is a noninvasive, painless, X-ray imaging procedure used to produce rapid, clear two-dimensional images of organs, bones, and tissues. The cross-sectional images generated during a CT scan can be reformatted in multiple planes, and can even generate three-dimensional images. Depending on the clinical indication, the scan can be performed with or without intravenous contrast injection.

When to order CT v/s MRI?

- CT scan is used in emergency neurological conditions, as it is quick, takes lesser time and easily available.
- CT is very good for imaging bony structures. Therefore, in all head trauma cases and accidents with multiple injuries, CT scan should be ordered as a screening test.
- CT scan can easily and quickly distinguish between ischaemic and haemorrhagic stroke. Thus, in all suspected stroke cases CT brain scan should be ordered immediately.
- In cases of severe headache or atypical headache or headache with warning signs, CT brain scan should be ordered.
- In any cases of altered mental status or coma, CT brain should be ordered.
- CT scan is used as a screening tool for migraine, tumours, transient ischaemic attacks (TIA), dizziness, seizures, congenital deformities of the skull or brain, etc.
- Patients having metallic implants, pacemakers cannot receive an MRI but can have a CT scan.

- CT scan may be done as a pre-requisite for surgical procedures of the brain and spinal cord (for e.g. CT guided biopsy).

Four basic steps of CT scanning:

1. X-Ray Production
2. Data Acquisition
3. Data Processing
4. Image Display

CT scan works much like other X-ray examinations in which different parts of the part being scanned absorb X-rays in varying degrees. It is this crucial difference in absorption that allows the body parts to be distinguished from one another on an X-ray film or CT electronic image.

The CT scanner takes X-ray images at various angles around the body with the help of rotating X-ray beams and X-ray detectors. These images are processed by a computer to produce cross-sectional pictures of the body. These pictures are seen as an X-ray 'slice' of the body, which is recorded on a film and called as a tomogram. Three-dimensional models of the body area also can be created by stacking the slices together.

Certain exams require a special dye, called contrast, to be delivered into the person's body through intravenous injection, orally or per rectum. Contrast CT scan helps to highlight structures such as blood vessels and obtain functional information about specific tissues.

CT scanning is used in medicine as a diagnostic tool and as a guide for interventional procedures.

Indications for head CT examination include the following:

- Head trauma
- Stroke
- Headaches
- Initial evaluation for space-occupying lesions, tumors
- Unexplained change in mental status
- Seizures
- Suspected hydrocephalus
- Suspected intracranial hematoma, infections
- Psychiatric disorders
- Dizziness
- Vascular occlusive disease and aneurysm evaluation
- Diseases or malformations of the skull
- Guide the biopsy of the brain

Indications for spine CT examination include the following:

- Guide diagnostic procedures such as the biopsy of a suspicious area to detect cancer, or the removal of fluid from a localized infection (abscess)
- Congenital anomalies of the spine
- Tumors of the spinal cord, spinal pain
- Spinal injury
- Detection of spinal canal stenosis, vertebral fracture, and infection of the spine and spinal cord.
- When MRI is not available/possible.

Special precautions to be taken for CT examination include the following:

- CT should be performed for pregnant patients only in critical situations and only after discussion of the potential risks and benefits.
- Repeated X-ray exposure may increase the patient's risk for cancer. However, the risk from any one scan is small, with the benefit of an accurate diagnosis outweighing the risks.
- In certain clinical situations, intravenous contrast administration is indicated. Contrast media is safe in most patients. However, adverse reactions may occur in patients who have an allergy to the IV contrast media, or patients suffering from renal impairment, hyperthyroidism, phaeochromocytoma, myasthenia gravis, etc.
- Checklist to be considered before ordering a CT scan with contrast:
    a) Presence of renal failure (as in alcohol abuse, angina, heart failure, kidney problems, liver disease, severe infection).
    b) If taking diabetes medication Metformin, medicine may need to be stopped temporarily for 48 hours (Since contrast medium affects the kidneys temporarily and kidneys are involved in removal of metformin, contrast medium can greatly increase the levels of metformin in the blood which increases the risk of lactic acidosis.)
    c) Any previous reaction to contrast.
    d) It is recommended that nursing mothers should wait 24 hours after contrast administration to resume breastfeeding.

Advantages of CT scan:

- The time taken for total testing is shorter in CT than for MRI. Thus, CT is used in emergency settings as well as a screening method for detecting suspected brain and spine disorders, wherein use of MRI is not possible due o unavailability and/or time constraints.
- MRI cannot be done on patients who are claustrophobic as the patient has to remain inside the noisy machine for about 20-45 minutes. CT is more comfortable.

- CT scan is cheaper than an MRI.
- CT is less sensitive to patient motion than MRI.

Disadvantages of CT scan:

- Risk of ionizing radiations is always there in CT scan.
- CT does not differentiate well between bone, soft tissue and blood vessels. It also does not give inter soft tissue differentiation.
- Contrast medium used in CT contains iodine, while MRI uses non iodine contrast medium.
- CT scan does not visualize the spinal cord adequately.

Common CT brain findings:

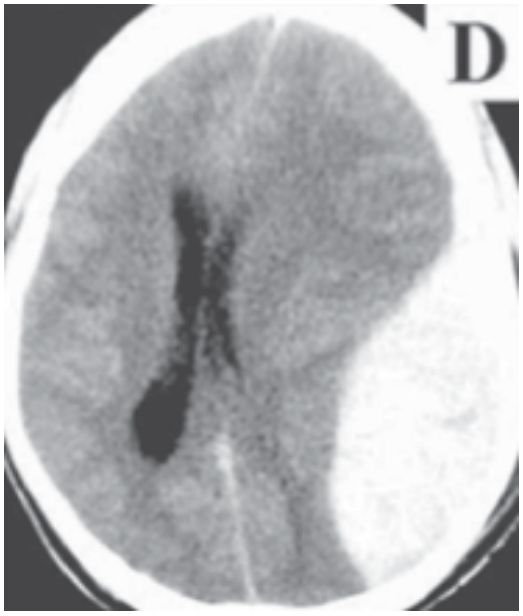


Fig 9.1 CT scan of brain in a case of head injury showing large left parietal extradural haematoma

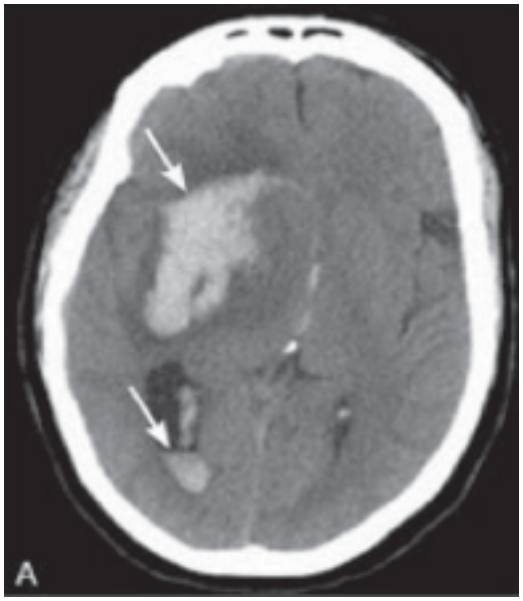


Fig 9.2 CT scan of brain showing acute intracerebral haemorrhage with midline displacement (Note: Acute haemorrhage appears hyperdense, i.e. white on CT scan)

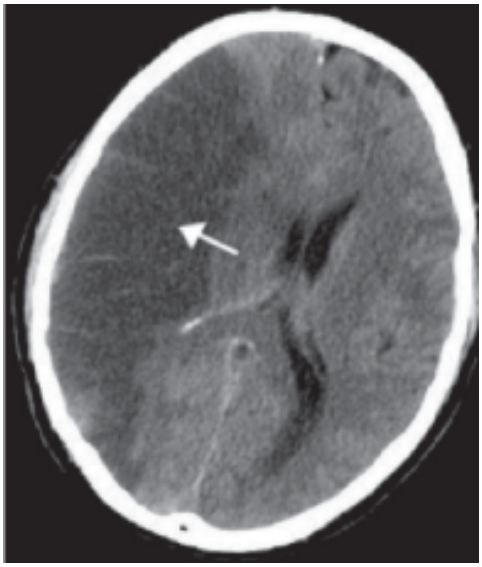


Fig 9.3 CT scan of brain showing right hemisphere ischaemic stroke with midline displacement

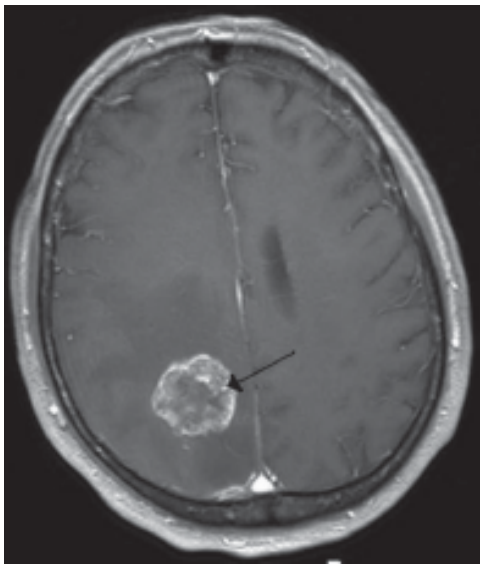


Fig 9.4 CT scan of brain showing right hemispheric intracerebral tumour

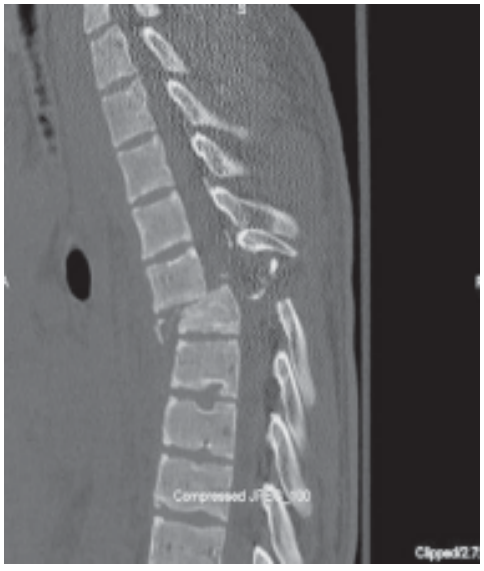


Fig 9.5 CT scan of spine showing compression fractures of T5 and T6 vertebrae with anterior subluxation of T5 over T6 with intraspinal fracture fragments and severe spinal cord injury

10. Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging (MRI) is a medical imaging technique that uses a powerful magnetic field and radio waves to produce detailed images of body structures including tissues, organs, bones, and nerves to study the anatomy and physiology of the body in both health and disease. An MRI differs from a CT scan, in that it does not use radiation. Brain and spine MRI is an excellent diagnostic and prognostic tool for various neurological and neuromuscular disorders like cerebrovascular diseases, tumours, demyelinating and infectious diseases of the brain and spinal cord.

When to order an MRI scan instead of CT scan?

- MRI is done once CT scan has already detected a brain tumour. MRI visualizes the brain and soft tissues very well, so, the extent, spread, type and staging of the tumour can be done in detail.
- MRI is done as a follow up scan in cases of stroke to know the area of damage and prognosis.
- In cases of spinal cord injury, degenerative disc disease, spinal cord tumour, meningioma, meningomyelocoele, transverse myelitis, infections of the spine, MRI is done. Spinal cord is visualized better with MRI than with CT scan.
- MRI is an imaging modality of choice in cases where a definitive diagnosis is suspected clinically or through previous imaging like CT scan. It is used to confirm the diagnosis and to better visualize the soft tissues and their abnormalities.
- In neurodegenerative conditions, for e.g. dementia, multiple sclerosis, multi system atrophy (MSA), Parkinson's disease, cerebellar ataxia, etc, an MRI scan is preferred.
- MRI is ordered in cases of behavioral problems and psychiatric disorders.

Principle of MRI

The hydrogen protons contained in water molecules of the body exhibit tiny magnetic fields which normally move around randomly. During an MRI scan, when short bursts

of radio waves are applied to the body, these tiny magnetic fields of the hydrogen protons align to the magnetic field and realign back into place alternately. This makes the protons' magnetic fields spin round in unison and emit a weak radio signal in resonance. The protons in different tissues of the body realign at different speeds and thus, emit signals of varying intensities. This forms the basis of differentiation of various soft and hard tissues of the part being scanned. A receiving device receives and transmits the resonance signals to a computer, where clear, cross-sectional black and white images of the body are created. Each of these images shows a thin slice of the body and differentiates between bone, soft tissues and fluid-filled spaces by their water content and structural properties. These images can be converted into three-dimensional (3-D) pictures of the scanned area. The field strength of the magnet is measured in tesla, and the majority of systems operate at 1.5T. T1 image weighting is useful for assessing the cerebral cortex and identifying fatty tissue, while T2 image weighting is useful for detecting edema and revealing white matter lesions.

Contrast MRI scanning

Chelates of gadolinium are the most commonly used intravenous contrast agents.

- These agents are safer than the iodinated contrast agents used in X-ray radiography or CT.
- Gadolinium agents are safe in patients with renal impairment, though precautions have to be taken before administering these agents in specific cases.
- In patients with severe renal failure requiring dialysis there is a risk of nephrogenic systemic fibrosis. Therefore, dialysis patients should receive gadolinium agents only when essential.
- Dialysis should be performed as soon as possible after the scan to remove the agent from the body promptly.

Indications of MRI brain

- To check for causes of muscle weakness, numbness and tingling.
- To check for causes of symptoms such as change in consciousness, confusion, or abnormal movements. These symptoms may be caused by brain diseases, such as Huntington's disease, multiple sclerosis, Parkinson's disease, or Alzheimer's disease.
- To look for tumors, infections, abscess, or conditions of the brain or brain stem, such as encephalitis or meningitis.
- To investigate birth defects and developmental anomalies.
- To investigate causes of epilepsy (seizure).
- To check for integrity of brain and other cranial structures in head trauma.
- To diagnose a stroke or blood vessel problems in the head.

- To investigate psychiatric disorders.
- To look for causes of hearing loss, memory loss, headaches, speaking difficulties, vision problems and dizziness.
- To diagnose vascular occlusive disease and aneurysm.

Indications of MRI spine

- To assess the spinal anatomy and alignment in injury and birth defects.
- To look for causes of muscle weakness in the limbs, numbness and tingling, abnormal movements.
- To look for problems in controlling or emptying urinary bladder.
- To assess intervertebral disc and joint for diagnosing sciatica, nerve root entrapment, spinal cord indentation.
- To assess compression of spinal cord and nerves.
- To help plan and monitor spinal surgical procedures, such as decompression of compressed spinal cord and nerves or spinal fusion.
- To image spinal infection or tumors.
- To assess inflammation of the spinal cord or nerves.

Contraindications of MRI scan

- Patients with metal implants (brain aneurysm clips , prosthetic metal heart valves, eye implants, intrauterine device, artificial joints, dental fillings and braces, tubal ligation clips, surgical clips or staples) and implanted electronic device (cardiac defibrillator, pacemaker, retained leads, implanted nerve stimulators, implantable cardioverter-defibrillator) can experience excess MRI related heating during the scanning procedure.
- These implants can also interfere with the MR signaling and produce artifacts which deteriorate the quality of images and also may produce false and misleading images of the inside of the scanned body part.
- The patients need to inform about these implants to the referring doctor and staff carrying out MRI scanning so that they are aware of the risks associated with MRI scanning and measures are taken to ensure the scan is as safe as possible.
- Some tattoo ink contains traces of metal, but most tattoos are safe in an MRI scanner.
- MRI scans are not usually recommended during pregnancy, particularly in the first three months.

Advantages of MRI scan

- MR images of the brain and other cranial structures are clearer and more detailed

than with other imaging methods. Thus, MRI should be preferred for imaging if available.

- MRI uses non iodine contrast medium which is safer than iodine containing contrast media used in X-ray and CT imaging.
- Risk of ionizing radiations is absent in MRI scan.
- MRI is the most sensitive means to detect and evaluate brain tumors.
- MRI can detect stroke at a very early stage (within less than 30 minutes) by mapping the motion of water molecules in the tissue.
- The MRI examination poses almost no risk to the average patient when appropriate safety guidelines are followed.

Disadvantages of MRI scan

- Implanted medical devices that contain metal may malfunction or cause problems in obtaining clear images during an MRI exam.
- Metallic implants, pacemakers may malfunction or cause problems during an MRI exam.
- Nephrogenic systemic fibrosis may occur as a complication of MRI caused by the injection of high doses of gadolinium-based contrast material in patients with very poor kidney function.
- A person who is very obese and large may not fit into the opening of certain types of MRI machines.
- The time taken for MRI scanning is longer than for CT. Also, traction devices and life support equipment used in emergency settings have to be kept away from the area to be imaged. Thus, MRI cannot be used in emergency settings.
- MRI is many a time uncomfortable for patients who are claustrophobic and cannot remain in the noisy machine for such long testing time.
- MRI costs more than CT.
- MRI is sensitive to patient motion. Patient motion can give rise to bad quality images.

MRI with DTI

Diffusion tensor imaging (DTI) is an MRI technique used to noninvasively visualize anatomical connections between different parts of the brain. It is used to study abnormalities in white matter fiber structure (location and orientation) and brain connectivity. DTI is useful in the investigation of stroke, epilepsy, multiple sclerosis, brain abscesses, brain tumors (localization, infiltration), mild traumatic brain injury (defining the severity), and hypertensive encephalopathy. It is used in surgical planning of brain tumors, to determine the proximity and relative position of the corticospinal tracts and a tumor.

DTI tractography is a 3D modeling technique used to visualize neural tracts. It can also visualize very short connections present among cortical and subcortical regions. It is used for measuring deficits in white matter (such as in aging), differentiation of brain tumour, distinguishing between acute-ischemic changes and chronic-ischemic changes in cases of stroke, diagnosing and follow up of MS lesions, determining the location and extent of epileptic foci, etc. It helps in preoperative planning in terms of determining the extent of diffuse infiltration of pathologic tissue (for e.g. tumour, abscess) to minimize functional damage and residual tumor volume.

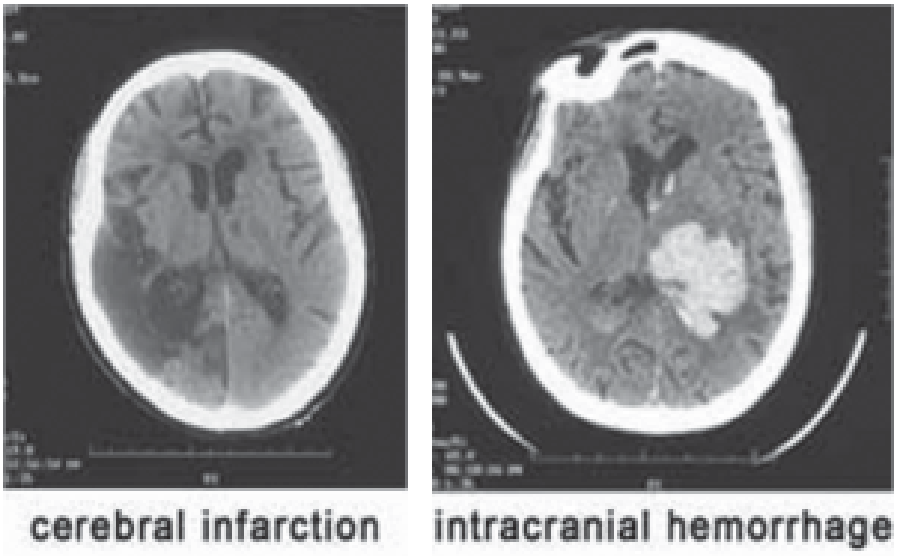


Fig. 10.1 MRI Scan of Brain

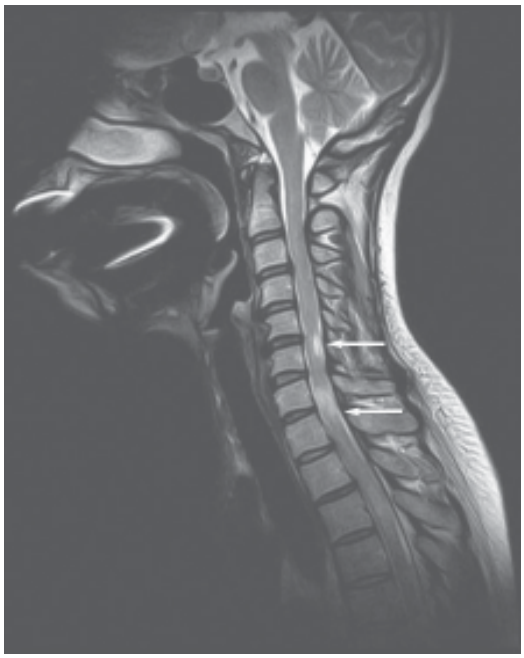


Fig. 10.2 MRI Scan of Spinal cord

11. Angiography

Angiography is a very specialized test which is ordered by a neurologist or a neurosurgeon. Angiography is a minimally invasive medical test that uses X-rays or MRI technology and an iodine or gadolinium containing contrast material to produce pictures of the blood vessels. Imaging of the vascular architecture of the brain is termed as Neuro-angiogaphy.

Angiography can be performed using:

- Digital X-ray technology (DSA)
- Computed Tomography (CT)
- Magnetic Resonance Imaging (MRI)

Digital subtraction angiography (DSA) is a type of fluoroscopy technique used to clearly visualize blood vessels in a bony or dense soft tissue environment.

Procedure: A pre-contrast image which includes all the structures within the head like skull, brain, CSF, meninges, blood vessels, etc. is acquired first by a digital X-ray using technology. In catheter angiography a catheter is introduced into the superficial femoral artery of the patient after giving local anaesthesia (general anaesthesia in children) and navigated under X-ray guidance up to the carotid artery where an iodine containing contrast material is injected and multiple X-ray images are taken. In IV-DSA, radiopaque iodine based dye is injected intravenously into the body. The contrast material flows along with the blood to the cerebral arteries and highlights the blood vessels on the X-ray. These images are simultaneously stored in the computer which then subtracts the 'pre-contrast image' from the 'post-contrast image'. Tissues and blood vessels on the first image are digitally subtracted from the second image, leaving a clear picture of the artery or vein for assessing the integrity of these blood vessels and abnormalities in them.

CT angiography uses a CT scanner to produce detailed images of both blood vessels of the brain. An iodine containing contrast is through intravenous route. A CT scan is then performed while the contrast flows through the blood vessels to the blood vessels of the brain. After scanning, the images are processed on a computer and reviewed in different planes and projections. In Digital Subtraction Angiography (DSA), images are electronically manipulated to remove (subtract) bones and other

structures obscuring the images taken to make the blood vessels stand out.

Magnetic resonance angiography (MRA) uses magnetic resonance imaging (MRI) technology to image blood vessels.

Various MRI techniques include:

- Flow-dependent angiography
  - Time-of-flight (TOF) or inflow angiography
  - Phase-contrast (PC-MRA)
- Flow-independent angiography
  - Contrast-enhanced Magnetic Resonance Angiography
  - Subtraction less Contrast-enhanced Magnetic Resonance Angiography
  - Non-enhanced magnetic resonance angiography

Indications of cerebral angiography

To diagnose and evaluate diseases of blood vessels and related conditions such as:

- Cerebral aneurysm
- Brain arteriovenous Malformation (AVM)
- Dural arteriovenous fistula
- Intracerebral Hemorrhage
- Dissections of arteries
- High-grade intracranial stenosis
- Acute stroke
- Multiple sub cortical strokes in cerebral vasculitis
- Intracranial tumor and its blood supply
- Cerebral venous thrombosis
- Congenital abnormalities in blood vessels

Indications of spinal angiography

Evaluating and diagnosing diseases of blood vessels and related conditions of the spine including:

- Bleeding into the blood vessels of the spinal cord.
- AVM
- Aneurysm
- Stenosis, thrombosis of spinal blood vessels

- Spinal stroke due to blockage of blood vessel
- Stroke due to blood vessel inflammation
- Suspected rupture of blood vessels of the spine
- Spinal tumour and its blood supply
- Suspected spinal dural fistula
- Unexplained spinal disease

Contraindications of angiography

DSA and CT angiography:

- Patients with bleeding disorders
- Patients who have an allergy to the IV contrast media
- Patients suffering from renal impairment, hyperthyroidism, phaeochromocytoma, myasthenia gravis, etc.
- Presence of renal failure (as in alcohol abuse, angina, heart failure, kidney problems, liver disease, severe infection).
- Patients taking diabetes medication Metformin. Medicine may need to be stopped temporarily for 48 hours
- Pregnant females should have the scan done only in critical situations after discussion of benefits and risks.
- Complications such as an allergic reaction to the anesthetic or the contrast medium, blockage or damage to the vessel punctured, thrombosis and embolism formation, bleeding or bruising at the site of puncture/injection, and anywhere along the vessel during passage of the catheter, increased risk of ionizing radiation can also occur.

MR Angiography:

- Patients with metal implants and implanted electronic device (cardiac defibrillator, pacemaker)
- Pregnancy (especially in the first trimester)

Advantages of DSA

- Results from cerebral angiography are more accurate than those produced by carotid Doppler ultrasound or other noninvasive imaging of the blood vessels.
- Use of a catheter makes it possible to combine diagnosis and treatment in a single procedure.

Disadvantages of DSA

- Risk of ionizing radiations and allergic reaction to iodine containing contrast is present.
- Risk to the foetus in pregnant females.
- Risk of catheter introduction causing damage to the vessels is present.
- Risk of stroke occurring due to dislodged thrombus from artery into the vessels supplying brain by the catheter is present.

Advantages of MR angiography

- It is a non-invasive technique not involving introduction of catheter into any blood vessel.
- It does not use ionizing radiations.
- Contrast medium used in MRA does not contain iodine and is less toxic and can be used in patients with renal impairment.

Disadvantages of MR angiography:

- It is unsafe and cannot be used for patients having metal and electronic implants.
- High cost of MRA makes it a less frequently used diagnostic test.

Common DSA findings

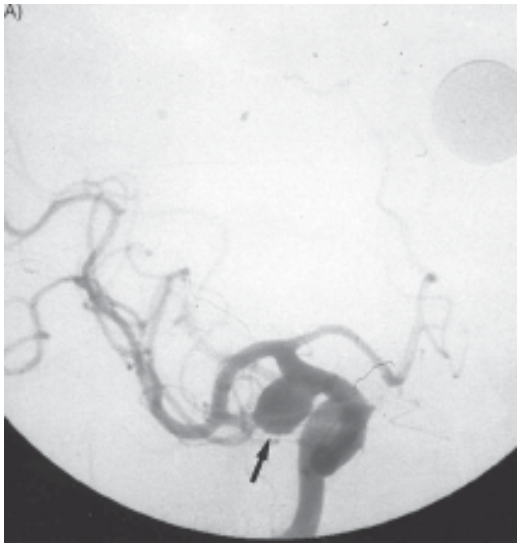


Fig 11.1 DSA showing right posterior communicating artery aneurysm (arrow)

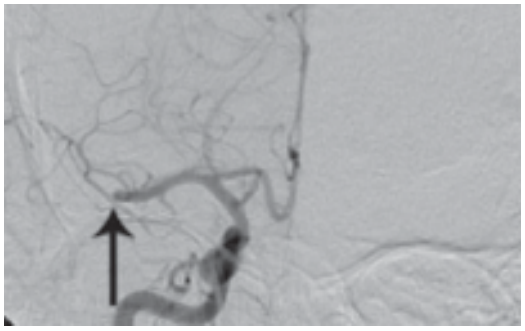


Fig 11.2 DSA showing occlusion of right middle carotid artery by a clot

Common CT angiography findings:

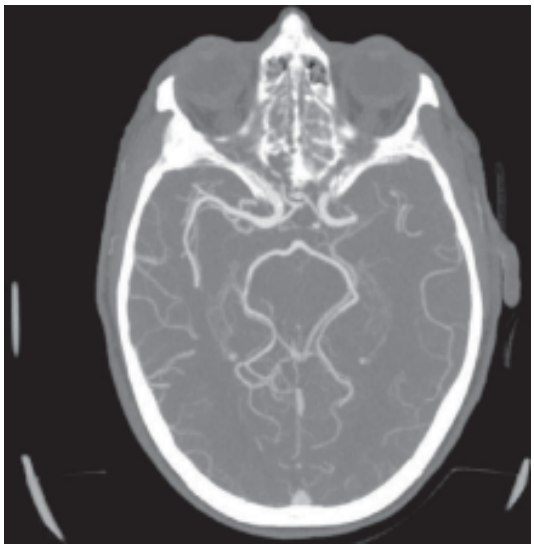


Fig 11.3 Cerebral CT angiogram showing occlusion of left middle carotid artery

Common MR angiography findings:

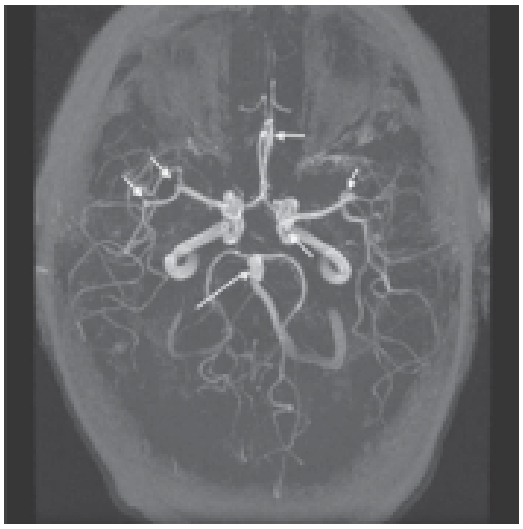


Fig 11.4 Cerebral MR angiogram showing multiple aneurysms

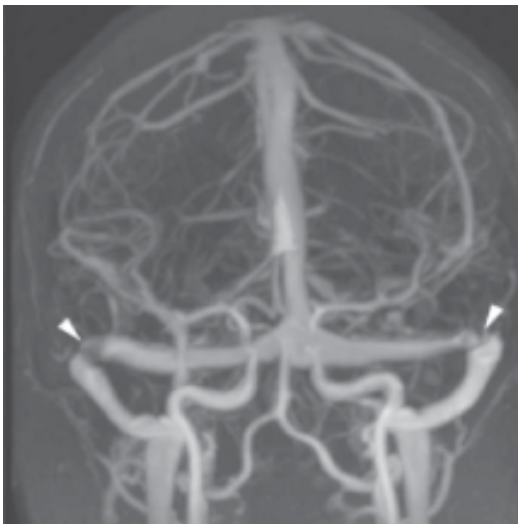


Fig 11.5 Cerebral MR angiogram showing bilateral transverse cerebral venous stenosis

12. Plain X-Ray

X-rays are a type of radiation called electromagnetic waves. When the body is exposed to X-rays, different parts of the body absorb different amounts of radiation and allow varying amounts of the X-rays to pass through depending on their densities.

X-rays pass through body tissues onto specially treated plates and a 'negative' type picture is made. Images are produced in degrees of light and dark, depending on the amount of X-rays that penetrate the tissues. The soft tissues in the body (such as blood, skin, fat, and muscle) allow most of the X-ray to pass through and appear dark gray on the film. A bone, metal or a tumor, which is denser than the soft tissues, allows few of the X-rays to pass through and appears white on the X-ray. At a break in a bone, the X-ray beam passes through the broken area and appears as a dark line in the white bone.

Radiographs are useful in the detection of pathology of the skeletal system as well as for detecting some disease processes in soft tissue of brain and spinal cord. Radiographs may show fractures, presence of foreign body intracranial air, midline shift of structures through shift of calcified pineal gland, etc.

For some types of X-ray tests, a contrast medium such as iodine or barium is introduced into the patient's body, either orally, intravenously, rectally or intrathecally (myelogram). In some people, the injection of a contrast medium can cause side effects such as feeling of warmth or flushing, a metallic taste in the mouth, lightheadedness, nausea, itching and rarely, severe reactions which include severe hypotension, anaphylactic shock and cardiac arrest.

Though X-rays of the skull are not used as often as in the past, due to the use of newer technologies such as computed tomography (CT scans) and magnetic resonance imaging (MRI), they remain valuable for evaluating the bones of the skull and spine for fractures and detecting other conditions of the skull, spine and their contents.

Indications of X-ray imaging

- Head trauma
- Spine trauma
- Suspected non-accidental injuries to detect previous injuries

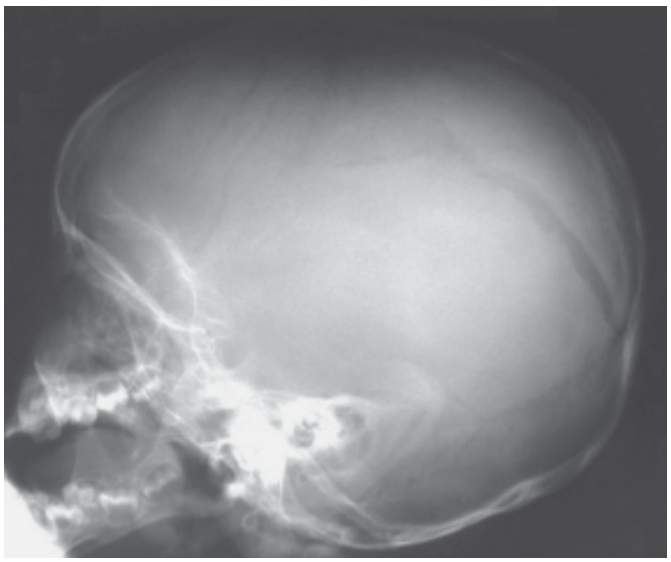


Fig. 12.1: X-Ray Brain

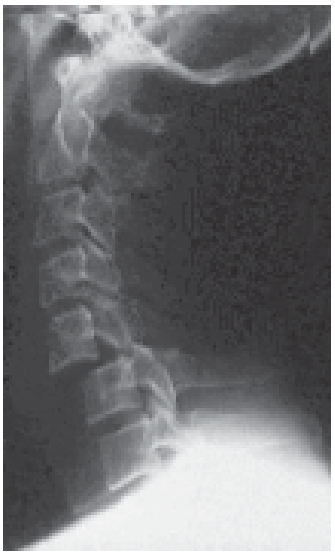


Fig. 12.2: X-Ray Spinal Cord

- To detect tumors
- Congenital anomalies of the cranial vault and spine
- Headache
- Certain metabolic and endocrine disorders that cause bone defects of the skull.
- Detect cerebral calcification
- Migration of the soft tissues inside the skull

Contraindications of X-ray imaging

- Risks associated with radiation exposure may be related to the cumulative number of X-ray examinations and/or treatments over a long period of time.
- Radiation exposure during pregnancy may lead to birth defects. When taking a skull X-ray, special precautions should be made to minimize the radiation exposure to the foetus.
- Patients having allergy to iodine or barium contrast agents are contraindicated for contrast induced X-ray imaging.
- Contrast media is safe in most patients. However, adverse reactions may range from mild to severe in patients suffering from renal impairment, hyperthyroidism, phaeochromocytoma, myasthenia gravis, etc

Common radiographic findings valuable in neurological diagnosis:

13. Positron Emission Tomography-Computer Tomography (PET-CT)

Positron emission tomography (PET) scanning is a very specialized scanning procedure, which is used only in specialized cases, where apart from structural imaging, a functional imaging of the body part is required (for e.g. tumours, Alzheimer's disease, epilepsy, behavioral disorders, etc.). PET is a functional imaging technique that produces a three-dimensional image of functional processes in the body.

Procedure: A positron-emitting radionuclide (tracer), usually fluorodeoxyglucose (FDG), an analogue of glucose is introduced into the body on a biologically active molecule intravenously, which is taken up by active tissues of the body. Gamma rays are created during the emission of positrons from these active tissues, and the scanner then detects the gamma rays. A computer then analyzes the gamma rays and uses the information to create an image map of the organ or tissue being studied.

Principle: PET neuroimaging is based on the principle that areas of high radioactivity are associated with brain activity. The amount of the radionuclide collected in the tissue affects how brightly the tissue appears on the image, and indicates the level of organ or tissue function. If blood flow and perfusion of an organ or tissue has to be studied, the radionuclide chosen may be a type of radioactive oxygen, carbon, nitrogen, or gallium.

Functional imaging obtained by PET can be more precisely aligned or correlated with anatomic imaging obtained by CT scanning. In modern PET-CT scanners, three dimensional imaging is often accomplished with the aid of a CT X-ray scan performed on the patient during the same session, in the same machine.

Uses of PET-CT scans

PET and PET-CT scans are performed to:

- To detect suspected brain and spinal tumours.
- To detect cancer metastasis and recurrence of tumors.
- To determine staging of patients with tumours where staging is difficult clinically, and also to help in radiotherapy planning.

- To evaluate the prognosis of a treatment plan, such as cancer therapy.
- To evaluate and diagnose memory disorders (Alzheimer's disease) and other central nervous system disorders such as Parkinson's disease, Huntington's disease, epilepsy, and cerebrovascular accident.
- To localize epileptic foci.
- To evaluate the perfusion (blood and oxygen flow) of the brain tissue using the tracer oxygen-15.
- To examine links between specific psychological processes or disorders and brain activity.
- To locate the specific surgical site prior to surgical procedures of the brain.
- To facilitate PET-image guided surgery of intracranial tumors, arteriovenous malformations and other surgically treatable conditions.
- To map normal human brain for research purposes.
- To compare the effects of a treatment intervention on brain function, using a pre and post intervention PET scan.

Contraindications of PET-CT scan

- Pregnant females should not undergo the scan since radiation is believed to be unsafe for developing fetuses.
- Recent chemotherapy or radiotherapy can make interpretation difficult.
- Patients having allergies or who are sensitive to radionuclide, contrast dyes, or iodine.
- Very obese people may not fit into the opening of a PET-CT scanner.

Precautions for PET-CT scan

- Other imaging methods should be considered for pregnant patients.
- Patients who are claustrophobic may find the test uncomfortable.
- High blood glucose levels in diabetics may interfere with the accuracy of a PET scan, since high levels lower the FDG tracer uptake in tissues and tumour cells. A diabetic patient may be instructed to take pre-procedure insulin dose with a meal several hours prior to the procedure. Also, fasting for a certain period of time prior to the procedure may be required. If plasma glucose level is <120 mg/dl the FDG PET study can be performed. If plasma glucose level is >120 mg/dl the FDG PET study may be rescheduled or the patient excluded depending on the patient circumstances and the need for the test being conducted.
- Since medications such as tranquilizers and sedatives, and alcohol act as CNS depressants, while caffeine and nicotine in tobacco and smoking act as CNS

stimulants, their consumption should be avoided a day prior to testing to avoid false results on scans.

- Some of the administered FDG might be excreted in small amounts in breast milk. Therefore, milk should be collected and discarded for 2 hours after the scan following which normal breast feeding can be resumed.

Advantages of PET-CT scan

- PET-CT scan provides information on both function and anatomic structure of the brain and spinal cord that is unattainable using other imaging procedures.
- PET-CT scan results help in more accurate diagnosis of various neurological disorders.
- PET-CT scans are less expensive than exploratory surgery and yield more precise information.
- By identifying changes in the body at the cellular level, PET imaging may detect the early onset of disease before it is evident on other imaging tests such as CT or MRI.

Disadvantages of PET CT scan

- Injection of the radiotracer may cause pain and inflammation.
- PET CT scans are time consuming.
- Test results of diabetic patients or patients who have eaten within a few hours prior to the examination can be adversely affected because of altered blood sugar or blood insulin levels.
- Because the radioactive substance decays quickly and is effective for only a short period of time, late arrival of the patient for the test may require rescheduling the procedure for another day.

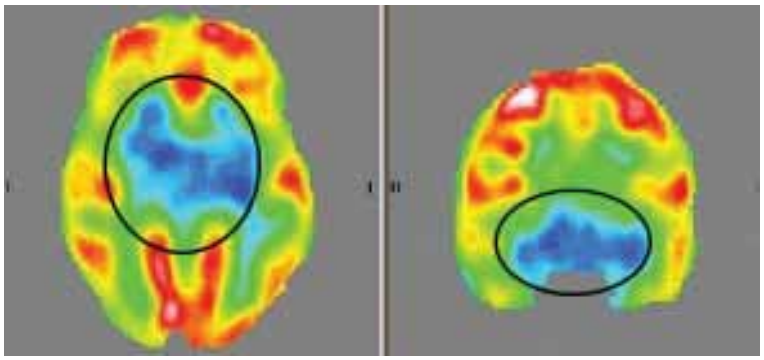


Fig. 13.1 : PET CT scan of the brain in autism. The areas of reduced metabolism and FDG uptake are seen in different shades of blue colour.

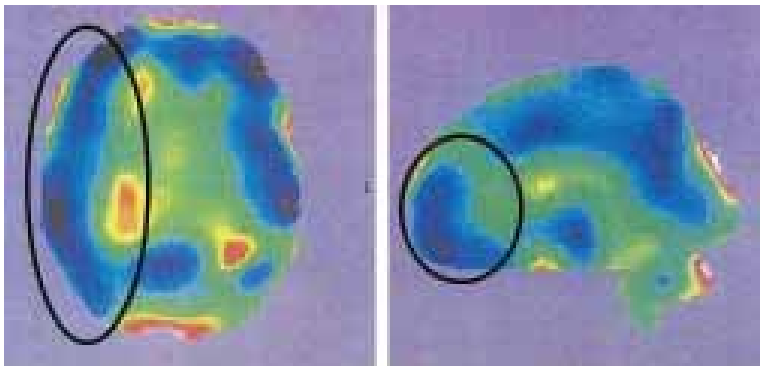


Fig.13.2: PET CT scan of the brain in cerebral palsy showing, blue/black areas as severe damage.

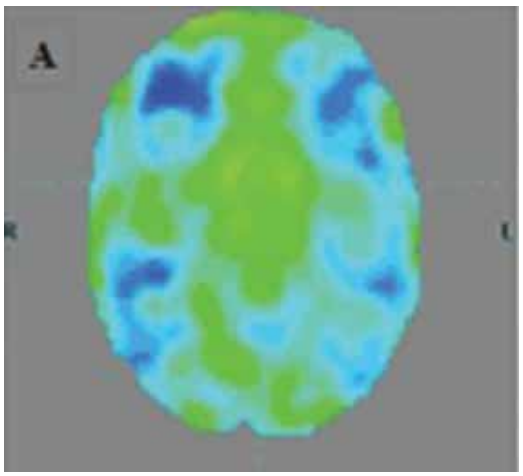


Figure 13.3: PET-CT scan brain in intellectual disability showing decreased FDG uptake in the frontal, parietal, temporal, occipital, mesial temporal structures bilaterally.

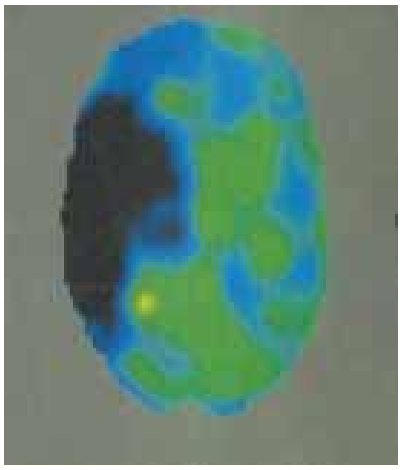


Figure 13.4: PET-CT scan brain in stroke showing blue and black areas as severely damaged.

14. Functional MRI

Functional Magnetic Resonance Imaging (fMRI) is a very specialized imaging test which is ordered by a neurologist or a neurosurgeon. It is a functional neuroimaging procedure that uses MRI technology to measure activity of neurons in the brain and spinal cord by detecting associated changes in blood flow in the area of activation. When neurons of a particular brain or spinal cord area become active, blood flow to that area increases bringing in more oxygenated haemoglobin which is diamagnetic (resistant to magnetism) than deoxygenated haemoglobin which is paramagnetic (attracted to magnetism). While performing an MRI scan, this difference in rising oxygenated haemoglobin level gives rise to an improved MR signal, since diamagnetic blood interferes less with the magnetic MR signal. This improvement is mapped and represented graphically by color coding according to the strengths of activation, to show which neurons are active at the time of a particular task during MRI scanning.

Procedure

fMRI detects differences in brain activity involved in a sensory, motor, cognitive function or a behavioral function. During the fMRI procedure, the patient is asked to alternatively perform a specific task or is stimulated to trigger several processes or emotions. The stimuli can be grouped in blocks (e.g. 30s-long) or presented as events. Each of the conditions is repeated several times and separated by rest periods. The combination of these conditions is called an fMRI paradigm. Tasks like tapping the fingers, toes, moving feet up and down are commanded to perform to study activation of the areas involved in motor function. To study areas of activation in sensory function, sensory stimuli like stroking with a brush along a particular dermatome (cutaneous), viewing pictures (visual), listening to an audio (auditory), smelling an odour (olfactory), tasting a substance (gustatory) may be presented. Many cognitive and language paradigms also exist, which include word generation (prompted by a letter), semantic decision making (e.g., is the displayed word a vegetable?), and even simple auditory presentation of words. Though motor tasks and cutaneous sensory stimuli are mainly used in clinical fMRI studies, other tasks and stimuli are used in studies conducting research.

Uses of brain fMRI

- To examine the anatomy of the brain.
- To help assess the effects of stroke, trauma or degenerative diseases (such as Alzheimer's disease) on brain function.
- Assessment of patients with disorders of consciousness (coma, vegetative state, minimally conscious state, locked-in syndrome).
- To determine precisely which part of the brain is handling critical functions such as thought, speech, movement and sensation, called brain mapping.
- To check the neural correlates of a seizure
- To study how the brain recovers partially from a stroke, test how well a drug or behavioral therapy works, detect the onset of Alzheimer's, and note the presence of disorders like depression
- To monitor the growth and function of brain tumors.
- To guide the planning of surgery, radiation therapy, or other surgical treatments for the brain so that damage to important functional areas of the brain is avoided and that primary functions (motor, language, etc.) are preserved as much as possible.
- To compare the effects of a treatment intervention with respect to function using a pre intervention and a post intervention fMRI.

Uses of spinal fMRI

- To map neuronal activity at different levels of the spinal cord in response to various stimuli, such as touch, vibration, and thermal changes, and with motor tasks.
- To detect a neuronal response in the spinal cord caudal to the injury site during both active and passive lower limb movement tasks, and in response to a noxious stimulus, even when subjects could not feel the stimulus. This is useful for revealing areas of impaired and preserved activity in spinal cord injured patients.
- To identify the pathogenesis of many chronic pain conditions such as irritable bowel syndrome, chronic lower back pain, or fibromyalgia.
- To determine whether the breakdown causing muscle weakness is at the spinal level, neuromuscular junction or within the muscle fibers themselves, as in muscular dystrophies.
- To track disease progression and prognosis.
- To localize function in pre-surgical mapping, in cortical tissue near areas intended for any spine surgery or resection.
- To study normal sensory and motor function and the effects of trauma to the spinal cord and multiple sclerosis for research purposes.

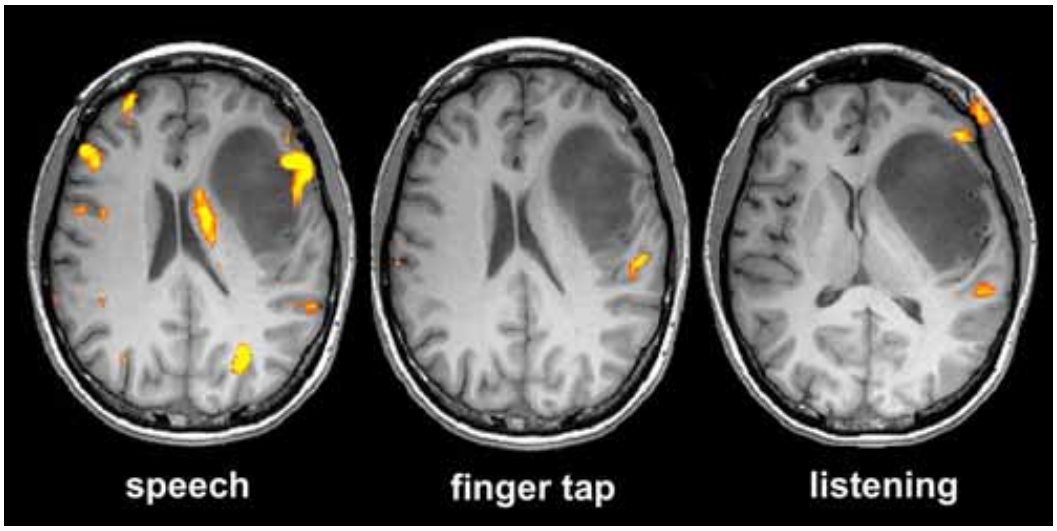


Fig. 14.1: fMRI of Brain

- To compare the effects of a treatment intervention with respect to function using a pre intervention and a post intervention fMRI.

Contraindications of fMRI

- Patients who are contraindicated for MRI scanning are also contraindicated for fMRI.
- Patients with metal and electronic implants
- Pregnant females, especially in the first trimester.

(II) Electrophysiological

15. Electroencephalography

Electroencephalography is the neurophysiologic measurement of the electrical activity of the brain OBTAINED by recording from electrodes placed on the scalp or, in special cases, subdurally or in the cerebral cortex. The resulting traces are known as an electroencephalogram (EEG) and represent an electrical signal (postsynaptic potentials) from a large number of neurons.

Clinical use

EEG in various forms is most useful as a tool for monitoring and diagnosis in certain clinical situations:

- Seizure and epilepsy: to detect seizure focus and monitor the effects of treatment
- Disorders with coexisting seizures: in cases of autism, cp, etc, where the patient may not have experienced a seizure attack or shown symptoms, EEG can efficiently detect a possible underlying epileptic focus
- Sleep disorders
- Eating disorders
- Coma and brain death
- Dementia

Procedure

In conventional scalp EEG, the recording is obtained by placing electrodes on the scalp, after preparing the scalp area BY applying a conductive gel to reduce impedance. Modern EEG systems have the subject wear a plastic cap where the electrodes are inserted in small holes.

Electrode placement is determined by measuring and marking the scalp using a system called the 10-20 system. Each electrode is connected to an input of a differential amplifier (one amplifier per pair of electrodes), which amplifies the voltage between them (typically 1,000-100,000 times, or 60-100 dB of voltage gain). The resulting voltage signal is filtered by a high-pass filter and a low-pass filter, typically set at 0.5 Hz and 35-70 Hz, respectively. The high-pass filter typically filters out slow electrogalvanic

signals, whereas the low-pass filter filters out electromyographic signals.

The filtered signal is then output on paper (in older systems), or displayed on a computer screen. The amplitude of the EEG is about 100 μV when measured on the scalp, and about 1-2 mV when measured on the surface of the brain.

Standard EEG: During a standard EEG, the patient is asked to breathe deeply for some minutes, look at a flashing light, etc. These activities change the electrical activity in the brain which shows on the computer. The patient is asked to keep as still as possible during the test. Any movement can change the electrical activity in the brain, which can affect the results.

Advantages

- Less expensive than other functional imaging tests.
- The time resolution is very high.
- EEG measures the electrical activity of the brain directly.

Limitations

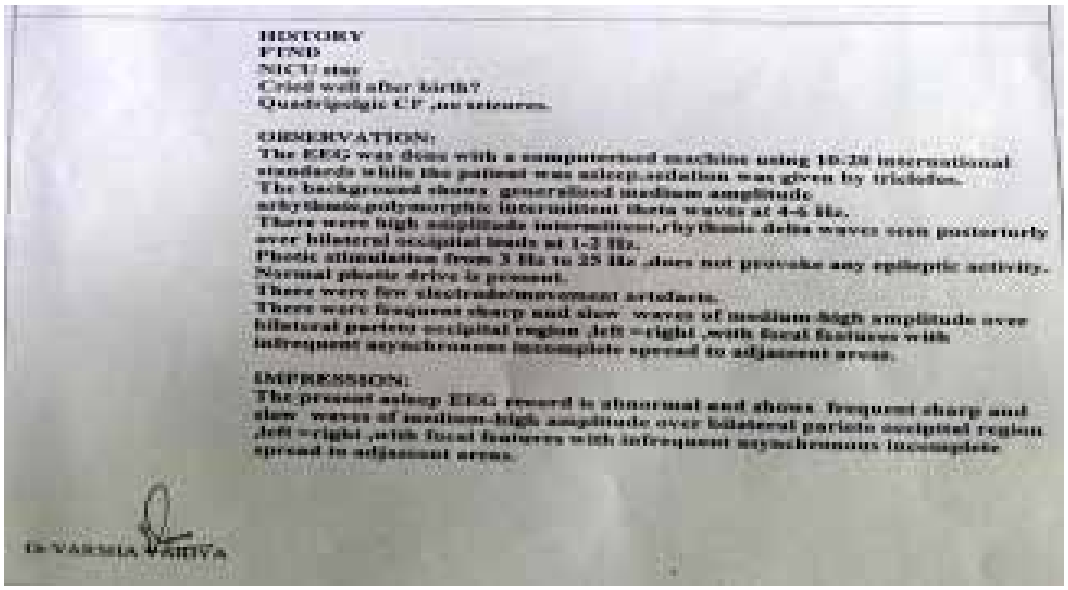
- Scalp electrodes are not sensitive enough to pick UP individual action potentials.
- It cannot differentiate whether the resulting electrical activity is releasing inhibitory, excitatory or modulatory neurotransmitters.
- EEG has limited anatomical specificity when compared with other functional brain imaging techniques such as functional magnetic resonance imaging (fMRI).

Activity types

The EEG activity is of two types: (1) rhythmic activity and (2) transients.

Rhythmic activity is divided into the following bands depending on the frequency:

- Delta: These waves are normally found only when a person is asleep or in young children. abnormal activity may indicate subcortical lesions, diffuse lesions, metabolic encephalopathy hydrocephalus, deep midline lesions
- Theta: These waves are normally found only when a person is asleep or in young children. abnormal activity may indicate focal subcortical lesions, metabolic encephalopathy, deep midline disorders, hydrocephalus
- Alpha: Alpha waves are present only in the waking state when eyes are closed but the person is mentally alert. present abnormally in coma
- Beta: Abnormal activity present in patients on benzodiazepines
- Gamma: A decrease in gamma band activity may indicate cognitive decline
- Mu: Limited Mu activity may indicate working of motor mirror neurons (as in autism).



HISTORY
PYNB
NICU stay
Cried well after birth?
Quadriplegic CP ,no seizures.

OBSERVATION:
The EEG was done with a computerised machine using 10-20 international standards while the patient was asleep.sedation was given by trichlofos.
The background shows generalised medium amplitude
arhythmic,polymorphic intermittent theta waves at 4-6 Hz.
There were high amplitude intermittent,rhythmic delta waves seen posteriorly over bilateral occipital leads at 1-2 Hz.
Photic stimulation from 3 Hz to 25 Hz ,does not provoke any epileptic activity.
Normal photic drive is present.
There were few electrode/movement artifacts.
There were frequent sharp and slow waves of medium-high amplitude over bilateral parieto-occipital region ,left =right ,with focal features with infrequent asynchronous incomplete spread to adjacent areas.

IMPRESSION:
The present asleep EEG record is abnormal and shows frequent sharp and slow waves of medium-high amplitude over bilateral parieto occipital region ,left =right ,with focal features with infrequent asynchronous incomplete spread to adjacent areas.

Dr VARSHA VAIDYA

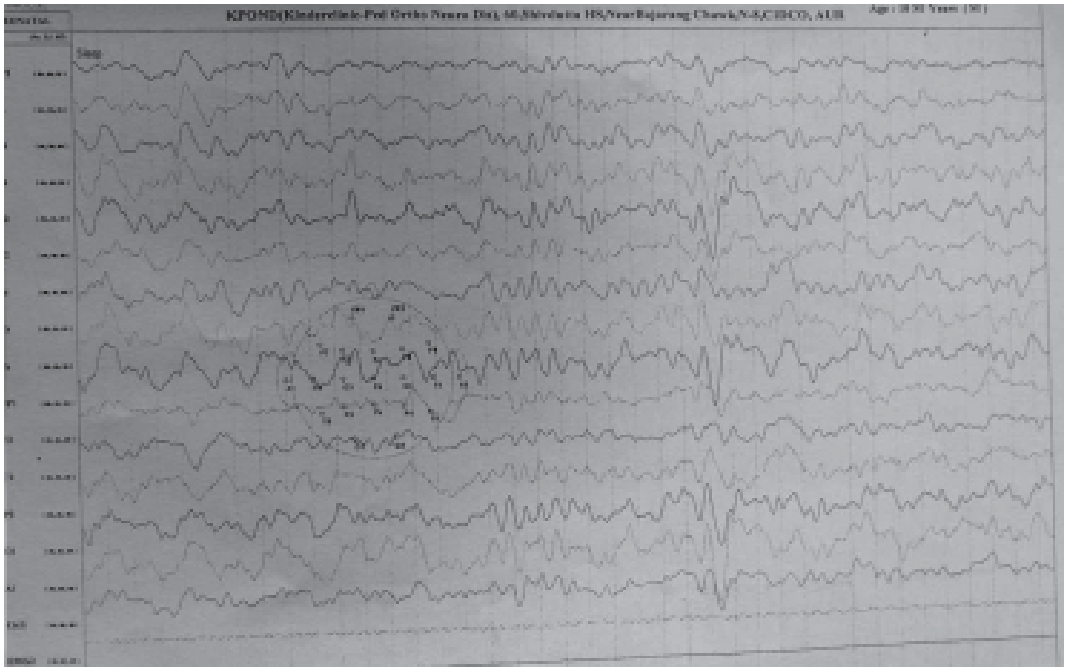


Fig. 15.1: EEG – Seizures

EEG REPORT

The international 10-20 system of electrode placement was used.

The patient was awake, un-cooperative, transiently drowsy and intermittent sleep tracing was recorded. The wake record shows medium amplitude 8-9 Hz alpha activity, reactive to eye opening.

The drowsy record shows a 4-5 Hz Medium amplitude thetoid activity.

Patient achieved sleep stage 2- Non REM sleep with the presence of vertex sharp waves and sleep spindles intermittently.

Fast beta activity noted due to sedation.

No generalized /focal epileptiform activity noted.

Hyperventilation: not possible as patient was not cooperative.

Photic stimulation: No photosensitivity response was recorded.

Intermittent movement and muscle artifacts were noted.

COMMENTS : Normal sleep EEG record.

No epileptiform discharges seen.

No focal slow wave abnormality recorded.

DR. SHEKHAR G PATIL
Paediatric Neurologist

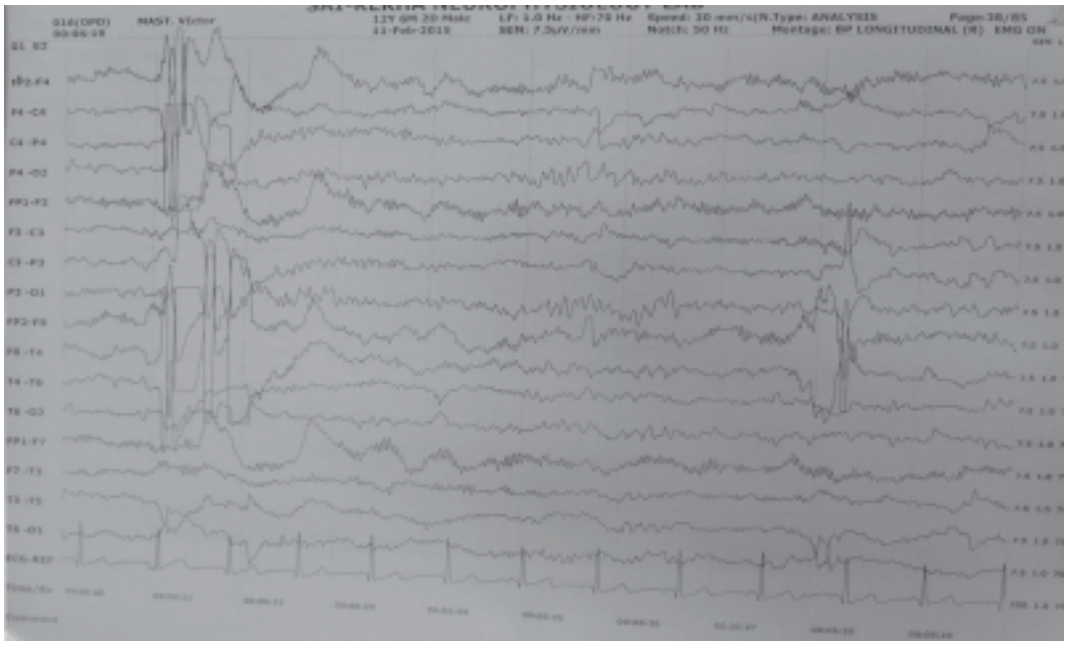


Fig. 15.2: EEG – Autism

Sleep EEG

Sleep EEG is ordered in cases where seizures occur during sleep, or in fatigued state, or when the awake EEG is normal.

Sleep-deprived EEG

A sleep-deprived EEG is done when standard awake EEG did not show any unusual electrical activity.

Normal EEG

- In adults who are awake, the EEG shows mostly alpha waves and beta waves.
- The two sides of the brain show similar patterns of electrical activity.
- There are no abnormal bursts of electrical activity.
- On photic stimulation, one area of the brain (the occipital region) shows a brief response after each flash of light, the brain waves being normal.

Abnormal EEG

- If the two sides of the brain show different patterns of electrical activity, it may indicate a problem in one area or side of the brain.
- Sudden bursts of electrical activity (spikes) or sudden slowing of brain waves may be caused by a brain tumor, infection, injury, stroke, or epilepsy. In many patients with epilepsy, the EEG may appear completely normal between seizures.
- Presence of delta waves or too many theta waves in awake EEG of adults may indicate presence of a brain injury or a brain illness.
- The EEG which shows no electrical activity in the brain (a flat or straight line EEG) means that the brain function has stopped. This may be due lack of oxygen or blood flow to the brain, or when a person is in coma, or even in cases of severe drug induced sedation.

16. Electromyography and Nerve Conduction Studies

Electromyography (EMG) is an electrodiagnostic technique used for recording the electrical activity produced by skeletal muscles. An electromyograph is used to detect the electrical potentials generated by muscle cells when they are neurologically or electrically activated. These signals are then analyzed to evaluate normal or abnormal activation level and recruitment of muscle fibers in various disorders of muscles and nerves of central nervous system as well as peripheral nervous system.

There are two kinds of EMG: surface EMG and intramuscular (needle and fine-wire) EMG using surface electrodes and needle electrodes respectively. Surface EMG is unable to assess the same muscle activity as when the needle is inserted through a muscle. Therefore, needle EMG is commonly used in clinical settings.

The activities recorded during an EMG are: A) Insertional activity - Normal muscles at rest generate some normal electrical signals when the needle is inserted into them. B) Spontaneous activity at rest - Nil muscle activity is seen normally. Abnormal spontaneous activity might indicate some nerve and/or muscle pathology. C) Voluntary recruitment - The patient is asked to contract the muscle and electrical activity is recorded. The shape, size, and frequency of the resulting electrical signals are analyzed.

EMG characteristics in neuropathies and myopathies.

- Neuropathic disease shows the following EMG characteristics:
  - An action potential amplitude that is twice normal due to the increased number of fibers per motor unit because of reinnervation of denervated fibers
  - An increase in duration of the action potential
  - A decrease in the number of motor units in the muscle
- Myopathic disease shows the following EMG characteristics:
  - A decrease in duration of the action potential
  - A reduction in the area to amplitude ratio of the action potential
  - A decrease in the number of motor units in the muscle

Abnormal EMG finding

- ***Insertional activity:***

  This activity is decreased in atrophied muscle or fatty tissue. Whereas, it is increased in conditions that cause membrane instability, such as neuropathies, radiculopathies, and inflammatory myopathies.

- ***Spontaneous activity at rest:***

  Abnormal fibrillation potentials result from motor axonal loss that is not balanced by reinnervation in conditions such as inflammatory myopathies and direct muscle injury. Low-amplitude fibrillation potentials suggest that denervation has occurred in the remote past, whereas high-amplitude fibrillation potentials suggest an ongoing active denervation process.

- ***Voluntary muscle recruitment:***

  Reduced recruitment signifies motor axonal loss or focal demyelination or conduction block. Whereas, increased recruitment with a small voluntary force suggests a myopathy.

- ***Interpretation:***

  EMG study is combined with nerve conduction studies for better interpretation of results.

Uses

- To identify neuromuscular disorders
- To diagnose peripheral nerve compression or injury (eg. Carpal tunnel syndrome, Cubital tunnel syndrome)
- To identify nerve root compression or injury (eg. due to herniated intervertebral disc, sciatica)
- To check for causes of muscle weakness and wasting and help differentiate between neuropathy and myopathy
- To diagnose muscle disorders such as muscular dystrophy
- To evaluate motor problems such as involuntary muscle twitching (eg. Motor neuron disease)
- To diagnose disorders those affect the motor neurons in the spinal cord, such as amyotrophic lateral sclerosis or polio
- To diagnose diseases affecting the neuromuscular junction such as myasthenia gravis

Indications

EMG is indicated when there is:

- Weakness in the limb/s

- Pain in the limb/s
- Suspected spinal nerve compression
- Suspected neurologic injury or disorder affecting peripheral nerves

Contraindications

- Patients with bleeding disorders (eg. haemophilia) and patients receiving anticoagulant therapy, since the needle electrodes may cause bleeding within the muscle.
- Patients with skin infections, since there is a risk of spreading infection from the skin to the muscle.
- Patients on medications such as skeletal muscle relaxants, cholinergics, and anticholinergics, since they affect muscle activity and EMG may show false test results. These medications may need to be stopped at least three days prior to EMG testing.
- Patients with impaired consciousness or cognition, who cannot understand commands given during the procedure.

Precautions

- In patients with gross oedema, skin puncture by needle electrodes may result in leakage of serous fluid for a long time. The fluid may also contain bacteria which may increase the risk of cellulitis. So, EMG study should be avoided or postponed.
- Swelling or bleeding in muscles or excess fat (obesity) may interfere with the transmission of electrical waves to the electrodes, and thereby alter the EMG results.

Limitations

- Excess of adipose tissue (fat) affects the EMG recordings.
- Needle and wire introduction into the muscles is painful.
- Even if surface EMG technique is used, it only measures potentials of superficial muscles and provide comparatively less information about the state of diseased muscle.

Nerve Conduction Studies

A nerve conduction study (NCS) is an electrodiagnostic test used to evaluate the electrical conduction, and thus the function of the motor and sensory nerves of the body.

Uses

- Uses of sensory NCS include evaluating parasthesias (numbness, tingling,

burning sensations) in a limb or a part of the limb (eg. Carpal tunnel syndrome, Guyon's canal syndrome, peroneal neuropathy), in two or more limbs or parts of the limbs (eg. Guillain-Barré syndrome, diabetic neuropathy)

- Uses of motor NCS include evaluating weakness in muscle/s of limb/s (eg. nerve root compression due to herniated disc, motor neuron disease, muscular dystrophy, poliomyelitis)

Indications

NCS is indicated when there is:

- Weakness in the limb/s
- Parasthesias in the limb/s
- Pain in the limb/s
- Suspected spinal nerve compression
- Suspected neurologic injury or disorder affecting peripheral nerves

The nerve conduction study consists of the following components:

- Motor NCS
- Sensory NCS
- F wave study
- H-reflex study

Nerve conduction velocity (NCV) is a common measurement made during this test. NCV refers to the speed with which electrical impulses travel through a particular nerve.

Procedure: Flat electrodes are placed on the skin at intervals along the nerve course. Low-intensity electrical impulses are passed through these electrodes to stimulate the nerve. The impulses (sensory/motor) produced by this electrical current are recorded and viewed on an oscilloscope or computer screen. The recorded impulses are then evaluated to determine the speed with which the impulses travel through the nerves.

Motor NCS

Motor NCS are performed by electrical stimulation of a peripheral nerve and recording from a muscle supplied by this nerve. The time taken by the electrical impulse to travel from the stimulation site to the recording site is called the latency and is measured in milliseconds (ms). The size of the response (amplitude) is measured in millivolts (mV). Stimulation is carried out at two or more different locations along the same nerve to determine difference in latencies. The distance between the different stimulating electrodes and the difference in latencies are used to calculate the velocity.

Sensory NCS

Sensory NCS are performed by electrical stimulation of a peripheral nerve and recording from a purely sensory portion of the nerve, such as on a finger. The sensory NCV is also calculated the same way as for motor NCV.

F-wave study

F-wave study uses supramaximal current intensity to stimulate a motor nerve, action potentials of which travel through the nerve in an anti-dromic direction, from the site of the stimulating electrode in the limb to the spinal cord's ventral horn and back to the limb in the same nerve that was stimulated. Action potentials from a muscle supplied by the nerve are recorded. The F-wave latency is used to derive the conduction velocity of nerve between the limb and spinal cord.

H-reflex study

H-reflex study uses stimulation of a nerve and recording the reflex action potential from a muscle in the limb. This also evaluates conduction between the limb and the spinal cord, but in this case, the afferent impulses are in sensory nerves while the efferent impulses are in motor nerves.

Interpretation

Different pathological processes result in changes in latencies, amplitudes of the motor and/or sensory nerves or slowing of the conduction velocities to differing degrees.

Possible causes for abnormal result:

- axonopathy (damage to the nerve cell)
- conduction block (an obstacle to the impulse conduction within the nerve)
- demyelination (damage to the myelin sheath)

Contraindications

There are no specific contraindications for this test. But, precautions need to be taken in the following cases:

- In patients with pacemakers, deep brain stimulators or spinal cord stimulators, stimulating electrodes placed in close proximity to these devices could induce a voltage of sufficient amplitude to inhibit the functioning of these devices. Thus, special precautions must be taken while performing NCS on them.
- Patients with impaired consciousness or cognition, who cannot understand commands given during the procedure and who cannot bear the electrical stimulations.

17. Evoked Potentials

Evoked potential (EP) tests measure the electrical activity in the brain in response to stimulation of specific sensory nerve pathways such as sight, sound, or touch. Minute electrical signals are evoked in the brain in response to these sensory stimuli. These signals travel along the sensory nerves and through afferent pathways of the spinal cord to respective regions of the brain and are picked up by electrodes, amplified, and displayed on a computer. EPs, thus, are able to detect the slowing or blockage of electrical conduction (eg. demyelination) along these pathways.

Uses of SSEP test:

- Primary use is to determine compromised central nervous system (CNS) conduction.
- To diagnose nerve entrapment syndromes such as carpal tunnel syndrome/ulnar nerve entrapment syndrome.
- To diagnose spondylytic myeloradiculopathy
- To diagnose thoracic outlet syndrome
- To diagnose and manage acquired metabolic disorders (e.g., lead toxicity, B12 deficiency)
- To help reveal asymptomatic lesions, for example in case of suspected multiple sclerosis.
- To confirm presence of demyelinating diseases such as multiple sclerosis; diagnosis of which requires evidence of demyelination in two distinct areas of the central nervous system.
- Abnormalities of trigeminal SSEPs may guide towards diagnosis of MS, Wallenberg syndrome, cerebellopontine angle tumors, trigeminal neuromas, or meningeal sarcoidosis with facial paralysis.
- To help confirm symptoms when few physical findings are noted
- To establish an anatomic region where the conduction disturbance or block occurs
- To detect tumors or other problems affecting the brain and spinal cord

- To check prognosis in comatosed patients in anoxic brain injury
- To study fundamental aspects of sensory physiology for research purposes

Indications

- To assess patients with acute spinal cord injury
- To evaluate acute anoxic encephalopathy
- To evaluate patients with suspected stroke
- To confirm or reject the presence of a suspected conduction block.
- To identify clinically silent brain lesions such as multiple sclerosis suspects, in whom neurological signs and other objective findings (brain plaques on MRI and/or positive oligoclonal bands in CSF) are present.
- To assess and follow up for prognosis in patients with spinocerebellar degeneration (e.g. Friedreich's ataxia, olivopontocerebellar degeneration)
- In unexplained myelopathy
- To evaluate radiculopathy, neuropathy

Different types of evoked potentials studies

- Somatosensory evoked potential (SSEP) test: This test helps detect problems with cutaneous sensations which may be due to segmental innervation disturbances, disturbances in the spinal cord, demyelination, etc.
- Visual evoked potential (VEP) test: This test helps detect problems with the optic nerves that affect sight.
- Brainstem auditory evoked potential (BAEP) test: This test helps detect problems with hearing due to nerve damage or brain stem tumors and multiple sclerosis.

Somatosensory evoked potential (SSEP) testing is commonly used in clinical settings. During the procedure, electrodes are attached to the wrist, the back of the knee, or other locations depending on the dermatome to be studied. A mild electrical stimulus is applied through the electrodes. Electrodes placed on the scalp then pick up the response from corresponding brain area and the time taken for the current to travel along the nerve to the brain is recorded. Abnormalities may include prolonged latencies or lack of development of the SSEP. The stimulation sites commonly used for clinical diagnostic SSEP studies are the median nerve at the wrist, the common peroneal nerve at the knee, and the posterior tibial nerve at the ankle.

The dorsal columns in the spinal cord are mainly responsible for conduction of the electrical activity that generates the SSEP. While in the brain, the lemniscal and thalamocortical pathways are involved. Because the diagnosis of multiple sclerosis requires evidence of demyelination in two distinct areas of the central nervous system, EP testing can help confirm multiple sclerosis.

Visual evoked potential (VEP) testing

Visual stimuli used in VEP testing are strobe flash, flashing light-emitting diodes (LEDs), transient and steady state pattern reversal and pattern onset/offset. The most common stimulus used is a checkerboard pattern, which reverses every half-second. The VEP is used to identify impaired transmission along the optic nerve pathways, which is a common early finding in MS, even in some patients who have never experienced any visual symptoms. It is used to detect problems with the conducting nerves and areas of the brain involved in vision in cases of optic neuritis, occipital trauma, or neurofibromatosis, etc.

Brainstem auditory evoked potential (BAEP) testing

In BAEP testing, broad-band clicks as stimuli are used for the neurologic applications of auditory evoked potentials. BAEPs reflect neuronal activity in the auditory nerve, cochlear nucleus, superior olive, and inferior colliculus of the brainstem. Abnormal test results may be a sign of hearing loss, multiple sclerosis, acoustic neuroma, brainstem stroke, or brainstem degenerative disorders, etc. BAEP testing may also be used for outcome prediction in cases of coma.

Contraindications

There are no specific contraindications for this test. But, precautions need to be taken in the following cases:

- In patients with pacemakers, deep brain stimulators or spinal cord stimulators, stimulating electrodes placed in close proximity to these devices could induce a voltage of sufficient amplitude to inhibit the functioning of these devices. Thus, special precautions must be taken while performing SSEP testing on them.
- Patients with impaired consciousness or cognition, who cannot understand commands given during the procedure and who cannot bear the electrical stimulations.

Advantages

- SSEP testing may help diagnose a problem even when the neurologic change is too subtle to be noticed by the patient or to show up on neurological examination.

Limitations

- Abnormalities demonstrated by these tests are etiologically nonspecific and do not guide towards a specific diagnosis. Therefore, the test results should be integrated carefully into the clinical situation by the concerned physician.
- Though evoked potential studies are considered safe procedures, the test may cause discomfort in hyperalgesic patients and children.

(III) Biochemical

18. Blood Tests

In neurological disorders, clinical history and examination is the key to identify the diagnosis. Radiological investigations, for e.g. CT, MRI, are required to confirm the diagnosis and differentiate between various causes. Blood tests are adjunctive and offer added information about systemic causes or effects of neurological disorders. Blood tests are especially important in CNS infections, seizures, nutritional deficiencies and metabolic disorders. Here we have described the commonly used blood tests in patients presenting with neurological complaints.

I. Routine blood tests

Complete blood count

White blood cells (WBC)

Normal ranges

- WBC - 4-10 x 109/L
- Neutrophils - 2.0-7.0×109/L
- Lymphocytes - 1.0-3.0×109/L
- Monocytes - 0.2-1.0×109/L
- Eosinophils - 0.02-0.5×109/L
- Basophils - 0.02-0.1×109/L
- Peripheral WBC count increases significantly after a generalized seizure and is probably transient in nature.
- High WBC count (consisting predominantly of PMNs) in bacterial meningitis
- Higher than normal numbers of lymphocytes or monocytes - some types of cancers
- Neutropenia - in cancer, viral infections such as influenza, bacterial infections such as tuberculosis, or deficiencies of vitamin B12 or folate (folic acid).
- Neutrophil granulocytes - May indicate bacterial infection. May also be raised in acute viral infections

- Monocytes - May be raised in bacterial infection, tuberculosis, malaria
- Eosinophil granulocytes - increased in parasitic infections, or allergic reaction.

Platelet

Platelet abnormalities could be the underlying cause of some of the neurological disorders.

Normal value: 150-400 × 109

- Thrombocytosis (increased platelet count) may present as:
  - Headache, transient ischaemic episodes, paraesthesias
  - Other transient symptoms may include dizziness, dysarthria, syncope, migraine, seizures, etc.
- Thrombocytopenia (low platelet count) may cause bleeding in the brain leading to stroke or hematoma.
- Thrombotic thrombocytopenic purpura may present as:
  - hallucinations, bizarre behavior, altered mental status, stroke, headaches

Haemoglobin level

Normal ranges:

- Men: 13.8 to 18.0 g/dL
- Women: 12.1 to 15.1 g/dL
- Children: 11 to 16 g/dL
- Pregnant women: 11 to 14 g/dL

Headache may be a symptom of anemia due to decreased oxygenation of the brain tissues.

Polycythemia vera (increased RBC count) may present as headaches, lack of concentration, fatigue and thromboembolic stroke (due to increased blood clotting tendencies).

Creatinine level

Normal value: 0.5 to 1.2 mg/dL

Renal failure can lead to increased levels of creatinine, which in turn can cause electrolyte imbalance leading to seizures. Also, drug dosing errors in patients with renal impairment can cause adverse effects and poor outcomes. Dosages of drugs cleared renally should be adjusted according to creatinine clearance or glomerular filtration rate.

Prothrombin time tests (PT-INR)

The prothrombin time (PT) test and international normalized ratio (INR) test examine the integrated function of all of the coagulation factors.

Normal PT:

12-13 seconds, Normal INR: 0.8-1.2

PT-INR should be checked in haemorrhagic stroke (bleeding tendencies). Regular PT-INR check up will be required in patients with ischemic stroke who are on anti-coagulants.

ESR

Normal ranges:

0-22 mm/hr for men and 0-29 mm/hr for women

Elevated ESR should raise suspicion of tuberculosis and malignancies. In these conditions, there is very high ESR level. A borderline increased ESR may be non-specific due to chronic inflammation.

II. Vitamins

Vitamin B12

Normal value: 130-700 ng/L

A full blood count which shows anaemia and macrocytosis should prompt the practitioner to look for a deficiency of vitamin B12 or folate. Tests commonly used for the detection of these vitamin deficiencies are serum folate, red cell folate and serum B12 concentrations.

Deficiency may cause:

- unexplained neurological or neuropsychiatric abnormalities.
- peripheral neuropathy and sub-acute combined degeneration of the spinal cord
- paraesthesias, weakness, clumsiness, and an unsteady gait (ataxia)
- senile dementia or Alzheimer disease; memory loss, irritability, and personality changes in elders

B12 toxicity may present with similar complaints of deficiency. For e.g. numbness, paresthesias, headaches, giddiness, etc. Therefore, B12 level is required to distinguish between toxicity and deficiency. Also, history of whether the patient was on B12 supplements will help to differentiate.

Vitamin E

Normal value: 5.5-17 µg/mL

Deficiency may cause:

- Ataxia
- Progressive spinocerebellar syndrome
- Peripheral neuropathy
- Cranial neuropathy with ophthalmoplegia
- Dysarthria
- Psychomotor impairment
- Myopathy

III. Serum Immunoglobulins

- IgG is increased in chronic phases of inflammatory diseases of CNS, multiple sclerosis, Lyme disease, neuromyelitisoptica, neurosarcoidosis and GBS

  Oligoclonal bands are bands of immunoglobulins that are seen in patient's blood serum or cerebrospinal fluid on protein electrophoresis. IgG in normal CSF migrates as a faint diffuse zone, but in demyelinating diseases, IgG migrates as discrete oligoclonal bands. The presence of oligoclonal bands in cerebrospinal fluid combined with their absence in blood serum often indicates that immunoglobulins are produced in central nervous system resulting from viral and bacterial infections, and autoimmune diseases. Therefore, when investigating CNS diseases, bands in serum are subtracted from bands in CSF. Presence of oligoclonal bands in serum as well as CSF may indicate presence of multiple sclerosis, myelitis, neoplastic meningitis and CNS inflammatory disorders.

IV. Disease specific tests

- **Myasthenia gravis**

The anti-acetylcholine receptor (AChR) antibody test is the most reliable test for diagnosing autoimmune myasthenia gravis (MG) in most of the patients.

The anti-striated muscle (anti-SM) Ab is present in about 84% of patients with thymoma who are younger than 40 years and less often in those without thymoma. Thus, a positive test result should guide towards checking the presence of thymoma in patients younger than 40 years.

Seronegative (negative for anti-AChR Ab) patients should be referred for antibodies to muscle-specific kinase (MuSK) testing. Anti-MuSK-positive individuals tend to have more pronounced bulbar weakness and may have tongue and facial atrophy. They may have neck, shoulder and respiratory involvement without ocular weakness. Also, response to acetylcholine esterase (AChE) inhibitors is oftenly less, with chances of symptoms getting worse.

Striational antibodies are found in almost all the patients with thymoma and MG, and late-onset MG patients; while rarely in anti-AChR-negative patients. Presence of these antibodies should raise a strong suspicion of thymoma in a young patient with MG.

Testing for rheumatoid factor and antinuclear antibodies (ANAs) is indicated to rule out systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA).

- **Muscular dystrophy**

Increased Creatine phosphokinase (CPK) levels are indicative of muscle disease. Thus, CPK testing is the most specific test for muscular dystrophy. CPK levels are 50-300 times greater than normal levels in the early phases of disease, but the levels decrease as the muscle mass decreases. The CPK level is highest in Duchenne MD, with comparatively lesser level in Becker MD.

- **GuillianBarre syndrome**

Antibodies to glycolipids and gangliosides are observed in the sera of most of the patients with GBS during the acute phase.

Antibodies to GM1 are frequently found in the sera of patients with the acute motor axonal neuropathy (AMAN) or acute demyelinating polyradiculoneuropathy (AIDP) variants of GBS.

Anti-GM1 antibodies titers may be elevated with C jejuni infections.

Anti-GQ1b antibodies are found in GBS patients with ophthalmoplegia and the Miller-Fisher variant.

Assays for antibodies to C jejuni, Cytomegalovirus, Epstein-Barr virus, Herpes simplex virus, HIV, and Mycoplasma pneumonia infections may be considered in GBS. HIV has been reported to precede GBS. Thus, testing should be done in high-risk patients to check for possible infection with this agent.

- **Cerebral malaria**

Rapid diagnostic tests (RDTs) are being used for emergency medical screening and in medical facilities with limited resources. These tests target antigen HRP-2 from P. falciparum.

Immunochromatographic tests detect antibodies to histidine-rich protein-2 (PfHRP2), parasite LDH (pLDH), or Plasmodium aldolase, and are very specific.

Polymerase chain reaction (PCR) tests target the detection of small-subunit 18S rRNA and circumsporozoite (CS) genes. In patients with low levels of parasitemia, PCR-based technique is the most reliable test for detecting malaria parasites.

V. Peripheral smears

- **Cerebral malaria**

Manifestations of cerebral malaria include impairment of consciousness (confusion, delirium, obtundation, stupor, or coma), convulsions, focal neurologic deficit, and psychosis.

Demonstration of asexual form of P. falciparum in peripheral blood smear, in thick and thin blood smear films stained by Giemsa stain is required for the diagnosis. Absence of parasites in some patients may be due to sequestration of parasitized RBCs in cerebral circulation or earlier treatment with antimalarial drugs. In such a situation, at least 3 smears 6 hours apart should be examined. At least 3 smears should be negative before excluding cerebral malaria.

- **Tuberculous meningitis**

AFB testing is used to identify an active tuberculosis (TB) infection caused by the Mycobacterium tuberculosis. An AFB smear is used as a rapid test to detect mycobacteria. A molecular test for TB called nucleic acid amplification test (NAAT) may be done in conjunction with an AFB smear.

AFB blood and CSF cultures are used to diagnose active M. tuberculosis infections, infections due to nontuberculous mycobacteria, or to determine whether TB-like symptoms are due to another cause. Susceptibility testing is done to determine the most effective antibiotic to treat the mycobacterial infection.

VI. Specific biomarkers

- **Homocysteine**
  - Significant in cases of stroke
  - Homocystinuria- causes mental retardation, seizures
  - Hyperhomocystinemia - associated with arterial and venous thrombosis and should be distinguished from autosomal recessive homocystinuria.
  - Elevated homocysteine levels are found in the elderly, in patients with vitamin B6 and B12 deficiency; and in renal insufficiency. Testing should be done in young adults in case of stroke. Fasting homocysteine level is measured by high-performance liquid chromatography (HPLC) with fluorescence detection.

Normal levels:

- Age 0-30 years: 4.6-8.1 µmol/L
- Age 30-59 years: 6.3-11.2 µmol/L (males); 4-5-7.9 µmol/L (females)
- Age >59 years: 5.8-11.9 µmol/L

VII. Thyroid hormones test

- **Hyperthyroidism:** Neurological manifestations can include tremors, chorea,

myopathy, and) periodic paralysis.

- **Hypothyroidism:** seizures, coma
- Typical adult limits for these hormones are: TSH (units): 0.45 - 4.50 uIU/mL; T4 Free/Direct (nanograms): 0.82 - 1.77 ng/dl; and T3 (nanograms): 71 - 180 ng/dl.

VIII. Electrolytes

Common electrolytes include:

v **Calcium** (Normal: 2-2.6 mmol/L)

- Hypocalcemia: Convulsions, Arrhythmias, Tetany and numbness/ parasthesias in hands, feet, around mouth and lips.
- Hypercalcemia: Psychiatric overtones (Depression 30-40%, anxiety, cognitive dysfunction, insomnia, coma)

v **Magnesium** (Normal: 1.5-2 mEq/L)

- Hypomagnesemia: increased irritability of the nervous system with tremors, athetosis, jerking, nystagmus and an extensor plantar reflex. In addition, there may be confusion, disorientation, hallucinations, depression, epileptic fits, hypertension, tachycardia and tetany.

v **Potassium** (Normal: 3.5-5 mmol/L)

- Hypokalemia: muscle weakness, myalgia, tremor, and muscle cramps (owing to disturbed function of skeletal muscle). With more severe hypokalemia, flaccid paralysis and hyporeflexia may result.
- Hyperkalemia: muscle weakness

v **Sodium** (Normal: 135-145 mmol/L)

- Hyponatremia: headache, nausea, vomiting, confusion, seizures, brain stem compression and respiratory arrest
- Hypernatremia: neuromuscular excitability, and edema. With more severe elevations of the sodium level, seizures and coma may occur.

v **Chloride** (Normal: 95-105 mmol/L)

- Levels decrease in metabolic acidosis which shows neurological symptoms like lethargy, stupor, coma, seizures.

IX. Blood sugar

- Hypoglycaemia manifestations - headache, cognitive disturbance, hemiplegia, coma, and seizures.
- Diffuse peripheral neuropathy primarily affects the limbs, damaging the nerves of the feet and hands. Autonomic neuropathy is the other form of diffuse neuropathy and it affects the heart and other internal organs.

- Focal or localized diabetic neuropathy affects specific nerves, most commonly in the torso, leg, or head.

Normal ranges:

- Fasting plasma glucose: 70-99 mg/dL
- Postprandial plasma glucose at 2 hours: Less than 140 mg/dL
- Random plasma glucose: Less than 140 mg/dL

X. Lipid profile

Hyperlipidaemia is a major risk factor of stroke. Therefore, it is very important to check the lipid profile and do preventive measures.

High LDL and Total cholesterol, low HDL significantly increase the chances of stroke.

Normal ranges:

- Triglycerides: 50-150 mg/dL
- Total cholesterol: 3-5.5 mmol/L
- High-density lipoprotein (HDL): 40-80 mg/dL
- Low-density lipoprotein (LDL): 85-125 mg/dL

XI. Liver function tests

- Hepatic encephalopathy manifestations - forgetfulness, confusion, irritability, altered level of consciousness, and coma
- These tests include serum liver transaminases (AST or SGOT and ALT or SGPT), albumin and bilirubin (direct and indirect), ammonia.

Normal ranges

- Alanine aminotransferase (ALT): 5-30 U/L
- Aspartate aminotransferase (AST): 5-30 U/L
- Total bilirubin: 2-20 µmol/L
- Albumin: 35-50 g/L
- Ammonia: 15-50 µmol/L

XII. Uremia

- **Normal Blood urea:** 5 to 20 mg/dl
- Increased levels of blood urea cause: Central nervous system - Diurnal somnolence, Night insomnia, Memory and concentration disorders, Asthenia, Headache, Confusion, Fatigue, Seizures, Coma, Encephalopathy

- Peripheral nervous system - Polyneuritis, Restless legs, Cramps, Peripheral neuropathy, Oxidative stress

XIII. Genetic testing

- **Congenital myopathies - muscular dystrophies**

  The PCR method rapidly screens for deletions of the dystrophin gene at exons 3-30 and at exons 44-55. PCR can be used to detect more than 98% of existing deletions, and it can be performed within 24 hours.

- **Spinal muscular atrophy**

  Homozygous SMN1 gene deletion is highly specific and sensitive for the diagnosis of SMA. In patients with suspected disease and no gene deletion, SMN1copy testing with sequencing of coding regions of SMN1 copy is suggested.

- **Epileptic seizures**

  Mutations in one of several genes can cause or increase susceptibility to juvenile myoclonic epilepsy. The genes commonly studied are the GABRA1 gene and the EFHC1 gene.

  Potassium channel subunit gene mutation (KCNQ2, KCNQ3) is found in benign familial neonatal seizures; while, mutations of LGI1 gene is found in autosomal dominant epilepsy with auditory features.

  Patients with the syndrome of epilepsy with myoclonic-atonic seizures show GLUT1 deficiency. The gene tested for the cause of deficiency is SLC2A1.

- **Huntington's disease**

  Huntington disease (HD) is an adult-onset, autosomal dominant inherited disorder. Genetic testing may not be necessary in a patient with a typical clinical picture and a family history of HD. However, in the absence of a family history of HD, patients should undergo genetic testing to exclude or confirm HD. In normal individuals, CAG - tri-nucleotide repeat occurs between 11 and 29 times. In people with Huntington's disease, the repeat occurs over and over again, from 40 times to more than 80. Genetic testing, thus detects CAG repeat number for each allele.

- **Hereditary ataxias**

  Various genes responsible for ataxia have been identified in spinocerebellar ataxia types 1, 2, 3, 5, 6, 7, 8, 10, 12, 13, 14, 17, 28; dentatorubropallidoluysian atrophy (DRPLA); ataxia-telangiectasia (A-T); Friedreich's ataxia (FRDA); ataxia with oculomotor apraxia types 1 and 2; Marinesco-Sjogren Syndrome; ataxia with Vitamin E deficiency; fragile X associated tremor/ataxia syndrome; mitochondrial recessive ataxia syndrome; autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS); and episodic ataxia types 1 and 2.

- **Amyotrophic lateral sclerosis**

  Various specific gene mutations have been described in familial ALS. Mutation in the copper/zinc superoxide dismutase 1 (SOD1) gene, also known as ALS1 is the most common finding in genetic testing. Other genes most commonly involved in familial ALS are C9orf72, FUS (ALS6) and TARDBP (ALS10).

19. Cerebrospinal Fluid

Cerebrospinal fluid (CSF) is a vital fluid found in the brain and spinal cord. CSF is examined to diagnose a variety of neurological disorders. CSF is collected by a method called lumbar puncture.

Procedure

Lumbar puncture is carried out under sterile conditions by inserting a needle into the subarachnoid space, usually between the third and fourth lumbar vertebrae. CSF is extracted through the needle, and tested for cell count, and physical, chemical and microbiological characteristics.

Risks

Risks associated with lumbar puncture include:

- bleeding from the puncture site into the spinal fluid (traumatic tap)
- discomfort during and after the procedure
- allergic reaction to the anaesthetic
- infection at the puncture site
- headache after the test
- adhesive arachnoiditis
- trauma to the spinal cord or spinal nerve roots resulting in weakness or loss of sensation, or even paraplegia

Indications

CSF testing is done in the presence of following signs and symptoms:

- severe, unremitting headache
- stiff neck
- hallucinations, confusion, or dementia
- seizures

- fever that persist or intensifies
- fatigue, lethargy, muscle weakness
- changes in consciousness
- severe nausea
- light sensitivity
- numbness or tremor
- dizziness
- speaking difficulties
- trouble walking or poor coordination
- severe mood swings
- intractable clinical depression
- In infants - when they are irritable, cry when they are held, have body stiffness, refuse food, and have bulging fontanelles

Contraindications

Lumbar puncture should not be performed in the following situations:

- Idiopathic increased intracranial pressure (ICP), because it can lead to brain herniation.
- Age >65, reduced GCS, recent history of seizure- A CT or MRI scan is indicated instead
- Bleeding disorders
- Skin infection at puncture site
- Sepsis
- Hypertension with bradycardia and deteriorating consciousness
- Cardiorespiratory compromise
- Skeletal deformities of the spine (scoliosis or kyphosis)

Common findings

Physical Characteristics

v Pressure of the CSF can be measured when starting CSF collection.

- Normal: 90-180 mm H2O
- Increased CSF pressure may indicate tumour, infection, hydrocephalus, or bleeding.

- Decreased pressure may be due to dehydration, shock, or leakage of CSF through an abnormal opening.

v Colour of the fluid - normally it is clear and colourless.

- Yellow, orange, or pink CSF may indicate the breakdown of blood cells due to bleeding into the CSF or the presence of bilirubin.
- Green CSF may indicate presence of bilirubin or infection.

v Turbidity - Cloudy or turbid CSF may indicate the presence of white or red blood cells, microorganisms, or an increase in protein levels.

v Viscosity - Normal CSF will have the same consistency as water. Thicker consistency of CSF may indicate certain types of cancers or meningitis.

Chemical Tests

- CSF glucose -Normal: 50-80 mg/dL (or greater than two-thirds of blood glucose). Glucose levels may decrease in the presence of bacteria or inflammatory cells (WBCs) or tumour cells.
- CSF protein - only a small amount is normally present in CSF. Normal: 15-60 mg/dL. Decreases in CSF protein are not generally considered significant. Increases in protein are most commonly seen with:
  - Meningitis and brain abscess
  - Brain or spinal cord tumors
  - Multiple Sclerosis
  - Guillain-Barré Syndrome
  - Syphilis

Additional CSF testing includes:

- CSF protein electrophoresis - specific types of proteins are detected. For e.g. Oligoclonal bands may be seen with multiple sclerosis and Lyme disease. Normal: 0 or 1 band present normally
- CSF IgG - increased in some conditions, such as multiple sclerosis, herpes encephalitis, connective tissue diseases.
- Myelin basic protein - seen in myelin breakdown, such as with multiple sclerosis.
- CSF lactic acid - often used to distinguish between viral and bacterial meningitis. The level will usually be increased with bacterial and fungal meningitis while it will remain normal or only slightly elevated with viral meningitis. Normal: 10-25 mg/dL
- CSF lactate dehydrogenase (LDH) - used to differentiate between bacterial and viral meningitis; the level is usually increased with bacterial meningitis and not with viral meningitis; may also be elevated with leukemia or stroke. Normal: <

2.0-7.2 U/mL

- CSF glutamine - may be increased with liver disease, hepatic encephalopathy or Reye syndrome. Normal: 6-15 mg/dL
- CSF C-reactive protein (CRP) - elevated with inflammation. It is markedly increased with bacterial meningitis.
- Tumor markers - Carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), and hCG may be increased in metastatic cancers.

Infectious Disease Tests

These tests may be performed to look for microorganisms if meningitis or encephalitis is suspected.

- CSF gram stain for direct observation of bacteria and fungi present in CSF under a microscope
- CSF culture and sensitivity is used to detect any microorganisms which will grow in the culture and to select antimicrobial therapy for the affected person and prophylaxis. Some amoebae, single cell parasites, may also be detected with a culture.

Additional CSF testing includes:

- Detection of viruses - detection of viral genetic material (DNA, RNA) by polymerase chain reaction (PCR) testing; for example, herpes virus and enteroviruses. The presence of viral antibodies and their increase over time indicates a recent infection by that virus.
- CSF Cryptococcal antigen - to detect a fungal infection caused by the yeast Cryptococcus neoformans
- Other CSF antigen and antibody tests - may be done depending on which organism(s) are suspected.

Other CSF tests for infectious diseases that are less commonly done include:

- CSF AFB smear and culture may be positive with tuberculosis and with other mycobacteria
- CSF syphilis testing (VDRL) positive with neurosyphilis.

Microscopic tests

- CSF total cell counts
  - Red blood cell (RBC) count -Normally no red blood cells are present in the CSF. The presence of red blood cells may indicate bleeding into the CSF or may indicate a "traumatic tap" - blood that leaked into the CSF sample during collection.

– White blood cell (WBC) count- Normally less than 5 cells are present in the adult. A significant increase in white blood cells in the CSF is seen with infection or inflammation of the central nervous system.

- **CSF WBC differential**

  Small numbers of lymphocytes, monocytes are normal in a sample of CSF. There may be:

  – an increase in neutrophils with a bacterial infection
  – an increase in lymphocytes with a viral or fungal infection, immune disorders (multiple sclerosis)
  – sometimes an increase in eosinophils with a parasitic infection

- **CSF cytology**

  A cytocentrifuged sample is treated with a special stain and examined under a microscope for tumour cells.

  – abnormal cells may be present with cancerous tumors

CSF analysis

CHARACTERISTICS	NORMAL	MENINGITIS		
		BACTERIAL	VIRAL	TUBERCULOUS
Pressure (mmH2O)	100-200	Normal or raised	Normal or raised	Normal or raised
Appearance	Clear	Turbid/purulent	Clear/cloudy	Clear/cloudy
Colour	Clear	White	Clear	Clear/white
Protein (g/L)	0.18-0.45	>1	<1	0.1-0.5
Glucose (mg/dL)	2/3 of serum	Decreased	Normal	Normal / Decreased
Glucose - Serum: CSF Ratio	0.6	<0.4	>0.6	<0.4
Gram stain	Normal	60-90% positive	Normal	
WBC	<3	>500	<1000	100-500
Other		Predominance of PMNs	Predominance of lymphocytes	Predominance of lymphocytes
Lactic acid (mmol/L)	<3.5	>3.5	<3.5	<3.5

Section C

Neurological Diseases and their Comprehensive Management

20. Brain Stroke

Stroke is a focal neurological deficit which occurs due to disruption of blood supply. The blood vessels are either blocked by a clot (ischemia) or they are ruptured leading to a hemorrhage. This further affects the oxygen supply to the brain causing brain damage.

Risk Factors:

A – Age and Anxiety and Atrial fibrillation

B – Body built (obesity)

C – Cigarette Smoking and Cardiac disease

D – Diabetes/ Diet

E – Exercise lack

F – Family History

G – Gout

H – Hypertension and hypercholesterolemia and homocystinemia

antiphospholipid antibodies, metabolic syndrome (obesity, hypertension and hyperlipidemia) are also risk factors for stroke.

Types

There are three main types of strokes namely ischemic stroke, hemorrhagic stroke and TIA (transient ischemic attack).

TIA (transient ischemic attack)

The sudden onset of a focal and transient (<24 hours) neurological deficit due to brain ischemia. This type of stroke is called a mini stroke. It is usually caused due to a temporary clot. However, it should be taken seriously as there are chances of it leading to ischemic stroke.

Warning Signs

- Numbness or weakness that starts suddenly, either on the left or right side of the body (face, arms, or legs are often affected)

- Confusion, difficulty comprehending language, or trouble talking that begins without warning
- Sudden vision problems (in one eye or both)
- Severe, piercing headache, with no clear cause, that starts suddenly
- Difficulty walking because of sudden loss of balance or dizziness
- In a TIA, symptoms generally last only about one minute, according to the American Stroke Association (ASA). Some can last up to five minutes.
- Blood pressure more than 180/110
- Any neurodeficit, headache with projectile vomiting.

Ischemic stroke *:*

This type of stroke occurs due to formation of a clot in the blood vessel obstructing the blood supply to the brain. 87% of all strokes are ischemic type. There are two sub-types of ischemic stroke. Embolic stroke in which, the blood clot forms in any part of the body and eventually reaches the brain. Thrombotic stroke is caused due to a clot formed in an artery which supplies blood to the brain called thrombosis. Thrombosis either results due to large vessel thrombosis or small vessel disease also called lacunar infarction.

Hemorrhagic stroke:

This type of stroke occurs when a weak blood vessel ruptures resulting in bleeding. Hemorrhagic stroke is further divided into two types. Intracerebral hemorrhage, wherein a blood vessel in the brain bursts and spills into the surrounding brain tissue, damaging brain cells. Subarachnoid hemorrhage, wherein the artery which is on or near the surface of the brain bursts and spills into the space between the surface of the brain and the skull. This bleeding is often signaled by a sudden, severe headache.

Causes of stroke:

Ischemic strokes are caused due to clots in the blood supplying arteries. These clots are formed in the already narrowed arteries due to atherosclerosis. Lifestyle risk factors for atherosclerosis include high cholesterol, smoking, heavy drinking, high blood pressure, diabetes, etc.

Hemorrhagic stroke is often caused due to conditions like high blood pressure, trauma, vascular malformations, overtreatment with anticoagulants and aneurysms and arteriovenous malformations (AVMs).

Examination

The F.A.S.T. test is often an easy way to examine and diagnose stroke

Using the F.A.S.T. test involves asking these simple questions:

Face : Check the patients face. Has their mouth drooped?

Arms : Can the patient lift both arms?

Speech: Is the patients speech slurred? Do they understand what the doctor speaks?

Time : Is critical. When was the patient normal? When did the symptoms start?

Basic examination of all patients includes a neurological and cardiovascular exam which includes vital signs and carotid auscultation. Check blood sugar by a finger prick test. The doctor should identify current medications, especially anticoagulants, and recent illnesses, surgery, or trauma. The patients should be immediately referred to the specialized hospital.

Differential Diagnosis

Differential Diagnosis for suspected stroke can include: hypoglycemia, hyperglycemia, hypercalcemia, seizure, migraine, brain tumor, peripheral vertigo, syncope, subdural hematoma, acute confusional state (delirium), vasculitis, drug side effect, transient global amnesia, encephalitis, functional disorder and paroxysmal symptoms of other neurological disorders including MS, upper cord lesions, radiculopathies and acute peripheral neuropathies.

Investigation

1. CT Scan of brain
2. MRI Brain
3. Blood test (CBC, Electrolytes, blood sugar, lipid profile, creatinine)
4. EEG in some cases where you suspect seizures

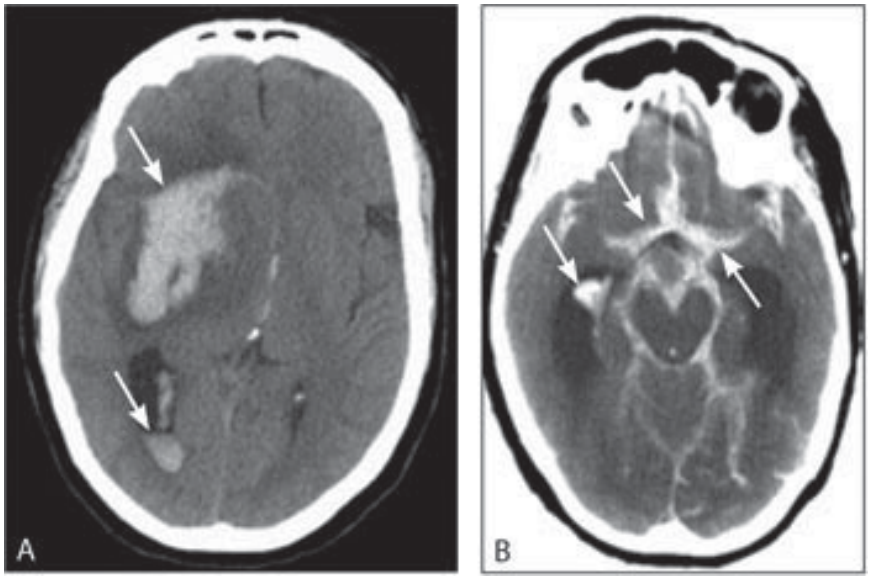


Fig. 20.1: CT Scan of brain

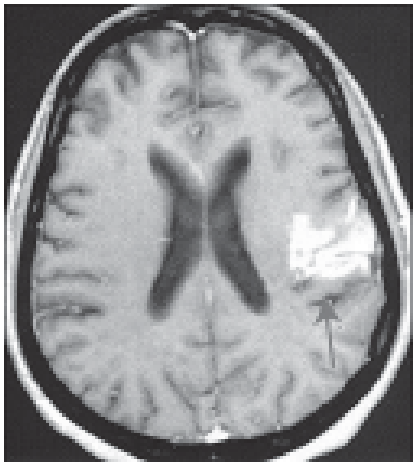


Fig. 20.1: MRI Scan of brain

Management

Acute ischemic stroke:

The only FDA approved treatment for ischemic strokes is tissue plasminogen activator which is given through IV to the patient. tPA dissolves the clot and improves blood flow to the brain. However, it should be administered within 3 - 4 hours to improve the chances of recovery. A significant number of stroke victims don't get to the hospital in time for tPA treatment; this is why it's so important to identify a stroke immediately. Refer to Section F for more details regarding tPA use.

The goal for the acute management of patients with stroke is to stabilize the patient and to complete initial evaluation and assessment, including imaging and laboratory studies, within 60 minutes of patient arrival. Critical decisions focus on the need for intubation, blood pressure control, and determination of risk/benefit for thrombolytic intervention.

Acute antiplatelet therapy (for secondary stroke prevention; patient assessed individually)

After intracranial hemorrhage exclusion - for patients not given tPA an immediate one time dose of 160mg ASA is recommended

For patients who have been given tPA withhold antiplatelet or anticoagulant therapy for first 24hrs, after which, ASA (50-325mg) should be given daily.

Initial Management:

- Temperature (treat >38°C, as fever may contribute to further brain injury or indicate complication such as pneumonia)
- Initial neurological vital signs (Q4H)

- O2 saturation
- Blood sugar (treat hypo and hyperglycemia)
- BP (treat >220 systolic or >120 diastolic cautiously in first 48hrs; aim for reduction by 10-15% unless otherwise indicated by medical conditions)
- Heart rhythm (to assess for atrial fibrillation)
- Swallowing screen (if fails keep NPO until full swallowing assessment)

Blood glucose	Treat hypoglycemia with D50 Treat hyperglycemia with insulin if serum glucose >200 mg/dL
Blood pressure	See recommendations for thrombolysis candidates and noncandidates.
Cardiac monitor	Continuous monitoring for ischemic changes or atrial fibrillation
Intravenous fluids	Avoid D5W and excessive fluid administration IV isotonic sodium chloride solution at 50 mL/h unless otherwise indicated
Oral intake	NPO initially; aspiration risk is great, avoid oral intake until swallowing assessed
Oxygen	Supplement if indicated (Sa02 < 94%)
Temperature	Avoid hyperthermia; use oral or rectal acetaminophen and cooling blankets as neede

Standard haematological and biochemical tests such as a full blood count, erythrocyte sedimentation rate, blood glucose, renal biochemistry and cholesterol level should be performed on patients with a stroke or TIA as a minimum

Thrombolytic therapy with rt-PA (alteplase 0.9 mg/kg up to maximum 90 mg) administered within four and a half hours of stroke onset according to protocols stated in the product licence significantly reduces death and disability at 90 days

Patients admitted with stroke within four and a half hours of definite onset of symptoms, who are considered suitable, should be treated with 0.9 mg/kg (up to maximum 90 mg) intravenous rt-PA.

Streptokinase should not be used for treatment of patients in the acute phase of stroke.

Aspirin 300 mg daily should be commenced within 48 hours of ischaemic stroke and continued for at least 14 days. ; In patients with dysphagia aspirin (300 mg) should be administered rectally or by enteral tube.

Aspirin should be avoided within 24 hours of IV or IA thrombolytic therapy.

Anticoagulants - Low molecular weight heparin (LMWH)

Dosage: 40 mg of enoxaparin subcutaneously daily or 5,000 U unfractionated heparin subcutaneously every 12 hours.

Indications:

- If early anticoagulation after ischemic stroke is indicated but UFH is contraindicated because of large brain infarctions, hemorrhagic infarctions, or pronounced microangiopathic changes in the brain, LMWH (in a body-weight-adapted dose) could be used since it carries lower bleeding risk.
- Conditions with potential high risk of early cardiogenic reembolization, such as atrial fibrillation with proven intracardial thrombus on echocardiography, artificial valves, left atrial or ventricular thrombi, or myocardial infarction during the last 4 weeks
- Symptomatic dissection of the arteries supplying the brain (after exclusion of subarachnoid hemorrhage on CT scan)
- Symptomatic extracranial or intracranial arteriosclerotic stenosis with crescendo TIAs or early progressive stroke
- Basilar artery occlusion before or after intra-arterial pharmacological or mechanical thrombolysis.
- Known hypercoagulable states (eg, protein C and S deficiencies, activated protein C [APC] resistance, antithrombin deficiency, relevant titer of antiphospholipid antibodies)
- Cerebral venous sinus thrombosis

Contraindications:

Patients with acute ischemic stroke treated with IV recombinant tPA should not be treated with anticoagulants for at least 24 hours post thrombolysis.

The use of LMWHs should be avoided in patients with known allergies to LMWHs, heparin, sulfites or benzyl alcohol, in patients with active major bleeding, or patients with a history of heparin-induced thrombocytopenia.

Advantages: Compared with UFH, LMW heparins display improved bioavailability and a more predictable dose response. LMWHs have fewer serious side effects, such as heparin-induced thrombocytopenia, heparin-induced osteopenia and severe bleeding.

Anti-Platelets and Anti-Coagulants:

They are effective at reducing the risk of another Ischaemic stroke in the future. These are long term treatments. They are contraindicated after a Haemorrhagic Stroke.

The anti-platelet medications used are:

Aspirin

Dosage - 75-325 mg daily.

Side effects: bleeding, low platelet, peptic ulcers

Clopidogrel

Dosage- Prophylaxis of Thromboembolic Events: Recommended Dose: 75 mg once daily.

Side effects: gastrointestinal hemorrhage, neutropenia, palpitation, syncope, asthenia, neuralgia, paresthesia and vertigo.

Warfarin

Warfarin is the most commonly prescribed anticoagulant. Warfarin is an anticoagulant used to reduce the risk of death, recurrent MI, and thromboembolic events such as stroke or systemic embolization after MI. Monitoring of INR (International Normalised Ratio) is necessary. The anticoagulant effect of warfarin should be kept at an international normalised ratio (INR) of about 2.5 (desirable range, 2.0-3.0).

Indications: Warfarin is recommended for Ischaemic stroke with atrial fibrillation and those who are at high risk of recurrent ischemic stroke.

Contraindications:

Absolute Contraindications to Warfarin

- Current active bleeding or bleeding disorders
- Platelet count <50,000
- Blood pressure consistently >160/90
- Noncompliance with medication or monitoring

Dosage: Initial: 2 to 5 mg orally or intravenously once a day for 1 to 2 days, then adjust dose according to results of the International Normalized Ratio (INR) or prothrombin time (PT).

Maintenance: the usual maintenance dose ranges from 2 to 10 mg orally once a day.

Side effects: bleeding, jaundice, oliguria

Dagibatran

It is a new type of anti-coagulant which acts by direct inhibition of thrombin. The main advantage offered by dagibatran is that it does not require INR monitoring. It is a tablet which is taken every day, but it more expensive that other treatments. One of the side effects of anticoagulants is bleeding.

Management of acute Haemorrhagic stroke is discussed in detail in Section D.

Management of Chronic Stroke

1. Reduction of high risk factors:

Reduce anxiety, and stress

Lifestyle modifications- healthy diet and exercise regularly, quit smoking

Control diabetes by diet and antidiabetic medicines

Control blood pressure by diet, exercise and antihypertensive medicines

Control cholesterol levels by low fat and low carbohydrate diet, and anticholesterol medicines

2. Comprehensive neurorehabilitation:

In the chronic stage of stroke, neurorehabilitation plays a key role in recovery. Physiotherapy, occupational therapy, speech therapy and psychological counseling will help in faster and higher degree of recovery.

3. Medicine:

Antiplatelet or anticoagulant therapy may be required to prevent recurrent ischemic stroke. Aspirin, clopidogrel may be prescribed by the neurologist for long term after ischemic stroke. Warfarin may have been started in the hospital by a specialist if there is an underlying cause of recurrent thromboembolic episode. In these cases, family doctor should keep a close watch on occurrence of side effects like bleeding. They should also closely monitor INR levels. In case of any episode of bleeding or high INR, patient should be referred to a neurologist immediately.

In cases of haemorrhagic stroke, blood pressure monitoring is very important. Blood pressure should be maintained around 120/80 mm Hg. Antihypertensive drugs should be prescribed. ACE inhibitors, beta blockers, angiotensin receptor blockers are prescribed according to the coexisting factors.

4. Prevention of stroke related complications such as:

- Deep vein thrombosis - Regular rehabilitation, maximize mobility and in some cases DVT prophylaxis may be required
- Spasticity or contracture - Regular rehabilitation will ensure that the range of motion and tone of the muscles are maintained which will prevent contracture formation. If the spasticity is hampering the ambulation or day to day activities, small dose of antispastic medicines may be tried.
- Shoulder displacement - It may happen because of flaccid shoulder girdle muscles which may lead to subluxation of shoulder joint. Therefore, it has to be prevented by giving appropriate shoulder braces and rehabilitation by a physical or occupational therapist.
- Pneumonia - In bulbar weakness, aspiration is common which leads to recurrent pneumonia. Regular speech and swallow therapy is required. Chest physiotherapy is needed in bed ridden patients.
- Urinary tract infection - In case of bowel bladder incontinence, proper care and the catheter hygiene is needed.
- Pressure ulcer - Pressure ulcers are the common complication in bed ridden patients, which has to be taken care of by advising proper positioning and

skin hygiene. Special mattresses like foam mattress, water or air bed which prevent pressure on pressure prone areas are required. The patient needs to be turned every two hourly. Keep the skin dry by powder application.

- Depression - Psychological counseling and family support are necessary to help the patient develop coping skills and improve his quality of life.

Summary

• Acute stroke is a medical emergency which needs immediate attention and treatment. Identify the signs and symptoms of acute stroke by FAST. Obtain a history regarding stroke in the past or a recent TIA. Identify the risk factors of stroke. Confirm the diagnosis of stroke by signs and symptoms, and exclude other stroke mimics like hypoxia, hypoglycemia, or hypotension. On suspicion of stroke, immediately hospitalize the patient and get a CT scan done to differentiate between an ischemic and hemorhhagic stroke.

• Post-stroke involves care for a patient who has had a stroke recently which includes comprehensive neurorehabilitation, prevention of complications, and medical treatment (antiplatelet, anticoagulants for ischemic and antihypertensive for hemorrhagic stroke and medicines to control other risk factors).

• Stroke prevention involves measures to prevent a first or recurrent stroke. This includes compliance to medical management and neurorehabilitation. Also, control of high risk factors is of utmost importance (lifestyle changes, diet, exercise, weight control, antidiabetic and anticholesterol medications).

Sample prescription for chronic ischemic stroke

Rx

1) Tb Aspirin 75 mg po 1 - 0 - 0
2) Tb Atorvastatin 20 mg po 0 - 0 - 1 (if the patient has high cholesterol)
3) Tb Lisinopril 5 mg po 1 - 0 - 0 (if the patient has high BP)
4) Tb Metformin 500 mg po 1 - 0 - 0 (if the patient has high blood sugar)
5) Low fat, low carbohydrate, low cholesterol diet
6) Low salt diet if hypertensive
7) Rehabilitation

21. Migraine

Migraine is a complex disorder characterized by recurrent episodes of headache, most often unilateral and in some cases associated with visual or sensory symptoms.It is severe paroxysmal headache which is throbbing in nature preceded by an aura.

It may be associated with nausea and vomiting.Migraine can be precipitated by red wine,menses,hunger,insomnia,perfumes.Symptoms accompanying migraine may be photophobia,scalp tenderness,paraesthesias,vertigo,syncope,seizures, etc.

Signs and symptoms

Throbbing or pulsatile headache, with moderate to severe pain that intensifies with movement or physical activity

Headache lasts 4-72 hours. Also the patient is sensitive to light and sound

Unilateral and localized pain in the frontotemporal and ocular area, but the pain may be felt anywhere around the head or neck

Pain builds up over a period of 1-2 hours, progressing posteriorly and becoming diffuse

Nausea and vomiting, including anorexia and food intolerance, and light-headedness

Features of migraine aura may precede or accompany the headache phase or may occur in isolation. Usually develops over 5-20 minutes and lasts less than 60 minutes. Most commonly visual but can be sensory, motor, or any combination of these

Visual symptoms may be positive or negative

Examination

- Cranial/cervical muscle tenderness
- Horner's syndrome (ie, relative miosis with 1-2 mm of ptosis on the same side as the headache)
- Tachycardia or bradycardia
- Hypertension or hypotension
- Hemisensory or hemiparetic neurologic deficits (ie, complicated migraine)

- Pupils may be poor in light reactivity, with near dissociation from light

Diagnosis

The diagnosis can be made on patient's history. International Headache Society diagnostic criteria are that patients must have had at least 5 headache attacks that lasted 4-72 hours (untreated or unsuccessfully treated) and that the headache must have had at least 2 of the following characteristics.

- Unilateral location
- Pulsating quality
- Moderate or severe pain intensity
- Aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)
- In addition, during the headache the patient must have had at least 1 of the following:
- Nausea and/or vomiting
- Photophobia and phonophobia

The most common positive visual phenomenon is the scintillating scotoma, an arc or band of absent vision with a shimmering or glittering zigzag border.

Investigations

1) MRI

Neuroimaging is indicated in cases of:

- Worst severe headache
- Change in the pattern of previous migraine
- Abnormal neurologic examination
- Onset of migraine after age 50 years
- New onset of headache in an immunocompromised patient (eg, one with cancer or HIV infection)
- Headache with fever
- Migraine and epilepsy
- New daily, persistent headache
- Escalation of headache frequency/intensity in the absence of medication overuse headache
- Posteriorly located headaches (especially in children, but also in adults)

2) CT (Is done when MRI is not available or is contraindicated)

Management

Management of migraine involves treatment of acute attack and prevention of recurrence.

Treatment of acute attack

Hospital admission for migraine is indicated for:

- Treatment of severe nausea, vomiting, and subsequent dehydration
- Treatment of status migrainosus
- Detoxification from overuse of combination analgesics, ergots, or opioids

Simple analgesics alone or in combination with other drugs are beneficial in cases of mild to moderately severe headaches. Acute treatment is most effective when given within 15 minutes of pain onset.

Analgesics used in migraine include acetaminophen, NSAIDs, and narcotic analgesics (eg, oxycodone, morphine sulfate).

(5-HT1) agonists (triptans) or opioid analgesics are used, for more severe pain, either alone or in combination with dopamine antagonists (eg, prochlorperazine).

Some commonly used triptans: Sumatriptan, Rizatriptan, Zolmitriptan, Naratriptan, Almotriptan, Eletriptan, Fovatriptan

All the triptans are most effective when taken early during a migraine. They may be repeated in 2 hours as needed, with a maximum of 2 doses daily. Triptans should not be taken by patients with known or suspected coronary artery disease, as they may increase risk of myocardial ischemia, infarction, or other cardiac or cerebrovascular events. Do not administer vasoconstrictors - ergots or triptans, to patients with known complicated migraine.

(The drugs with dosages are explained in detail in Section E and a quick reference in Section A [Chapter 1])

Antiemetics (eg, chlorperazine, promethazine) are used to treat vomiting associated with acute migraine attacks. Intravenous prochlorperazine can be given in patients with severe nausea and vomiting at the onset of an attack. Adequate hydration should be maintained.

Prophylactic migraine therapy: It is indicated if -

- Frequency of migraine attacks is greater than 2 /month
- Duration of each attack is longer than 24 hours
- The headaches cause significant disability that lasts 3 or more days
- Abortive therapy fails or is overused
- Symptomatic medications are contraindicated or ineffective
- Use of abortive medications more than twice a week
- Migraine variants such as hemiplegic migraine pose risk of permanent neurologic injury

The goals of preventive therapy are to reduce attack frequency, severity, and/or duration, improve responsiveness to acute attacks and reduce disability

An immediate neurologist referral should be made in case of status migrainosus, complicated migraine or if there is no response to previous treatment.

Prevention of migraine attacks

Reduction of Migraine Triggers: Patients should avoid factors that precipitate a migraine attack (eg, lack of sleep, fatigue, stress, certain foods, use of vasodilators). Patients may need to discontinue any medications that exacerbate their headaches. If an oral contraceptive is suspected to be a trigger, the patient should be advised to modify, change, or discontinue.

Biofeedback, cognitive-behavioral therapy, and relaxation therapy are also beneficial for migraine headaches.

Summary

Migraine is a very common form of headache. It is important to differentiate migraine from other serious headaches. Migraine can be triggered by various factors which should be identified. Investigations are not usually required unless other causes are suspected or patient is not responding to treatment. Management of migraine consists of treating the acute attack, and patient education to reduce further attacks. In unresponsive cases or status migrainosus or complicated migraine, neurologist referral needs to be sought.

Sample prescription

Rx

Migraine headache

1) Tb Rizatriptan 10mg 1 tablet stat followed by Tb Naproxen 250mg 8 hourly with Tb Pantoprazole 40 mg 1-0-1

Migraine prophylaxis

1) Tb Propranolol 40 mg(slow release) 1-0-0 x 3 months with
2) Tb Amitriptyline 10 mg 0-0-1 x 1 month or
3) Tb Flunarizine 10 mg 0-0-1 x till relief is obtained
4) Tb Pantoprazole 40 mg 1-0-1 x 1 week

22. Spondylosis

Spondylosis is a spinal degeneration of the discs or spinal joints and is universally present in all people above 50 years. However in some cases it becomes severely symptomatic and requires investigations and treatment accordingly.

Degenerative changes in the vertebrae may occur at cervical or lumbar level with subsequent impingement of neural elements in the canal.

There are 2 types of spondylosis: cervical and lumbar spondylosis

When to Suspect Spondylosis

Cervical

1) Neck pain radiating to arms (1 or both),the pain is almost always on the outer aspect of the arm(cardiac pain is almost always at the inner aspect of the arm)
2) Restricted neck movements-loss of neck extension & lateral flexion
3) Scapular pain may or may not be associated with neck pain
4) Tingling & numbness of upper limb (1 or both)
5) Dizziness or vertigo or tinnitus or blurring of vision - these symptoms are exacerbated by extremes of movement or minor neck jerk in case of cervical spondylosis.
6) Arm weakness with pain

Examination

1) Tenderness of posterior neck region, scapular muscles & trapezius, biceps, pectoralis major, and triceps
2) Reduction in or loss of sensation of touch, prick or hypersensitiveness in the area of distribution of cervical segments
3) decreased power in upper or lower limb, poor grip, difficulty in raising arms against resistance, difiiculty raising legs against resistance,foot drop.
4) Brisk reflexes-biceps,triceps, brachioradialis & sometimes in lower limb,knee jerk & ankle jerk

5) Babinski sign positive

6) Imbalance on Romberg's test positive on eyes closed only (when eyes are open patient has good balance)

Lumbar Spondylosis

1) Gait disturbance

2) low back pain, radiating pain from back to thighs

3) Sciatica

5) tingling & numbness of lower limb only

6) weakness in lower limb only

7) bladder or bowel - difficulty in control or incontinence in case of lumbar spondylosis

Examination

Tenderness of lumbar & paraspinal muscles, sacro-iliac region,

Straight leg raise test (SLR) -positive

Reduced power in lower limb

Brisk lower limb reflexes, Babinski-absent,

sensory deficit in lower limb

bowel bladder incontinence

restricted back movemen - ,bending, extending & lateral movements

Warning Signs

1) Neck pain or low back pain with weakness in upper limb or lower limb (neurodeficit)

2) Sensory loss in cervical or lumbar segment innervation

3) Severe imbalance with nausea, vomiting associated with neck pain

4) Severe blackout associated with neck pain

5) Severe back pain with restricted movements

6) bowel bladder incontinence

IF ABOVE WARNING SIGNS ARE PRESENT DO IMMEDIATE INVESTIGATION THAT IS MRI OF CERVICAL SPINE OR LUMBAR SPINE & URGENT REFERENCE TO NEUROLOGIST OR NEURSURGEON

1) MRI of cervical / lumbar spine with whole spine screening. MRI is the preferred & diagnostic imaging technique for spondylosis.

Findings may show either posterior osteophytes compressing the cord or the

nerve roots, disc prolapse compressing the cord and reduced canal size (canal stenosis).

MRI will show the presence of disc pathology & severity. I t depicts cord changes, enlargement, compression, or atrophy.

This investigation will guide to make decision about management choices, conservative or surgical.

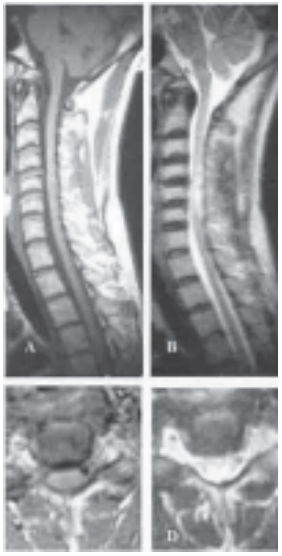


Fig. 22.1: X-Ray of Cervical spondylosis

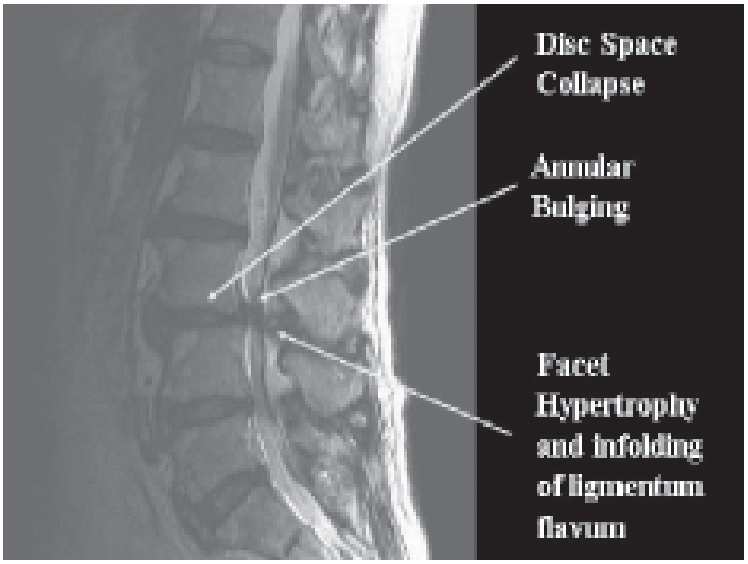


Fig. 22.2: X-Ray of Lumbar spondylosis

2) X ray cervical / lumbar spine

This is a basic investigation which will show loss of cervical lordosis, osteophytes reduction in joint space or spur formation, etc.

3) CT spine

CT spine to be done only if MRI is not available

4) EMG/NCV

EMG and nerve study is done if above warning signs are present. It is also done if the MRI findings are not conclusive. The study shows the level of nerve root compression. It will confirm the diagnosis and rule out other differential diagnoses.

5) Blood routine -Blood tests are done to rule out infection & to check kidney & liver function, so that appropriate medication or side effect of any analgesic medicines can be monitored.

If Creatinine levels are high, then NSAIDS are to be avoided & other pain medications are prescribed.

Management

A. Conservative Management:

1. Medication

   A) **Analgesics** - Acetaminophin, NSAIDS like

   Tb (diclofenac 50+paracetamol 500) 1-0-1,

   Or Tb (ibuprofen 400mg +paracetamol 325mg) 1-0-1

   Tb (naproxen 250mg +domperidone 10mg) 1-0-1,

   If creatinine at higher side give Tb Tramadol 100 mg 1-0-1

   If the pain is neuropathic in nature, then Amitriptyline or Pregabalin or Gabapentin should be prescribed. (Dosages mentioned in Section E)

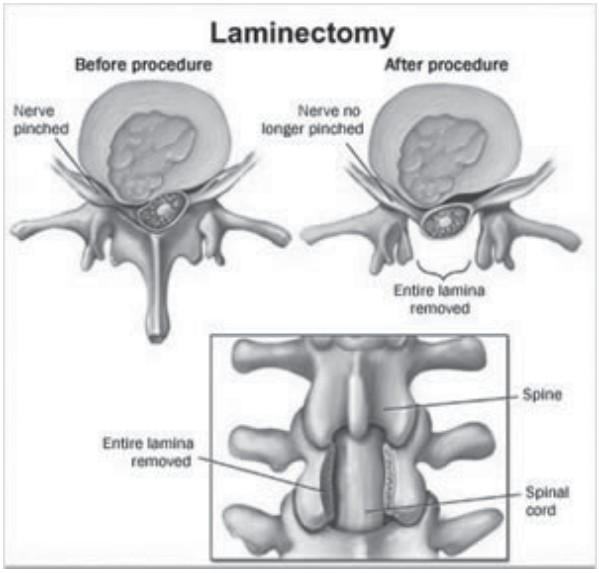
   B) **Muscle relaxants**-chloroxoazone(250/500mg 3-4 times a day), methocarbomol (1.5 g four times a day in divided doses)

   C) **Sedative**- Sedatives like Tb Alprazolam 0.25mg or Tb Amitriptyline 25 mg can be give in the night before bed .

2. Cervical (neck) support collar
3. Rehabilitation-Physiotherapy: gentle exercises, passive manipulation techniques
4. Avoidance of lifting heavy weights
5. Yoga under supervision
6. Traction may be considered in severe cases.

B. Surgery

If no relief with the above mentioned then surgery is considered. Also, if there are signs of cord compression, surgery should be considered early and neurosurgery referral should be done immediately. Options are anterior or posterior fusion of spinal vertebrae and decompression only or decompression along with stabilization.



Anterior approach: This is the most preferred one now days.

Indications:

1. Single level disc protrusion
2. Anterior cord compression

Procedure: Is done under general

anesthesia. A transverse 4 to 5 cm incision is made in the neck. The disk is removed along with the posterior osteophytes and the cord is decompressed. The empty space is filled either with a bone graft from the iliac bone or a titanium cage. Some cases require additional fixation with plates and screws.

Result and complications: Majority of patients report an immediate relief of symptoms after the surgery. Complications are rare and include displacement of the graft and neurological deterioration of power in all or some of the limbs.

Post op: Patient can start walking within one to two days of surgery (with a collar on). Patient can resume normal work after three weeks. The collar has to be worn for three to six months.

Posterior Approach: This involves doing a laminectomy, in which the spinal process and lamina on either side are removed.

Indications: Done in cases of cervical canal stenosis.

In this operation the spinal cord is decompressed. Post operatively the patient has to wear a collar for three to six months.

Results and complications: It is a safe procedure if done with correct indications. If not done properly it can cause severe neurological complications such as weakness of all four limbs.

Summary:

Spondylosis is a degenerative condition of the spine, observed commonly in the age group of 40 years and above. Most of the cases are treated conservatively, however if the patient does not show any sign of relief with the conservative management, surgery should be considered. Also, if any warning signs of cord compression are suspected, patient should be hospitalized and immediate MRI is warranted along with neurosurgery consultation.

Sample Prescription For Spondylosis

Rx

Tb Diclofenac sodium + paracetemol 1-0-1,

Tb Pantoprazole 40 mg 1-0-1,

Tb Chlorzoxazone 250/500mg 1-0-1,

Tb Amitryptiline 25 mg 1-0--1

23. Brain Tumors

Brain tumors are broadly classified into two types.

Benign Tumors: grow slowly and are curable, once totally excised surgically.

- **Meningiomas:** are very vascular tumors that can grow to a very large size.

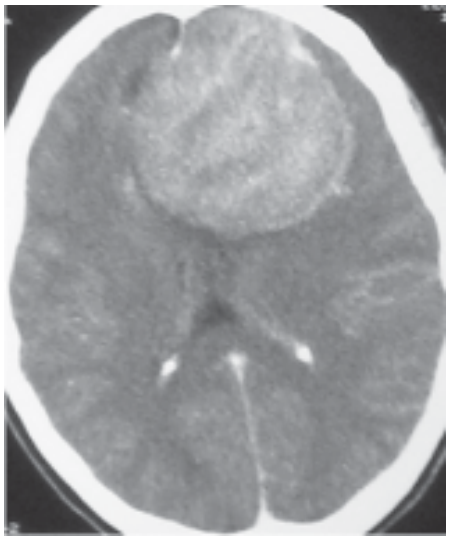


Fig 23.1 CT Scan of a Meningioma

- **Acoustic Neuromas:** arise from the 8th cranial nerve, in the angle between the cerebellum and pons, so are called CP angle tumors. They are slow growing and present with one sided hearing loss with tinnitus, along with difficulty in walking, headache, giddiness. In most of the patients the hearing loss is permanent. Patients present with decrease hearing in one ear along with tinnitus. At this stage the tumor is very small, can be removed easily. If not diagnosed early, it grows very large in size. Hence should be diagnosed early by doing a CTscan and a MRI scan.
- **Pituitary tumors:** arise from the pituitary gland and are slow growing. They initially cause hormonal and then visual symptoms. In women an early manifestation is ammenhorea or galactorhea. In men, it may present with

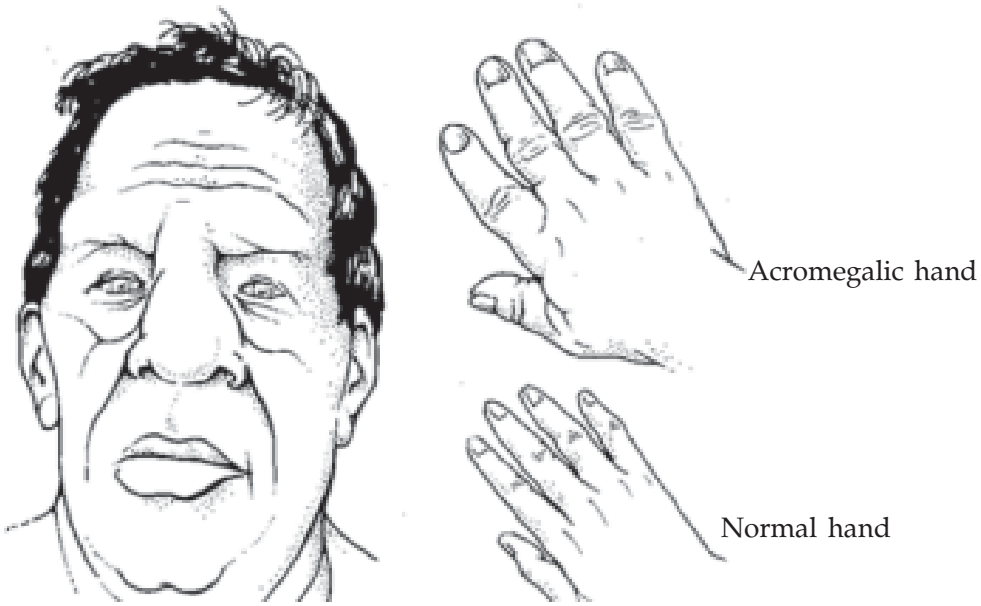


Fig 23.2 Acromegaly in pituitary tumours

thickened face and jaw bones, along with visual disturbances with restriction of the field of vision i.e. they can see only what is straight ahead and not on the sides (bitemporal hemianopia). Gradually they present with headaches and other signs of raised intracranial pressure. Hence early diagnosis is very essential as larger the tumor the more difficult it gets to excise it completely.

Tumors can be divided into primary tumors that started within the brain and those that spread from somewhere else i.e. brain metastasis.

Malignant tumors: grow very rapidly and hence a complete cure is difficult, since they recur after surgery and other treatments. The symptoms may include headaches, seizures, problem with vision, vomiting, and mental changes. The headache is classically worst in the morning and goes away with vomiting indicating raised intracranial pressure. Other symptoms may be difficulty in walking, speaking and altered sensorium.The most common malignant brain tumors are called gliomas or astrocytomas. They have 4 grades i.e. 1 to 4. Grades 1 and 2 are slow growing and have a relatively good prognosis. Grades 3 and 4 are fast growing and have a poor prognosis. Grade 4 astrocytomas are also called glioblastomamultiforme, these are the most malignant tumors of the brain. The average survival of the patients with grade 1 and 2 is 5 Years and that of grade 3 and 4 is 10 - 12 months.

Brain Metastasis

The most common brain tumor in older people is metastasis from another malignancy. After the lungs and the liver the brain is the most common site for malignancy.

Malignancy can be single or multiple, can be detected early as well as late. The symptoms are headache, severe and generalized with one sided limb weakness.

Note: Headache in any known case of malignancy should always be taken seriously and an urgent CT scan or MRI should be requested. Single large metastasis causing pressure effects on the brain need surgical excision. Small multiple metastases are treated with radiation and chemotherapy.

Investigations: Urgent CT scan of the brain (contrast and plain) or MRI brain.

Reference: Urgent reference to a neurosurgeon.

Treatment:

All brain tumor patients should be admitted once diagnosed.

Anticonvulsants(Eptoin 100 mg iv 8 hrly), antioedema measures (mannitol 100 mg iv 8 hrly with dexamethasone 4 mg iv 6 hrly)

Surgery:

Craniotomy: open surgery with attempt to totally excise the tumor. Done for all benign tumor as well as all large malignant tumors that are causing severe brain compression and increase of the intracranial pressure. Done under general anaesthesia, multiple holes are drilled in the skull using an electric drilling system. The bone between these holes is cut and removed (measuring 6 cm to 12 cm in size).Then the dura lining the brain is cut. Surface tumors are visible at this point and are removed. For deep tumors we have to delicately go through normal brain to reach the tumor. The use of advanced modern operating microscopes and sophisticated tumor removal devices such as CUSA (Cavitory ultrasonic suction aspiration) has made brain tumor removal very safe and satisfactory.

Stereotactic biopsy: with this the skull is not opened completely but with a small hole a needle is put in the brain and a biopsy is done. To do this a frame has to be put on the head and the patient is taken to the CT scan or the MRI Scan. Where the coordinates are obtained as to where the tumor is. These are then set on the frame to get accurate biopsy. It is done under local anaesthesia and only two to three days hospitalization is required with less of complications and patient discomfort. It is indicated and deep seated or small malignant tumors or infected lesions such as suspected tuberculomas. Overall the procedure is cost effective.

Endoscopic Surgery: Pituitary tumors can be removed from the nose with an endoscope. It is a stitchless surgery which takes care of the patient comfort and safety. Tumors within the ventricles can also be easily removed with a neuro endoscope.

Adjuvant Therapy:

Benign brain tumors require no adjuvant therapy however malignant tumors may require, radiation therapy and chemotherapy. Radiation therapy is given over six

weeks (5 times a week). Chemotherapy is given for grade 3 and grade 4 malignant tumors. Presently 2 regimes are commonly used PCV and Temozolamide. PCV's to be given in an injectable form and has side effects, but is cheaper. Temozolamide is the preferred one which is available as tablets and has much less side effects but is expensive. In selected types of tumors radiosurgery can be done using the gamma knife or X-knife. This is a one-time treatment with focused radiation. The advantage is absence of any side effects but the limitations are that it works only in selected indications, in only certain size tumors and is very expensive.

Follow Up:

All Brain tumors patients need to be on anti convulsant medications regularly (One year to lifelong)

Since possibilities of recurrence are high family physicians should take all symptoms of these patients seriously.

If any doubt get a CT Scan or an MRI done and refer back to neurosurgeon.

Counseling and rehabilitation are important to the patients.

Summary

- Brain tumours can be either benign or malignant.
- Most common tumours are gliomas in adults
- Second most common are meningiomas
- Common symptoms are headache, vomiting and seizures
- Diagnosed by CT scan or MRI scan
- Management is generally surgery followed by chemotherapy or radiotherapy

24. Head Injury

A head injury is any trauma that leads to injury of the scalp, skull, or brain. These injuries can range from a minor bump on the skull to a very serious brain injury. The most common cause of which are vehicular accident, falls, assaults, etc.

Head injury can be classified as either closed or penetrating. In a closed head injury, the head sustains a blunt force by striking against an object. A concussion is a type of closed head injury that involves the brain.

In a penetrating head injury, an object breaks through the skull and enters the brain. (This object is usually moving at a high speed like a windshield or another part of a motor vehicle)

Symptoms

The signs of a head injury can occur immediately or develop slowly over a few hours. Even if the skull is not fractured, the brain can bang against the inside of the skull and be bruised. (This is called a concussion.) The head may look fine, but complications could result from bleeding inside the skull.

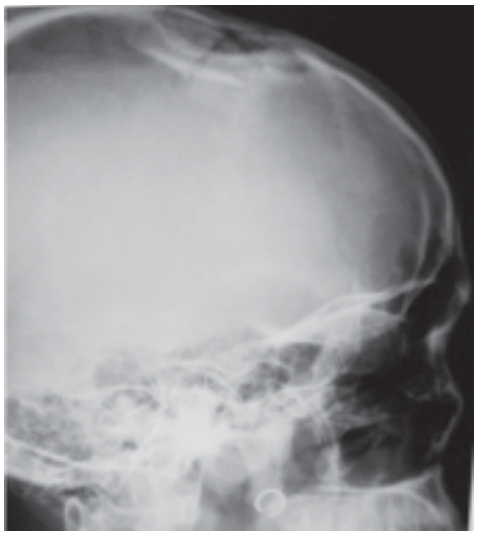


Fig 24.1: Depressed fracture of the skull

When a person who just had a head injury comes to you, try to find out what happened. Try to take the full history from the patient or the person accompanying him. In any serious head trauma, always assume the spinal cord is also injured.

Serious head injury

The following symptoms suggest a more serious head injury that requires emergency medical treatment:

1. Loss of consciousness, confusion, or drowsiness
2. Low breathing rate or drop in blood pressure
3. Convulsions
4. Fracture in the skull or face: Usually the break occurs at the site of impact. Skull fractures are generally linear or depressed. Typically, if the skull is fractured, the underlying brain has been injured. Fracture of the skull vault may be linear or depressed

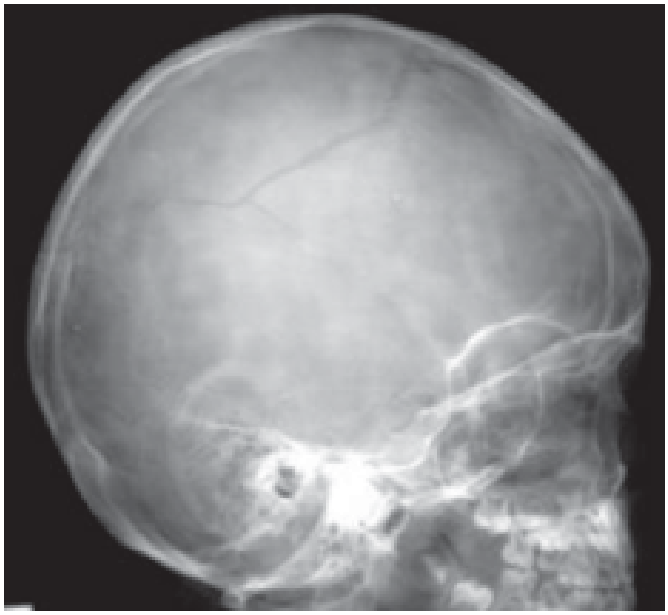


Fig .2 Linear Fracture of the skull

- Linear Fracture of the skull:The most common sites of linear fractures involve the temporal and parietal bones. If the auditory meatus is injured in a temporo-pareital fracture, the patient may have hearing loss, tinnitus or even vertigo.
- Fracture of the skull base: This is rare and if present may result in injury to the cranial nerves.

- Open Fracture (with scalp defect): If the dura is torn the brain is often injured as well. Moreover, if the dura has been torn the patient becomes vulnerable to infection, particularly if pieces of hair or other debris enter, it may give rise to a host of symptoms including the possible development of meningitis
- Closed Fractures (No Scalp Defect)

5. Facial bruising, swelling at the site of the injury, or scalp wound
6. Discharge from nose, mouth, or ears (may be clear or bloody):If the cribriform plate is damaged, itmay result in a laceration of the meninges leading to cerebrospinal fluidleak into the nose. The only symptom may be a continually "running nose". This may eventually lead to meningitis and therefore has to be treated in emergency.
7. Severe headache: This may occur due to intracranial haemorrhage.
8. Initial improvement followed by worsening symptoms
9. Irritability (especially in children), personality changes, or unusual behavior
10. Restlessness, clumsiness, lack of coordination
11. Slurred speech or blurred vision
12. Inability to move one or more limbs
13. Stiff neck or vomiting - signs of meningeal irritation.
14. Pupil changes: size is unequal or one of the pupils is not reacting.
15. Inability to hear, see, taste, or smell

Investigations:

CT scan should be done and should be admitted immediately or shifted to another hospital.

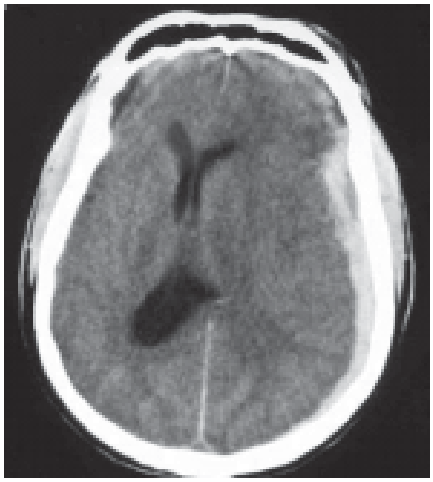


Fig 24.3: CT Scan Brain after a head injury

Treatment:

1. If you suspect a skull fracture, do not apply direct pressure to the bleeding site, and do not remove any debris from the wound. Cover the wound with sterile gauze dressing.
    a. Linear Fracture: No Surgical treatment required, analgesics, needs 24 hours observations admission.
    b. Depressed Fractures: Have to be operated and surgically evaluated, anti convulsants to be started. These patients have high chances of post injury epilepsy.
    c. Fractures of Cranial Base: Require hospitalization, to be treated with high antibiotics as there might be the case of CSF leak and meningitis.
2. Management of CLW's: Even if the patient is referred to another hospital, it is always advisable to suture the CLW of the scalp. If patient is not shifted to another hospital then start with broad spectrum antibiotics and continue till suture removal. That is after 10 days.

Reference: refer the patient urgently to a neurosurgeon.

For a moderate to severe head injury, take the following steps:

- Check the person's airway, breathing, and circulation. If necessary, begin rescue breathing and CPR.
- If the person's breathing and heart rate are normal but the person is unconscious, treat as if there is a spinal injury. Stabilize the head and neck by placing your hands on both sides of the person's head, keeping the head in line with the spine and preventing movement.
- Stop any bleeding by firmly pressing a clean cloth on the wound. If the injury is serious, be careful not to move the person's head. If blood soaks through the cloth, DO NOT REMOVE it. Place another cloth over the first one.

For a mild head injury, no specific treatment may be needed. Advice to, closely watch the patient for any concerning symptoms over the next 24 hours.

Patient's relatives should watch for -

- Vomiting
- Headache not relieved after a few hours
- Drowsiness
- Irritability
- Seizure
- Unusual or confused behaviour
- Bleeding or discharge from the ear or nose
- Weakness or numbness in arm or leg

- Altered vision

The symptoms of a serious head injury can be delayed. While the person is sleeping, wake him or her every 2 to 3 hours and ask simple questions to check alertness, such as "What is your name?"

Treatment: Analgesics may be used for a mild headache. Do not advice aspirin, because it can increase the risk of bleeding.

Brain Hemorrhage

Can be classified as three types that is

a. Extradural: Extradural hematomas are often secondary to a skull fracture and tear of the meningeal arteries below the site of primary impact.

b. Subdural: Subdural haemorrhagedevelops immediately at the time of injury, or slowly thus causing symptoms few days after the original head injury also.

c. Intracerebral: They are uncommon after a head injury except in case of gunshots or penetrating injuries.

In most cases a patient will lose consciousness for a little interval. He may seem lucid on waking up but then as the hematoma develops begins to increasingly complain of headache, irritability, confusion. If these haematomasare large and are causing increase in the ICP they have to be removed surgically by craniotomy.

Hematomas are potentially life threatening and can cause extensive brain injury, including coma, and even death. This is due to the effects of compression and raised ICP.Because of the compression the brain will press the varioustentorial compartments, or even be forced down into the foramen magnum at the base of the skull (herniation)thus compressing the brainstem, which can lead to death.

Usually the oculomotor nerve becomes compressed resulting in pupillary dilation, and loss of eye movement. As the brainstem gets compressed, patient begins to experience rapid changes in conscious-awareness, becomes stuporous, and may become comatose with irregular respiration. It may result inhemiplegia or decerebrate rigidity (i.e. extension of the extremities).

Brain Injury

These are further two types contusions that occur in the outer part of the brain and diffuse axonal injury that occur in the central part of the Brain. These require ICU management with ventilator support for upto 48 hours, and are treated medically with

a. Mannitol 100cc IV 8 hrly
b. Dexamethasone 4 mg IV 6 hrly
c. Eptoin 100 mg IV 8 hrly

Brain Death

Occurs when the brain is irreversibility damaged. These patients can be declared dead for the purpose of organ transplantation. The clinical signs of Brain death are:

a. Deep unconsciousness
b. Fully dilated and non-reacting pupils.
c. Absent doll's eye movements
d. No motor response, to deep central pain.
e. No spontaneous respiration.

Summary

Priority should be given to immediate assessment and stabilizing airway breathing and circulation.

Look out for signs and symptoms that suggest immediate hospitalization is required.

If sending the patient home, give a list of warning signs to the care taker, so that the patient can be brought back to the doctor immediately. See management of neurological emergencies for acute head injury management.

25. Spine injury

Spinal injury is a devastating event that occurs suddenly and whose consequences range from minimal symptomatic pain to a tragic quadriplegia (total paralysis of all four limbs). The key element in management is prevention of secondary neurological damage occurring during transportation, so whenever a family physician sees a patient with suspected spinal injury the first thing to be done is immobilize the spine which is done with cervical color and belts for thoracic and lumbar spine.

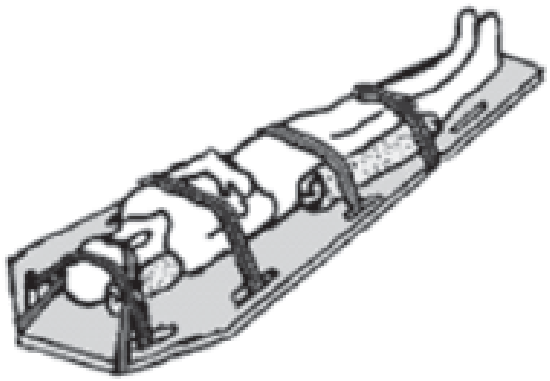


Fig 25.1 Immobilization of Spine

Classification :

1. Region wise:
    a. Cranio - Vertebral junction
    b. Cervical
    c. Thoracic
    d. Lumbar
2. Type:
    a. Fracture
    b. Dislocation

c. Fracture dislocation

3. Complete / Incomplete

   In complete spinal cord injury the entire cross section of the spinal cord has been injured resulting in loss of all sensory & motor function below the level of injury

   In incomplete spinal cord injury the spinal cord has been partially injured preventing some communication between brain & spinal cord below the level of injury. There is some preservation of either motor or sensory function

4. Cause of injury

   The spinal cord can be injured by transection, distraction, compression, bruising, haemorrhage or ischaemia of the cord or by injury to blood vessels supplying it. These injuries can all result in permanent cord injury and may be complete or incomplete.

5. Concussion of the spinal cord can result in temporary loss of function for hours to weeks

   Cause of spinal cord injury

   Injury results from primary & secondary insults

   Primary injury occurs at the time of the traumatic insult

   Secondary injury occurs over hours to days as a result of a complex inflammatory process, vascular changes and intracellular calcium changes leading to oedema and ischemia of the spinal cord. Irreversible damage occurs to nerve cells leading to permanent disability

Symptoms of an acute spinal injury are-

- Flaccid paralysis below level of injury
- Loss of spinal reflexes below level of injury
- Loss of sensation (pain, touch, proprioception, temperature) below level of injury
- Loss of sweating below level of injury
- Loss of sphincter tone and bowel & bladder dysfunction

Investigations:

1. Plain X-rays - AP and Lateral views
2. MRI - best diagnostic tool for spinal injury, as it shows the exact damage to the spinal cord nerves and help in deciding whether surgery is required along with what type of surgery to be done.

Note that CT scan is not useful diagnostic tool, since structures cannot be visualized and should be done only if MRI is not available.

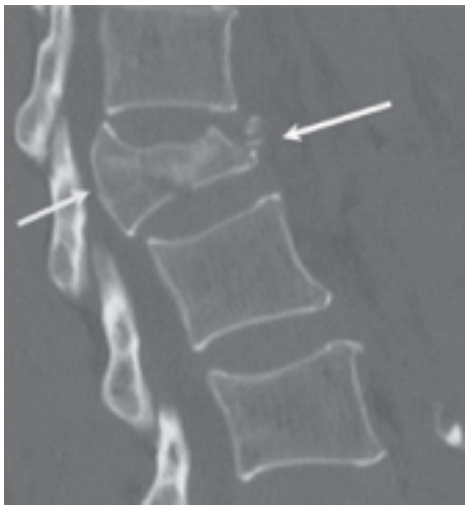


Fig 25.2 Burst fracture spine X-ray

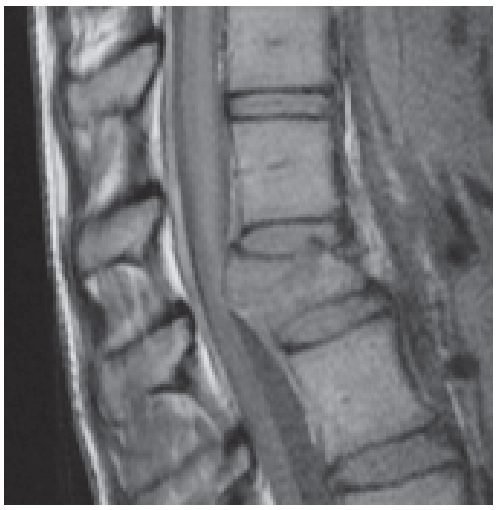


Fig 25.3 Burst fracture spine MRI

In order to confirm the level of injury, neurological assessment is required

- Assess the sensory level
- Assess the motor function
- After 72 hours, use the ASIA guidelines -

ASIA Scale:

A = Complete No motor or sensory function (for definitions, see note below) is preserved in the sacral segments S4-S5

B = Incomplete : Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5

C = Incomplete : Motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade of less than 3

D = Incomplete : Motor function is preserved below the neurological level, and at least half of the key muscles below the neurological level have a muscle grade of 3 or more

E = Normal : Motor and sensory function are normal.

Treatment:

1. At the site of accident / clinic of the family physician :
    a. Patient should be immobilized with the help of sand bags, plastic IV bottles along the neck/head and should be fastened to the stretcher.

b. Airway, breathing should be assessed and maintained. Regurgitation and aspiration should be managed accordingly.

c. Patient should be transported with no spinal movements and care should be taken while doing so, three persons should help in shifting / lifting the patient, they should lift the patient from the same side only.

d. For family physicians having to manage in their clinics due to transportation problem 2gm of Methyl prednisolone sodium succinate (MPSS) in 200 ml of normal saline should be given over a period of 1/2 hr .

2. In the hospital :

a. Resuscitation and maintaining the airway with intubation / ventilation if required.

b. Hemodynamic state is maintained.

c. Methyl prednisolone sodium succinate (MPSS) -Should be started within 3 hrs. of the injury and should be continued for next 24 hrs. If started within 3-8 hrs of injury then it should be given for 48 hrs. MPSS is given as a loading bolus dose of 30 mg/kg over ½ hr and a maintenance dose of 5.4 mg/kg/hr for the required period accordingly.

d. In dislocation patients traction needs to be applied by the neurosurgeon.

e. If patient has no evidence of spinal cord compression on MRI and shows improvement on MPSS and traction then there is no need for the surgery. However in patients with spinal cord compression or progressive neurological deterioration surgery must be considered.

f. Physiotherapy - is given for rehabilitation.

3. **Surgery :** Basic aims of surgery are decompression of the neural elements, reduction of misalignment and restoration of spinal stability.

a. Anterior /Posterior

b. Decompression / Stabilization

4. Operative procedure in spinal injury:

a. Cranio - Vertebral junction :

i. Anterior surgery - Trans oral excision of odontoid

ii. Posterior surgery - Cranio cervical decompression and or stabilization.

b. Cervical spine :

i. Anterior Corpectomy /Disc excision with anterior stabilization.

ii. Posterior Decompressive Laminectomy

c. Thoracic spine :

i. Trans thoracic Anterior Corpectomy with screws and rods/plate fixation.

ii. Posterior Decompressive Laminectomy and stabilization using pedicular

screws and rods /plate fixation.

d. Lumbar spine :

i. Trans abdominal Anterior Corpectomy.

ii. Posterior Decompressive Laminectomy and stabilization using pedicular screws and rods /plate fixation.

Many patients require both anterior as well as posterior surgery so it is done as a single and a two stage procedure.

5. Recent Advances: Availability and development of stem cell therapy is slowly revolutionizing the management of spinal cord injury. All the surgeries listed above are focused on the musculo skeletal system and none of them correct the neurological injury. The central nervous system (CNS) i.e. the brain and the spinal cord is the only tissue in the body which is incapable of degeneration, therefore any damage to CNS is irreversible. However with availability of the stem cells this is now no longer valid. Despite the surgery many patients are left with neurological deficits and are given rehabilitation in form of physiotherapy. The main aim of rehabilitation is to get the patient back to activities of daily living and achieve maximum possible degree of functional independence, therefore when stem cells are implanted to damage spinal cord they help to reestablish broken connections and thereby help in return the loss neurological functions.

Complications to watch for

- Pressure sores

  Patients who have a spinal cord injury are at high risk of damage to their skin. The spinal cord injury causes loss of sensation of pain, pressure & temperature. They also have lost motor control and have poor autonomic nervous system function. Pressure mattress should be used for such patients

  Air mattress should not be used for unstable spines. Change position 2 hourly of the patient.

- Pneumonia

  Regular ches physiotherapy and assisted coughing will help the patient.

- Urinary tract infections

  Long term management includes clean intermittentcatheterisation; condom drainage suprapubic catheter. Reduce bladder spasm by prescribing anti-cholinergics.Watch for recurrent UTI, renal & bladder calculi by maintaining good hydration and good hygiene of theperineal area to reduce infection.

- Constipation

  Increased fluid and fibre in diet.

- Deep venous thrombosis

  Thromboprophylaxis to be carried out so that DVT is averted.

Summary

Patients with spinal cord injury usually have distressing neurologic deficits and disability. Priority should be given to immediate assessment and stabilizing airway breathing and circulation. Patients with suspected spinal cord injury should be given a collar and transported on a hard back board. Watch out for hypotension, neurogenic shock and breathing in spinal cord injury patients. Patients with spinal cord injury should receive a comprehensive program of physical and occupational therapy as a part of management.

26. Dementia and Alzheimer's Disease

Definition:

Dementia is defined as an impairment in memory and atleast one other cognitive domain that is sufficiently severe to impair social and occupational functioning.

What are the early signs of dementia?

- Forgetfulness-forgets name & context
- Language & communication problem-difficulty to find correct words while speaking
- Personality hanges-agitated, anxious, apathetic, depressed, irritable, suspicious
- difficulty in performing familiar tasks
- confusion & disorientation
- odd behavior
- difficulty in following strong lines

What is MMSE

Mini mental state examination is a sensitive reliable 30 questionnaire that is used in clinical and research settings to measure cognitive impairment. It is also used to estimate the severity and progression of cognitive impairment and to follow the course of cognitive changes in an individual over time & makes it an effective way to document an individual's response to the treatment given.

What are the types of dementia?

1) Mild Cognitive Impairment(MCI)

   This is a condition which involves mild cognitive impairment, but is not significant to interfere with the daily activities.

Mild cognitive impairment (MCI) is an intermediate stage between the expected cognitive decline of normal aging and the more serious decline of dementia. It involves problems with memory, language, thinking and judgment that are greater than normal age-related changes. More than the patient, the family and friends will notice the memory lapses. But, it is not very evident as the patient continues to do the daily activities routinely.

On MMSE score 25 to 28

Investigations:

MRI shows bilateral hippocampal atrophy

Management:

Conservative management:

a) Treat the associated conditions that can also affect the memory. For eg. Treat hypertension or depression or sleep disturbances if present.

b) Start neuroprotective vitamins. For eg. Vit B12, folic acid, CoQ10, omega3 fatty acids

c) Start cognitive rehabilitation. Refer to a psychologist for specialized rehabilitation. Studies have shown computer use, playing games, reading books and other intellectual activities may help preserve function and prevent cognitive decline.

d) Regular physical exercise may also help prevent or slow cognitive decline.

e) Dietary advice: A diet low in fat and rich in fruits and vegetables

f) Social engagement may help to preserve mental function and slow mental decline.

2) Alzheimers Disease

Alzheimers is a condition of behavior and cognitive impairment which interferes with social and occupational functioning. It is a progressive brain disease which is irreversible in nature. This is characterized by development of amyloid plaques and neurofibrillary tangles,these plaques are seen on hippocampus(a structure which helps to encode memory) also the plaques are seen on other areas of cerebral cortex which helps in thinking and making decisions

Signs and symptoms:

The most prominent feature is memory impairment for recent events,language dysfunction,apraxia,behavioral disturbance.

MMSE- 12 TO 24

Mild Alzheimer	Moderate Alzheimer	Severe Alzheimer
Memory loss	Loss of impulse control through behavior	cannot recognize family or loved ones and cannot communicate in any way
Taking longer to accomplish normal, daily tasks	Shortened attention span	completely dependent on others for care
Confusion about the location of familiar places	Difficulty organizing thoughts and thinking logically	All sense of self seems to vanish.
Compromised judgment, often leading to bad decisions	Increasing memory loss and confusion	Other associated symptoms may include Groaning, moaning, or grunting
Mood and personality changes; increased anxiety	Restlessness, agitation, anxiety, wandering especially in the late afternoon or at night	Seizures, skin infections, difficulty swallowing
Trouble handling money and paying bills	Problems recognizing friends and family members	Lack of bowel bladder control
Loss of spontaneity and sense of initiative	Perceptual-motor problems: Such as trouble getting out of a chair or setting the table	

Etiology

-family history, advancing age, vascular factors, inflammatory markers, APOE 4 genotype, insulin resistance, dyslipidemia, hypertension, downs syndrome, traumatic brain injury.

Prognosis

Patients with alzheimers can display with anxiety, agitation, depression, insomnia, paranoia.Patients with alzheimers requires assistance for their ADLS that is for dressing, bathing, toileting they may also have symptoms of dyphagia and they may require the feeding tube to be inserted also they may have difficulty in walking.

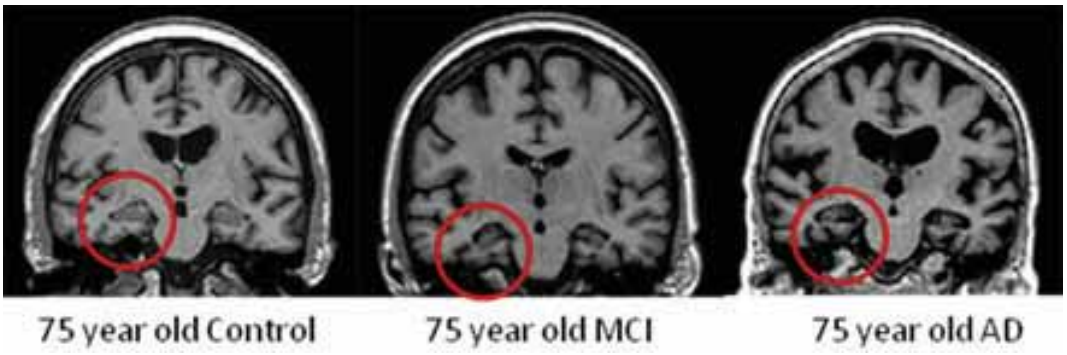


Fig. 26.1 : MRI Brain Of Mild Cognitive Impairment(mci)

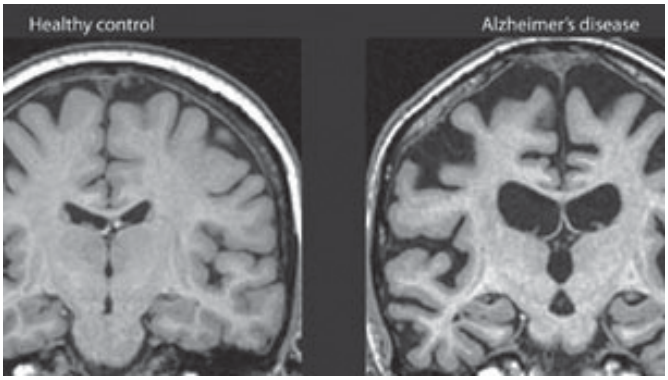


Fig. 26.2 : MRI Brain of Alzheimers Disease

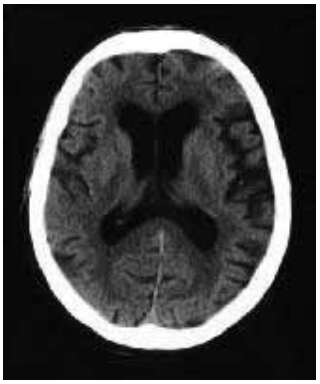


Fig. 26.3 : CT Scan of Alzheimers Disease

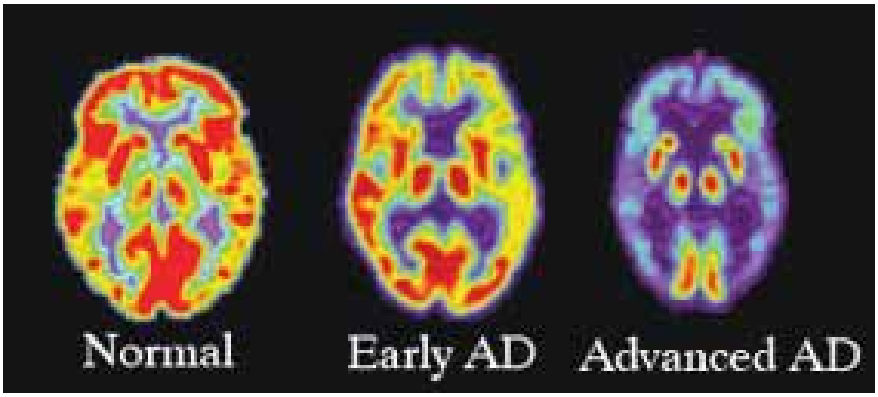


Fig. 26.4 : PET CT Brain of Alzheimers Disease

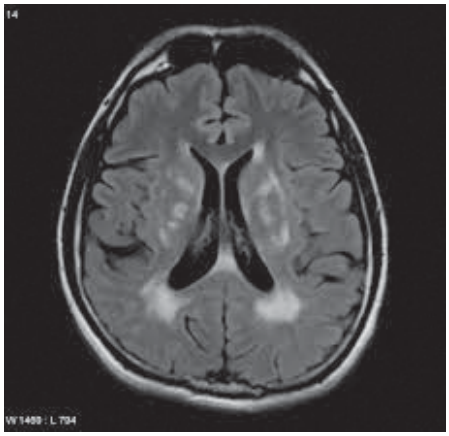


Fig. 26.5 : MRI of Vascular Dementia

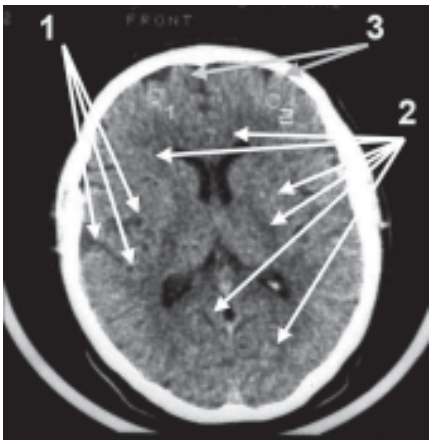


Fig. 26.6 : CT Scan of Vascular Dementia

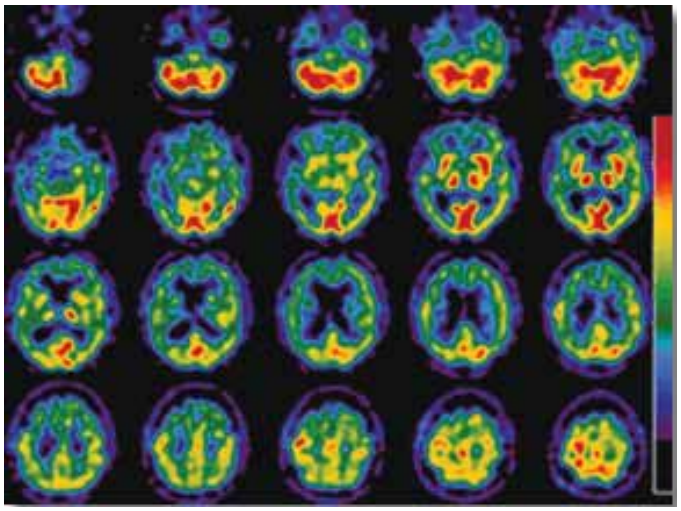


Fig. 26.7 : PET CT Scan of Vascular Dementia

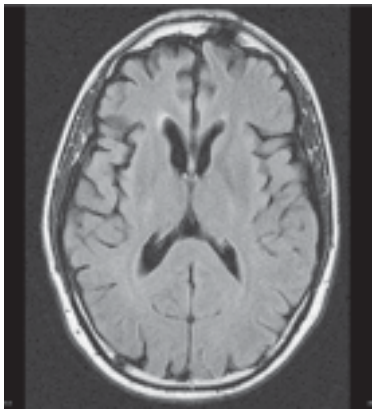


Fig. 26.8 : MRI of Frontotemporal Dementia

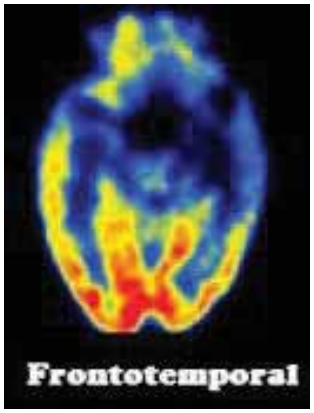


Fig. 26.9 : PET CT Scan of Frontotemporal Dementia

Investigations:

- MRI - medial temporal lobe atrophy (MTA) and parietal atrophy, bilateral hippocampal atrophy,eventual atrophy in temporal,parietal,and frontal cortex.
- mild atrophy: opening of sulci
- moderate atrophy: volume loss of gyri
- severe (end-stage) atrophy: 'knife blade' atrophy.

PET CT brain:- FDG-PET can show hypometabolism in the temporoparietal regions and/or the posterior cingulum, or the hippocampus.

This may help differentiate AD from FTD, which shows frontal hypometabolism on FDG-PET.

CT: CT should be done only if MRI is contraindicated (for eg. Presence of metallic implants)

Management of Alzheimers Disease

Pharmacology

1) Cholinesterase inhibitors

Tablet Donepezil to give 1 tablet of 5 mg at bedtime may increase to 10 mg in 4 to 6 weeks for mild to moderate disease

Tablet Galantamine extended release start 8 mg every morning with food may increase 16 mg after 4 weeks

Tablet Rivastigmine 1.5 mg twice a day may increase to 3 mg twice a day after 2 weeks

2) NMDA receptor antagonist

Memantine start with tablet 5mg daily at weekly intervals to maximum 20 mg/ day doses greater than 5 mg should be divided in bid.

Extended release tablet start 7 mg per day,increase at weekly intervals to target dose of 28mg/day,for renal impairment reduce to 14mg/day

Management of the associated symptoms & non pharmacological treatment given in the end of this chapter(pg number)

3) Vascular Dementia

This is also called as multi-infarct dementia,and this occurs because the blood supply to the brain is affected typically due to a series of minor strokes.Here the features of cognitive decline is associated with atleast one cerebral infarct which is temporary in nature.

Investigations:

Radiological findings may show one or more cerebral infarcts of varying sizes,or severe diffuse white matter abnormalities

- MRI may show global atrophy, diffuse white matter lesions, lacunes and 'strategic infarcts' (infarcts in regions that are involved in cognitive function).
- PET CT: Hypometabolism in the areas of infarct
- CT: Multiple lacunar infarcts

Management of vascular dementia

a) Control blood pressure with antihypertensives like tablet amlodepin 5mg od or tablet telmisartan 20 mg od or Tb Lisinopril 5 mg od

b) Control diabetes with antidiabetic medicines like tablet metformin, glyboride

c) Control cholesterol levels by medications like tablet atorvastatin 40 mg at night,tablet rosuvastatin 20mg at night.

d) Anticholinesterase medicines like Donepezil is also used as cognitive enhancer.

Management of the associated symptoms & non pharmacological treatment given in the end of this chapter(pg number)

4) Dementia With Lewy Bodies (DLB)

This is a type of dementia closely associated with parkinsons disease,this is characetrised by presence of lewy bodies which are clumps of alpha-synuclein & ubiquitin proteins in neurons.

Features like Impaired attention,concentration are seen,whereas visuospatial functioning,memory and naming is preserved.Parkinsonism,fluctuations and visual hallucinations are highly suggestive of DLB.

MMSE 15 to 28

Investigations:

MRI may often be normal or may have hippocampal and cortical atrophy if coexisting Alzheimers disease

Management of DLB

medications such as tablet donepezil or tablet rivastigmine or tablet carbidopa or levodopa

Management of the associated symptoms & non pharmacological treatment given in the end of this chapter(pg number)

5) Frontotemporal Dementia

This is a type of dementia where the frontotemporal area of brain is affected.

It may be associated with motor neuron disease.

Prominent features are personality/behavioural change,apathy or language dysfunction.

MMSE score-30 in initial 3 years

Investigations:

MRI -Frontal or/and temporal cortical atrophy

PET CT - Hypometabolism in frontal and temporal lobes

Treatment of FTD

medications such as tablet donepezil or tablet rivastigmine or tablet carbidopa or levodopa

Management of the associated symptoms & non pharmacological treatment given in the end of this chapter(pg number)

Normal pressure hydrocephalus or NPH ia also and important differential diagnosis which is described in Section A.

Management of Associated Symptoms With Dementia

Sun-downing, Aggressive Behavior

Antipsychotic drugs such as haloperidol or respiridone 0.5-1.0mg at bedtime to be given

Depression

Amitriptyline 25 mg bd, or Nortryptyline 20-50 mg twice a day or serotonin reuptake inhibitors like sertraline to be given.

Sleep Disturbance

Tablet zolpidem 5 mg qhs, or Tb alprazolam 0.2 mg, or

Tb Temazepam 15 mg 0-0-1

Neuroprotective Drugs (Supplements)

As Supplements are very helpful along with the medicines

Tablet CO Q or Tablet Ubiquinol also tablet vitamin c,vitamin e,multivitamin especially B complex including B12 & folic acid.

Other alternating medicines like gingko biloba are also being used.

Non Pharmacological Management is discussed in detail in section a

Summary

The major types of dementia are Alzheimer's, vascular, FTD and DLB. The clinical history, examination remain the mainstay of diagnosis. MRI and PET CT scans' findings are used to confirm the diagnosis and differentiate between the various types of dementia. Treatment of dementia needs a multidisciplinary approach which includes medications, rehabilitation, neuroprotection, environmental modifications and caregiver education.

Sample prescription

1) COGNITIVE IMPAIRMENT

   TB DONEZEPIL 5MG 1-0-0 OR

   TB RIVASTIGMINE 1.5MG 1-0-1

   OR TB GALANTAMINE 4MG 1-0-1

2) SLEEP DISTURBANCE

   TB TEMAZEPAM 15 MG 0-0-1 OR

   TB ZOLPIDEM 5 MG 0-0-1

3) DEPRESSION

   TB NORTRIPTYLINE 25 MG TDS

4) NEUROPROTECTION

   Tb COQ10 300 mg bd or Tb Ubiquinol 100 mg bd

   TB VIT C 1-0-0, CAP VIT E 400 MG 1-0-0

   CAP MECOBALAMIN 0-1-0, TB FOLIC ACID 1-0-0, TB OMEGA3 FATTY ACIDS 1-0-0

27. Movement Disorders

Movement disorders are the disorders which affect fluency, speed, quality, and ease of movements. Abnormal fluency or speed of movement is called dyskinesia. It may involve excessive or involuntary movements known as hyperkinesias; or slowed or absent voluntary movements known as hypokinesia.

Common Types of Movement Disorders

- Tremors
- Parkinson's
- Tics
- Dystonia
- Chorea
- Ataxia
- Restless leg syndrome

1) Tremors

Tremors could occur at rest or are intentional (on performing activity).

If they are at rest it could be-

a) Essential tremors - these are also called as benign tremors & are aggravated on activity. In old patients they are called senile tremors.

b) Secondary tremors - these occur due to anxiety, alcohol, hyperthyroidism , secondary to medications (eg-salbutamol, amytryptilin), etc

c) Parkinson's tremors- these are resting pill rolling tremors reduced with activity & sleep &may be associated with other features of Parkinson's such as bradykinesia (slow movement) and rigidity (stiffness).

d) Intentional tremors - These tremors are absent at rest & present only on doing activity. They may be associated with other cerebellar signs.

Management of Essential Tremors

1) Assure the patient that the tremors are benign
2) Propanalol 10-40 mg twice a day

3) Neuracetam 400 mg 1 tablet tds
4) B complex 1 daily
5) Rehabilitation: physiotherapy and Occupational therapy

If the above treatment is not responding then give gabapentin, alprazolam or clozapine

If medications are unable to suppress the tremors then consider referring the patient to neurologist or neurosurgeon for further management.

2) Parkinson's Disorder

Parkinson's is a degenerative disorder of the nervous system involving degeneration of dopamine generating cells. In the early stages of Parkinson's disease, the face may show little or no expression or the arms may not swing on walking. The speech may become soft or slurred. Symptoms worsen as the condition progresses over time.

Although Parkinson's disease cannot be cured, medications may markedly improve the symptoms.

Signs and symptoms

Symptoms are related to movement disorders like shaking, rigidity, difficulty walking.

Resting pill rolling tremors

Bradykinesia-slow handwriting, slow shuffling gait, slow daily activity, slow speech

Rigidity-lead pipe type (stiffness throughout flexion,extension of the elbow)or cogwheel type (intermittent)

Associated

Gait-no arm,swing,mass turning,freezing episode, slow shuffling gait,short steps

Mask faces-decreased expression on the face

Leaning posture

Blapharospasm or decreased blinking

Dementia

Investigations

Blood tests may be done to check for abnormal thyroid hormone levels or liver damage. An imaging test (such as a CT scan or an MRI) may be used to check for signs of a stroke or brain tumor.

PET CT sometimes may detect low levels of dopamine in the brain, a key feature of Parkinson's.

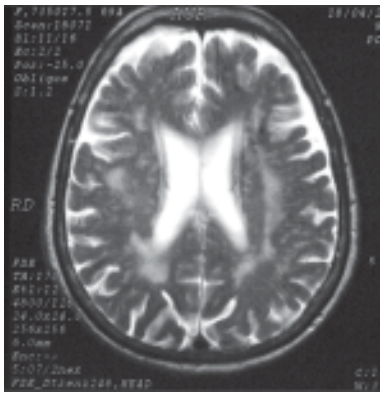


Fig. 27.1: MRI of Parkinsons Disease

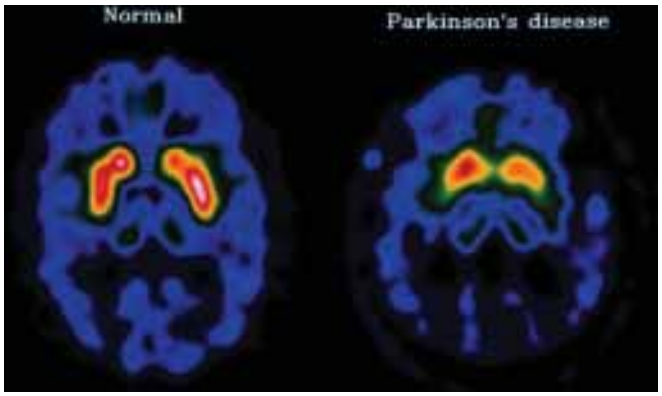


Fig. 27.2: PET CT of Parkinsons Disease

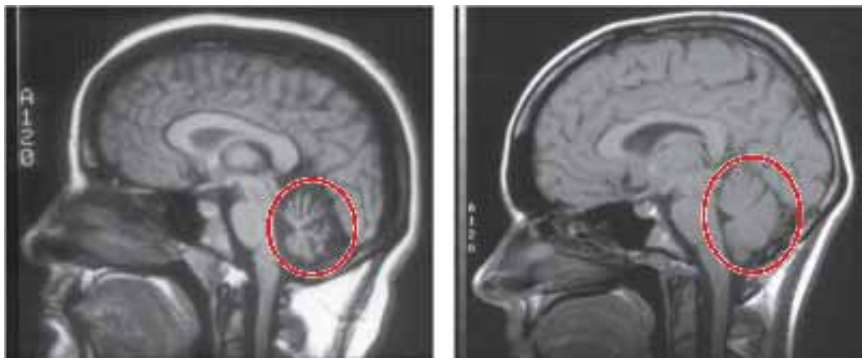


Fig. 27.3: MRI of Cerebellar Ataxia

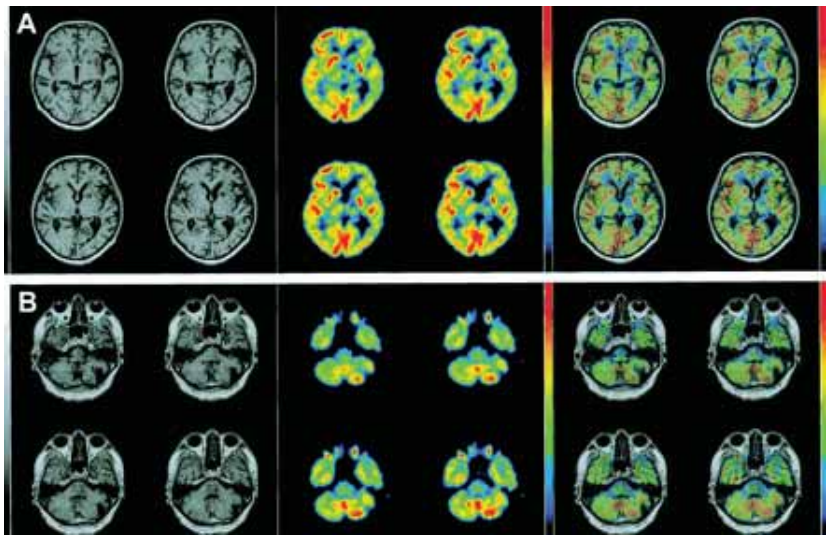


Fig. 27.4: PET of Cerebellar Ataxia

Risk factors for Parkinson's

Age : Young adults rarely experience Parkinson's disease. It ordinarily begins in middle or late life, and the risk increases with age. People usually develop the disease around age 60 or older.

Sex: Men are more likely to develop Parkinson's disease than are women

Heredity: Having a close relative with Parkinson's disease increases the chances of developing the disease.

Exposure to toxins: Ongoing exposure to herbicides and pesticides may be a risk factor of Parkinson's.

Management

Pharmacologic treatment of Parkinson disease can be divided into symptomatic and neuroprotective (disease modifying) therapy.

A) Symptomatic treatment

1) Levodopa, coupled with carbidopa, remains the gold standard of symptomatic treatment for Parkinson disease. Carbidopa allows for greater levodopa distribution into the central nervous system. The time when medication is providing benefit for bradykinesia, rigidity, and tremor is called "on" time, and the time when medication is not providing benefit is called "off" time.

   For details regarding Levodopa and Carbidopa dosage refer to Section E.

   Levodopa provides the greatest benefits for motor signs and symptoms, with only few adverse effects. However, its long-term use is associated with the development of motor fluctuations ("wearing-off") and dyskinesias.

   Dopamine agonists (ropinirole, pramipexole) provide moderate symptomatic benefit and delay the development of dyskinesia compared with levodopa.

   Levodopa in combination with a dopa decarboxylase inhibitor is started at a low dose and slowly titrated to control clinical symptoms. Most patients experience a good response on a daily levodopa dosage of 300-600 mg/day (usually divided 3 or 4 times daily) for 3-5 years or longer.

   Anticholinergic agents are used when tremors are not adequately controlled with dopaminergic medication. However, they have limited efficacy and may cause neuropsychiatric side effects.

   One of the most commonly used anticholinergic is trihexyphenidyl. The initial dose of trihexyphenidyl should be low and gradually increased. It is recommended to begin therapy with a single 1-mg dose. Dosage can be titrated by 1 mg each week or so, until a total of 4-6 mg is given daily or until satisfactory control is achieved. Some patients may require higher doses. Benztropine (Cogentin) is also commonly used, with an initial dose of 0.5-1 mg daily at

bedtime. Dose can be titrated at weekly intervals in increments of 0.5 mg to a maximum of 6 mg/day.

Amantadine is an antiviral agent that has antiparkinsonian activity. Amantadine offers additional benefit in patients experiencing waxing or waning effects from levodopa.

Amantadine is commonly introduced at a dose of 100 mg per day and slowly increased to an initial maintenance dose of 100 mg 2 or 3 times daily. Potential side effects of amantadine are confusion and hallucinations.

Possible strategies for advanced stage or when the response time for levodopa is decreasing include the following:

- Adding a dopamine agonist, COMT inhibitor, or MAO-B inhibitor
- Dosing levodopa more frequently
- Increasing the levodopa dose
- Switching from immediate release to sustained release levodopa/carbidopa/ entacapone

Surgical treatment includes deep brain stimulation and neuroablative surgeries. This may be an option for advanced stages. A neurosurgeon referral is thus required for uncontrolled advanced cases.

Rehabilitation - A comprehensive neurorehabilitation consisting of physiotherapy, occupational therapy, and psychological counseling is required.

B) Neuroprotective therapy aims to slow down or reverse the disease progression. This includes CoQ 10 and multivitamin prescription. For details refer Section E.

3) TICS

Rapid repetitive involuntary contractions of a group of muscles are known as tics.

They are of two types-

Motor tics (involving bodily movement)such as facial twitching, grimacing, binking& shrugging the shoulders.

Phonic or vocal tics (involving sounds)such as coughing,grunting,clearing the throat &sniffing

Causes

Anxiety,stress,excitement,fatigue,medications, other diseases like CP

Treatment

a) Habit reversal therapy-this therapy concentrates on other movements which compete with the tic movement.

b) Exposure with response prevention-this teaches techniques to suppress unpleasant feelings proceeding a tic.

In severe cases where day to day life is affected a new surgical treatment option of deep brain stimulation can be discussed by a neurosurgeon.

4) Dystonia

This is a syndrome of involuntary sustained or spasmodic muscle spasm &the movements are slow, sustained & often occur in a repetitive & patterned manner but are unpredictable & fluctuant. There may be abnormal posturing & twisting.

Causes-dystonia occurs due to

- damage to basal ganglia
- infection,stroke,drug interactions, CP,brain trauma.

Common types are writers cramp,cervical dystonia or torticollis,tardive dystonia-due to medication

Treatment

1) Medicine-Pacitane,levodopa,syndopa,clonazepam,lorazepam,baclofen
2) Sensorytrick-Control the movement by touching or stimulating affected or nearby body part.
3) Rehabilitation-Occupational and physical therapies

Stress management

In severe cases deep brain stimulation (Refer to a neurosurgeon)

5) Chorea

Excessive, spontaneous, irregular, non repetitive, random movements of arms or legs with unstable (dance like gait) are called chorea.

Causes

Levodopa induced Huntington's disease, Wilson's disease, and Sydenham's chorea-in acute rheumatic fever

Investigations

TSH & PTH, serum copper & ceruloplasmin level, serum ammonia, anti streptococcal antibody titers.

MRI brain, PET CT brain.

Treatment

1) Neuroleptics-Fluphenazine, risperidone, olanzapine, clozapine & quetiapine Or
2) Gaba ergic -gabapentin& valproate & clonazepam.

3) CoQ 10

6) Ataxias

Common types of ataxia:

cerebellar ataxia, spinocerebellar ataxia, Friedreichs ataxia, ataxia teleangectesis, ataxia with vit E deficiency.

Invetigations :

Basic routine blood tests-TSH,VIT E levels,Co Q 10 levels,vit B 12 levels, metabolic screening.

MRI brain, PET CT brain

Genetic testing

Treatment-

vit E, Co Q 10, B complex

Multivitamin (treat the specific cause)

Propanalol or primadone,clonazepam,baclofen for spasticity,amantadine,

acetazolamide for episodic ataxia.

Treat any underlying secondary cause if present.

Rehabilitation : Occupational and physical therapy

7) Restless Leg Syndrome

This is a neurological movement disorder of the limbs which is associated with a sleep complaint. Patient has irresistible urge to move legs.

Signs and symptoms :

An urge to move the legs that occurs due to uncomfortable and unpleasant sensations in the legs which may worsen during periods of rest or inactivity and worsens in evening & at night. This urge is partially relieved by movement.

These symptoms are not attributed to any mental disorder.

Other features associated with RLS are sleeplessness,daytime fatigue,involuntary repetitive jerky movements either during sleep or while awake or at rest.

Diagnosis:

The patients of RLS should be tested for iron deficiency anemia.

If any secondary cause is suspected on the basis of initial history, abnormal neurological findings, other laboratory tests which include CBC, creatinine, fasting blood glucose, magnesium, TSH, vit b12, folate should be done.

EMG, NCV should be considered if suspected for polyneuropathy or radiculopathy

Management

Pharmacology

Medications for primary RLS can be given on the basis of the symptoms. In case of secondary RLS Dopaminergic agents, benzodiazepines, opiods, anticonvulsants are to be given accordingly

Non Pharmacology

To avoid caffenine,alcohol,nicotine

Sleep hygiene measure

Medications which exacerbate RLS such as like Serotonin reuptake inhibitors,dopamine antagonists should be discontinued if possible.

Physical modalities before bedtime such as hot or colds water bath.

Summary

One of the common movement disorder is Parkinson's disorder. It is caused by dysfunction of dopaminergic neurons. It is important to distinguish between Parkinson's tremors from benign tremors as the management will differ. Family physician plays a key role in multidisciplinary treatment of Parkinson's. Monitor for dose response and side effects of medications. CT or MRI may be normal in early stages of Parkinson's. Therefore, if there is suspicion of Parkinson's , referral to a neurologist is required.

Ataxias can be very debilitating and affect the daily and social life of the patient. They are progressive and can affect the lifespan. Rehabilitation plays a major role and should be started at early stage.

Sample prescription for Parkinson's tremors

Rx

Tb Levodopa/Carbidopa 100 mg / 25 mg one Tb 1 - 1 - 1 (empty stomach)

Tb Pan 40 mg 1 - 0 - 1

Tb CoQ 10 300 mg 1 - 0 - 1

Tb multivitamin 0 - 1 - 0

Rehabilitation

Neurologist referral

28. Demyelinating Disorders

Demyelinating disorders are characterized by loss or dysfunction of myelin in the central or peripheral nervous system which occurs due to damage to the myelin sheath of neurons. This damage impairs the conduction of signals in the affected nerves. In turn, the reduction in conduction ability causes deficiency in sensation, movement, cognition, or other functions depending on which nerves are involved.

The most common demyelinating disorder is multiple sclerosis.

1) CNS :

Here the demyelinating process involves the central nervous system. The cause can be primary or secondary.

Primary

In primary demyelinating disorders, cause is unknown, but an autoimmune mechanism is suspected, since the disorder sometimes follows a viral infection or viral vaccination.

a) Multiple sclerosis
b) Neuromyelitis optica
c) optic neuritis
d) acute transverse myelitis
e) acute disseminated encephalomyelitis,
f) acute hemorrhagic leukoencephalitis

Secondary

Demyelination is secondary to an infectious, ischemic, metabolic, or hereditary disorder or to a toxin (eg, alcohol, ethambutol)

a) toxins-alcohol, ethambutol
b) infections-JC virus causes progressive multifocal leukoencephalopathy
c) nutritional- Vit B12 deficiency, Vit E,Vit B6, Thiamine ,osmotic demyelination syndrome.
d) hypoxic

e) hereditary - Adrenoleukodystrophies, metabolic storage disorders.

2) Peripheral demyelination:

Here the demyelinating process occurs within the peripheral nervous system .The most common type is Polyneuropathy.

When to suspect a demyelinating disorder

- diffuse or multifocal neurological deficit
- sudden onset,particularly in young adults
- onset within weeks of an infection or vaccination
- neurodeficits that wax & wane
- symptoms suggesting a specific demyelinating disorder

Signs and symptoms

Visual--Blurred vision, unilateral loss of vision, Oscillopsia, Diplopia

Motor--Trunk/limb weakness, Spasticity, Hyperreflexia

Gait disturbance & Balance problems

Sensory-Numbness, paraesthesias, dysesthesias,trigeminal neuralgia,hyperpathia, proprioception deficits

Cerebellar-Tremor, ataxia, incoordination

Genitourinary-urgency/frequency/retention of urine, Incontinence, constipation, impotence, dyspareunia

Neuropsychiatric-Impairment of memory, concentration, attention, Depression, irritability, anxiety

Other symptoms-Prominent intractable fatigue with no other cause

Here we describe the most common demyelinating disorders.

Multiple Sclerosis

Multiple sclerosis is an autoimmune disorder that affects the central nervous system and optic nerves by causing destruction of the myelin sheaths. This is a life-long chronic disease diagnosed primarily in young adults. During an MS attack, inflammation occurs in areas of the white matter of the central nervous system in random patches called plaques. This process is followed by destruction of myelin. Myelin destruction causes nerve conduction defects.

Usually a young adult will present with diplopia or other visual disturbance, weakness in limbs, fatigue, paraesthesia or sensory loss, incoordination, gait imbalance, bladder and bowel dysfunction. Memory problem and speech disturbance may also be present. These symptoms may wax and wane.

Multiple sclerosis is of four types

1) Benign multiple sclerosis
2) Relapsing remitting multiple sclerosis
3) Secondary progressive multiple sclerosis
4) Primary progressive multiple sclerosis

Investigations

1) MRI - MRI typically shows more than one hyperintense white matter lesions (plaques) particularly in periventricular white matter, corpus callosum, brainstem, cerebellum and/ or spinal cord. Ovoid lesions perpendicular to the ventricles (Dawson's bar or fingers) may be seen. In chronic advanced stage, global cerebral atrophy is seen.

   Gadolinium enhanced T1 weighted MRI scans may show enhancing white matter lesion which depict acute active MS lesions.

   Newer FLAIR MRI and MR spectroscopy have increased the sensitivity for detection of MS lesions.

   MRI also helps in excluding any other cause of neurological complaints.

   MRI is also an efficient monitoring tool to study the progression of the disease and also useful for treatment.

2) CT scan - In MS CT scan may show enhanced white matter lesion but the appearance is nonspecific. Therefore, it is used only to rule out other causes of neurodeficit.

3) Lumbar puncture - LP is not routinely done in MS. It is done only if the MRI findings are non diagnostic.

   CSF abnormalities found in MS include a mononuclear cell pleocytosis and an increased level of intrathecally synthesized IgG. The total CSF protein is usually normal or slightly elevated. Oligoclonal bands are detected in the CSF.

4) Evoked Potentials- EP testing assesses function in afferent (visual, auditory,and somatosensory) or efferent (motor) CNS pathways. VEP may show delay in latencies, SSEP may show delayed latencies in posterior column conduction of the spinal cord, the brainstem and cerebral cortex.

   BAEP may show delayed auditory pathways.

5) In Neuromyelitis optica serum antibodies aquaporin 4 may be present.

Treatment

Goals of therapy

1) Minimizing the effect of acute attack

An exacerbation of MS is the appearance of the new neurologic deficit or reappearance and/or worsening of an old deficit due to MS that lasts longer than 24 hours and is not due to fever or other systemic process.

Methylprednisolone- IV 1g for 5 days followed by tapered oral prednisolone for acute attacks

2) Modify the course of the disease (to prevent the relapse)

Interferon is given nowadays to modify the disease progression.

Interferons are listed below

a) Interferon Beta-1b

Dose-8 MIU (250mcg) to be given subcutaneously on alternate days

Side effects-Flu like symptoms may be seen, elevated liver enzymes can be seen.Leukopenia and psychiatric symptoms can be seen.

b) Interferon Beta-1a

Dose- 6 MIU (30 mcg) to be given intramuscularly weekly.

Side effects-Flu like symptoms can be seen

c) Glatiramer acetate

Dose- 20 mcg to be given subcutaneously daily

Side effect-mild injection site reaction may occur,transient flushing,chest tightness,shortness of breath.

3) Symptomatic management

a) Bladder dysfunction-to treat and prevent incontinence and urinary retention,hyperreflexic bladder(urgency,frequency,urge incontinence) it is better to keep a cathether after taking advice of a urologist.

Tb Oxybutynin 5 mg thrice a day, Tb Tolterodine (long acting) 2mg once a day

b) Spasticity

Simple exercises should be tried for example stretching,riding a bicycle.

When physical measures fail, start on tb baclofen,tizanidine,benzodiazepines

c) Constipation-Stool softner or laxatives for example lactulose, bisacodyl

d) Fatigue -Multivitamins ,rehabilitation,dietary advice

e) Depression or emotional lability- Amitryptiline 25 mg qhs

f) Musculoskeletal pain - NSAIDs .

g) Paraesthesia-Carbamazepine 100-200 mg once or twice a day.

4) long term rehabilitation including visual rehabilitation is important

Transverse myelitis

Transverse myelitis is a sudden onset of acute inflammation of the spinal cord. This

inflammation damages nerve fibers, and causes them to lose their myelin coating, thereby leading to decreased electrical conductivity in the spinal cord.

Causes

The disease is presumed to be caused by viral infections, spinal cord injuries, immune reactions, schistosomiasis or insufficient blood flow through spinal cord vessels.

This condition may be associated with

Bacterial Infections - Mycoplasma pneumoniae, Lyme borreliosis, syphilis (tabes dorsalis), tuberculosis

Viral Infections - herpes simplex, herpes zoster, cytomegalovirus, Epstein-Barr virus, enteroviruses (poliomyelitis, Coxsackie virus, echovirus), human T-cell, leukemia virus, human immunodeficiency virus, influenza, rabies

Post-Vaccination - Rabies, cowpox

Paraneoplastic syndromes

Vascular - thrombosis of spinal arteries, vasculitis secondary to heroin abuse, spinal arteriovenous malformations

Signs and symptoms

Symptoms typically develop over the course of hours or days and may progress over weeks. There is sudden onset of weakness and numbness of the limbs along with bladder bowel incontinence or dysfunction. Patient experiences pain and there may be associated fever. Typically, the patient suddenly falls down due to paralysis in both lower limbs.

Sensory symptoms of transverse myelitis may include a sensation of pins and needles traveling up from the feet. Back pain can occur at the level of the inflamed segment of the spinal cord. The degree and type of sensory loss will depend upon the extent of the involvement of the various sensory tracts, but there is often a sensory level. Motor weakness occurs due to involvement of the pyramidal tracts and mainly affects the muscles that flex the legs and extend the arms. Involvement of the autonomic nervous system is common and frequently leads to impaired function of the bladder and bowel and can also lead to episodes of high blood pressure. Bladder paralysis often occurs and urinary retention is an early manifestation.

Examination

If all the four limbs are involved this means the upper cervical cord is involved. And also there is risk of respiratory paralysis (segments C3, 4, 5 to the abdominal diaphragm).

A lesion of the thoracic spinal cord (T1-12) will produce upper motor neuron signs in the lower limbs, presenting as a spastic diplegia.

A lesion of the lower part of the spinal cord (L1-S5) often produces a combination of upper and lower motor neuron signs in the lower limbs.

Differential diagnosis

Acute spinal cord trauma, Lyme disease, acute compressive lesions of the spinal cord such as epidural metastatic tumour and infarction of the spinal cord (eg. due to insufficiency of the anterior spinal artery).

Investigation

1) MRI Spinal cord-The T1 weighted images show decreased signal intensity and myelomalacia in chronic stage.MRI is preferred as it is diagnostic. It also shows the severity and extent of spinal cord involvement.
2) If MRI is not available CT SCAN is done to rule out any compression of spinal cord by abscess or tumor.

Management

Stabilise the patient after checking the vitals

If you suspect tranverse myelitis then neurophysician consultation is required immediately.

1) ABC Airway breathing Circulation

   Start O2, IV fluids, and shift the patient to nearby hospital.
2) In hospital management

   Methylprednisolone - IV 1g for 5 days followed by tapered oral prednisolone for acute attacks or Dexamethasone is used as an acute line of treatment
3) Plasma exchange is used for moderate or severe cases who do not improve with IV steroids.
4) If any infective cause is found it is treated with Antibiotics and in case of herpes zoster treatment should be with acyclovir.

In chronic patients of demyelinating diseases long term care is required.

1) Pulmonary care-Patient should be ventilated properly if the saturation is low, also aspiration precaution needs to be taken care.
2) Bedsore prophylaxis needs to be taken care.
3) Urinary rehabilitation in consultation with a urologist.
4) Comprehensive neurorehabilitation should be started at the earliest.

Polyneuropathy

The demyelination of peripheral nerves leads to polyneuropathy. Polyneuropathy

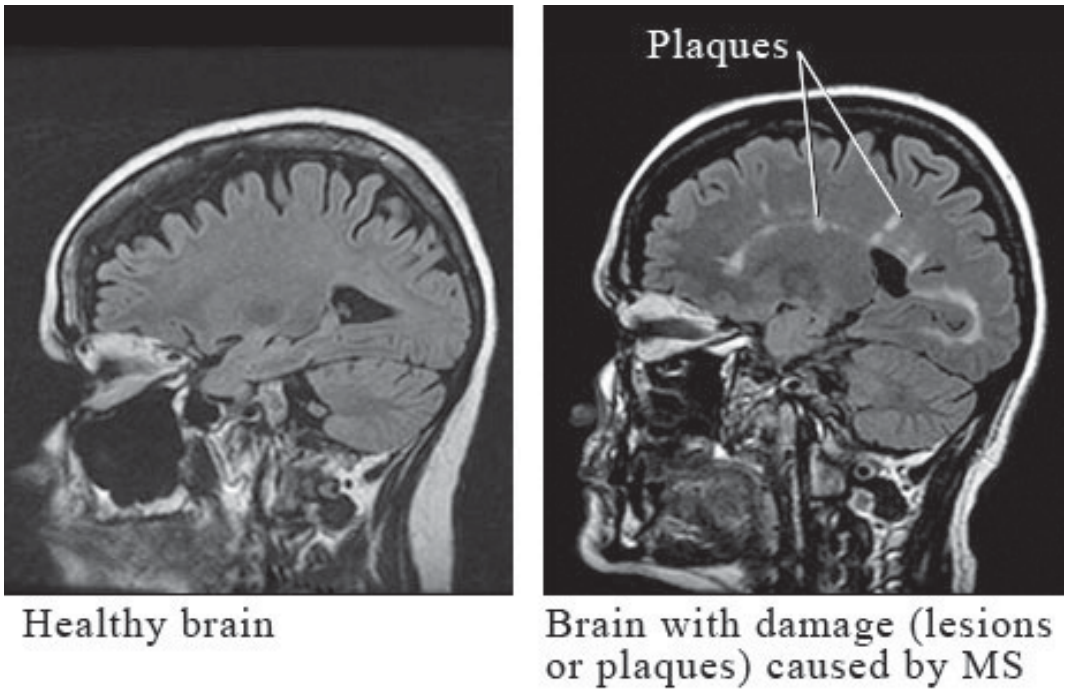


Fig.28.1: MRI of Multiple sclerosis

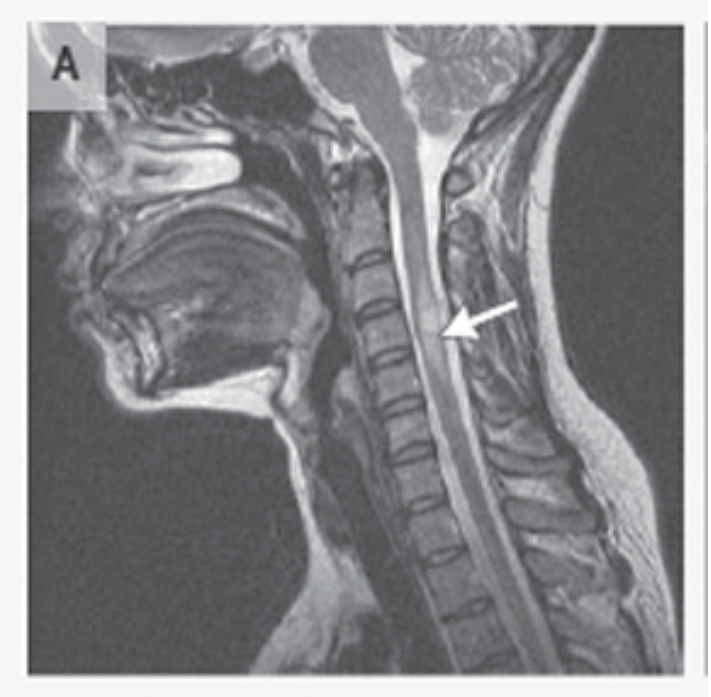


Fig.28.2: MRI of transverse myelitis

may affect primarily motor fibres or primarily sensory fibres or it may be mixed (sensory & motor).

Causes

Toxic - Alcohol, lead toxicity

Infections - Lyme disease, Diphtheria, leprosy, AIDS

Diabetes

Cancer

Medications - Colchicine, ethambutol, chloroquine, amiodarone.

Vasculitis

Signs and symptoms

One should suspect polyneuropathy when a patient has diffuse or multifocal sensory deficit, weakness without hyperreflexia. If the findings are diffuse but had asymmetrical onset, then it may suggest multiple mononeuropathy.

The patient may have distal symmetric stocking-glove distribution of loss of sensation.

Acute neuropathies suggest an autoimmune cause,a toxin,infection or a postinfectious cause

Symmetric distal neuropathies suggests toxic or metabolic

Rash, skin ulcers, and Raynaud's syndrome with polyneuropathy suggest vasculitis.

Weight loss,lymphadenopathy, with polyneuropathy suggests paraneoplastic syndrome.

Investigations

EMG/NCV is a diagnostic tool which gives information about the sensory and motor fibres.

Blood tests- CBC, Electrolytes, Renal profile, Blood sugar, VIT B12,Folate levels,TSH.

Coagulation studies,ProteinC & S, antithrombin III,anticardiolipin antibody and homocystine levels if one suspects vasculitits or hypercoagulable state as a cause of polyneuropathy.

Urine toxicology for heavy metal.

Treatment

1) For neuropathy amitryptiline 25 mg once a day or gabapentin 100 mg tds
2) Rehabilitation - Physiotherapy & Occupational therapy can minimize the disability and pain .

3) Treat the underlying cause - Remove the toxins, correct the nutritional deficiency
4) Vitamin B12, folic acid can be given for neuroprotection.
5) Corticosteroids for acute polyneuropathy.

Summary

The common demyelinating disorders include multiple sclerosis, transverse myelitis and peripheral polyneuropathy. Multiple sclerosis is a progressive disorder and eventually affects the whole body rendering the patient bed ridden. Recent advances in disease modifying agents have somewhat improved the prognosis. MRI of the brain and spine is diagnostic and can be used as a monitoring tool. A multidisciplinary team of specialists from the field of medicine, surgery, rehabilitation and nursing would be required. Family physician serves as an important link between the patient and the members of this team.

29. Infections of CNS

Infection of the central nervous system (CNS) can be viral, bacterial, fungal, or parasitic in origin. Infectious microorganisms most often enter the CNS by direct penetration after trauma or by travelling in the bloodstream.

The common types of infections involving the CNS are described below

1) Meningitis
2) Encephalitis
3) Brain abscess
4) Cerebral malaria

1) MENINGITIS

The protective membranes covering the brain and the spinal cord are called meninges. Infection of the meninges is called meningitis. The infection may occur due to bacteria, virus, fungus or protozoa.

They are classified according to the cause which has been described below.

Causes

1) Bacterial -a) pyogenic & b) tuberculous
2) Viral
3) Fungal
4) Protozoal

Bacterial meningitis

The most common bacteria that cause meningitis is S. pneumoniae and N.meningitidis.They initially colonize the nasopharynx by attaching to nasopharyngeal epithelial cells. Once in the bloodstream, the blood borne bacteria can reach the intraventricular choroid plexus, directly infect choroid plexus epithelial cells, and gain access to the CSF.

Signs & Symptoms

The classic triad of bacterial meningitis consists of the following:

- Fever
- Headache
- Neck stiffness

Other symptoms can include nausea, vomiting, photophobia, sleepiness, confusion, irritability, delirium, and coma.

Risk Factors

Otits media, immunocompromised, trauma, exposure to drugs,recurrent meningoencephalitis or meningitis,history of recent resection of acoustic neuroma, recent injection into subarachnoid space.

Tuberculous Meningitis

Tuberculous meningitis (TBM) develops in 2 steps. Mycobacterium tuberculosis bacilli enter the host by droplet inhalation. Localized infection escalates within the lungs, with dissemination to the regional lymph nodes. In persons who develop TBM, bacilli seed in to the meninges or brain parenchyma.

The second step in the development of TBM is an increase in size of a Rich focus until it ruptures into the subarachnoid space. The location of the expanding tubercle (ie, Rich focus) determines the type of CNS involvement

This can also occur after a primary infection in childhood or as a part of miliary tuberculosis.

Unlike bacterial meningitis Tuberculous meningitis in adults does not develop acutely from hematogenous spread of tuberculous bacilli to the meninges. Rather, millet seed-size (miliary) tubercles form in the parenchyma of the brain during hematogenous dissemination of tubercle bacilli in the course of primary infection. These tubercles enlarge and are usually caseating. The propensity for a caseous lesion to produce meningitis is determined by its proximity to the subarachnoid space and the rate at which fibrous encapsulation develops. Subependymal caseous foci cause meningitis via discharge of bacilli and tuberculous antigens into the subarachnoid space.

Signs & Symptoms

TBM may have an acute presentation. Sometimes it may present with cranial nerve deficits, or it may have a more indolent course involving headache, meningismus, and altered mental status. The prodrome is usually nonspecific; including headache, vomiting, photophobia, and fever also symptoms such as lassitude, depression, papilloedema, occulomotor palsies can also be seen.

Viral meningitis

Viral meningitis is inflammation of the meninges as a manifestation of central nervous system (CNS) infection. Viral meningitis is also often referred to as aseptic meningitis.

In uncomplicated viral meningitis, the clinical course is usually self-limited, with

complete recovery in 7-10 days. However, when the viral pathogen causes meningoencephalitis or meningomyelitis, the course can be significantly more protracted.

Based only on clinical symptoms, viral meningitis cannot be differentiated from bacterial meningitis. Both appear as headache, fever, and neck stiffness but viral meningitis has no evidence of bacterial presence in CSF. However, viral meningitis is less serious than bacterial meningitis. Therefore, CSF analysis is needed to identify the disease. In general, there are no medications to fight the virus that cause meningitis, so treatment is usually aimed at relieving the patient's symptoms by having rest and fever-reducing medication.(IV Acyclovir may be used in few cases.)

Investigations of Meningitis

1) CSF Finding is one of the most important tests which helps us in diagnosing the cause and type of meningitis

   CSF findings-

   a) Pyogenic - presence of polymorphonuclear (PMN) leukocytosis, decreased glucose concentration, increased protein concentration, increased opening pressure.

   b) Tubercolous- increased CSF pressure, it is usually clear but if allowed to stand may form a clot, AFB seen on staining

   c) Viral-Typical profile is lymphocytic pleocytosis, a normal or slightly elevated protein concentration, organisms are not seen on gram or AFB stain.

   d) Fungal-the CSF findings are similar to tuberculous with culture positive for fungal infection

Type of meningitis	Glucose	Protein	Cells
Acute bacterial	low	high	PMNs, often > 300/mm^3
Acute viral	normal	normal or high	mononuclear, < 300/mm^3
Tuberculous	low	high	mononuclear and PMNs, < 300/mm^3 lymphocytosis
Fungal	low	high	< 300/mm^3

2) CT scan

   The CTscan may show Watershed and lacunar infarcts and may show cerebral oedema in patient with bacterial meningitis, also it may show subdural effusion.

   Contrast-enhanced CT scans may also help in detecting complications such as venous thrombosis, infarction, and ventriculitis. Ventriculitis is a complication of bacterial meningitis that is seen commonly in neonates. Ependymal

enhancement can be seen on contrast-enhanced CT scans.

In case of tuberculous meningitis the scan may show hydrocephalus or may show tuberculoma.

3) MRI findings

MRI helps to detect the presence and extent of inflammatory changes in the meninges as well as complications. Noncontrast MRI of patient with uncomplicated acute bacterial meningitis may demonstrate obliterated cisterns and the distention of the subarachnoid space with widening of the interhemispheric fissure, cortical hyperintensities that represent edema.

In complicated cases with seizures and evolving focal signs, MRI is superior to CT in demonstrating parenchymal lesions due to meningoencephalitis or vasculitic complications. MRI helps in diagnosing intraventricular rupture of pyogenic abscess.

4) Blood tests

Complete blood count (CBC) with differential counts

Serum electrolytes

Serum glucose (which is compared with the CSF glucose)

Blood urea nitrogen (BUN) or creatinine and liver profile

Blood culture

Complications

- Hypotension or shock
- Hypoxemia
- Hyponatremia
- Cardiac arrhythmias and ischemia
- Stroke
- Exacerbation of chronic disease

Management of Bacterial Meningitis

Firstly to check the vitals & stabilize the patient,if the patient is dehydrated due to vomiting or the BP is low start him on IV fluids immediately

If you suspect meningitis in the patient the patient has to be referred for hospitalization.

Antibiotics

After CSF testing start on empiric antibiotics

Ceftriaxone-1-2 g BD or 12 hrly or

Cefotaxime- 1-2 g BD or 12 hrly.

Vancomycin - Starts with 0.5-2 g/day maximum is till 500 mg 6 hrly

Gentamicin - starts with 3-5 mg/kg/day in divided doses

Meropenum - starts with 500 mg

Augmentin -1.2 gm

Management Of Tuberculous Meningitis

Standard therapy nowadays includes combination of Rifampicin, isoniazid and pyrazinamide

(rifampicin 120 mg, isoniazid 50 mg and pyrazinamide 300 mg: <40 kg: 3 tab/day; 40-49 kg: 4 tab/day; 50-64 kg: 5 tab/day; 65 kg: 6 tab/day)

Ethambutol dosage is 15-30mg/kg.

Blood tests are to be done such as liver profiling as these medicines are hepatotoxic in nature.Other routine blood tests should also be done like Renal function tests,CBC,Electrolytes.

Compliance to medications is necessary in these conditions.

Also see post infection chronic care at the end of this chapter.

Encephalitis

Encephalitis means infection of the brain parenchyma .The causes are similar to meningitis.Encephalitis presents as diffuse or focal neuropsychological dysfunction.

Sign & Symptoms

Fever,confusion,behavior abnormality,altered level of consciousness,evidence of either focal or diffuse neurological symptoms, Neck pain, stiffness, photophobia, lethargy, flaccid paralysis .

Acute confusion or amnestic states.

Patients may also have hallucination,agitation,personality changes,behavior change,focal or generalized seizures may also occur.

Investigations

1) Blood tests-Complete blood count (CBC),Serum electrolyte levels,Serum glucose level,Blood urea nitrogen (BUN) and creatinine levels

2) Urine electrolyte levels,Urine or serum toxicology screening

   Blood cultures for bacterial pathogens

3) Lumbar puncture-A lumbar puncture (LP) should be performed in all cases of suspected viral encephalitis.

   Examination of the cerebrospinal fluid reveals increased amounts of protein

and white blood cells with normal glucose, though in a significant percentage of patients, the cerebrospinal fluid may be normal.

Bleeding is also uncommon except in patients with herpes simplex type 1 encephalitis.

4) CT SCAN

CT scan without contrast reveals marked hypodensity representing edema within the frontal and temporal lobes with sparing of the basal ganglia and cerebellum. The findings are typical of herpes encephalitis.

5) MRI scan

MRI offers better resolution in patients with herpes simplex encephalitis.

Characteristic MRI findings in viral encephalitis - FLAIR sequence shows bilateral thalamic, globus pallidus and caudate involvement, bilateral midbrain involvement

6) EEG- electroencephalograph may show sharp waves in one or both of the temporal lobes.

Management

To refer the patient to neurology department for hospitalization

Specific treatment to be started according to the cause

Supportive management-Stabilize the patient by checking the vitals like blood pressure, SPO2,pulse,HGT and accordingly giving O2,IV fluids ,antihypertensives and immediate shifting of the patient for hospitalization.

IV acyclovir dose-

Adult: 10 mg/kg every 8 hr for 10 days.

Child: 3 months: 20 mg/kg every 8 hr for 10 days

Also see post infection chronic care at the end of this chapter.

Brain Abscess

Brain abscesses are uncommon, serious, life-threatening infections. Brain abscess is Focal suppurative lesion in brain parenchyma.

Brain abscesses can originate from infection of contiguous structures (eg, otitis media, dental infection, mastoiditis, sinusitis) secondary to hematogenous spread from a remote site (especially in patients with cyanotic congenital heart disease), after skull trauma or surgery

Signs & Symptoms

The clinical presentation depends upon its location.

More than an infectious process this presents as expanding intracranial lesion.It presents with headache which is of dull, constant character either hemicranial or generalized and is progressive in nature.Headache may be associated with nausea and projectile vomiting .

There may be focal or generalized seizure,focal neurological deficit including hemiparesis,aphasia or visual field defects.

Signs of raised intracranial pressure may be seen-Change in mental state and Papilloedema.

Investigations

1) MRI

   MRI scan in an abscess patient will show a mass effect with surrounding edema.

   Gadolinium-enhanced coronal T1-weighted MRI in a patient also shows the midline shift by the abscess.

   On T1 contrast-enhanced MRI the abscess may be seen as an irregular mass with moderate peripheral enhancement.

2) CT scan

   Brain abscess will appear as an ill-defined hypodensity on non-contrast CT scan. They are frequently ring-enhanced with the addition of intravenous contrast.

   The CT scan will show the cerebral oedema and also it will show the thickness of cerebral abscess wall.

3) Lumbar puncture-LP should not be performed in patients with known or suspected intracranial infections,since it increases the risk of herniation.

4) Blood profile- Complete blood count, Serum electrolytes

   Serum glucose, Blood urea nitrogen (BUN) and creatinine and liver profile.

Management

Treatment involves high dose parenteral antibiotics & neurosurgical drainage.

Third generation cephalosporins such as cefotaxime & ceftriaxone are being used.Meropenum & vancomycin are also being used.

Dosages- Cefotaxime- 1-2 g 4-12 hrly

Vancomycin - Starts with 0.5-2 g/day maximum is till 500 mg 6 hrly

Gentamicin - starts with 3-5 mg/kg/day in divided doses

Meropenum - starts with 500 mg

Augmentin -1.2 gms

Also see post infection chronic care at the end of this chapter.

Cerebral Malaria

Cerebral malaria refers to a life threatening infection of the cerebrum caused by protozoa plasmodium falciparum.

The earliest manifestation is nonspecific fever. Loss of appetite, vomiting and cough are common. The history of symptoms preceding coma may be as brief as one to two days.

The primary symptoms which are seen in Cerebral Malaria are:

(a) Impaired consciousness with non-specific fever.

(b) Generalised convulsion and neurological sequelae and

(c) Coma, initially arousable which becomes unarousable later.

Cerebral malaria manifests as diffuse symmetric encephalopathy accompanied by focal neurologic signs. Some passive resistance to head flexion may be detected.

Examination

In cerebral malaria the tendon reflexes are variable, and the plantar reflexes may be flexor or extensor; the abdominal reflexes are absent. Flexor or extensor posturing may be documented.Patients are seen to have retinal hemorrhages with pupillary dilatation.

Funduscopic abnormalities include discrete spots of retinal opacification, papilledema, cotton wool spots, and decolorization of a retinal vessel or segment of vessel (occasional cases).

Convulsions may be generalized and often repeated, commonly seen in children. History and clinical findings of convulsion, coma and altered sensorium are important.

Investigations

1) Blood tests -These include CBC,creatinine,Liver profile,electrolyte,bleeding time clotting time,PT,INR,BUN, also blood tests for malarial parasite,malarial antigen,blood culture.

2) Peripheral smear: Asexual form of P. falciparum is seen in peripheral blood smear, in thick and thin blood smear films stained by Giemsa stain. In some patients with prior antimalarial treatment or sequestration of parasitized RBCs in cerebral circulation, peripheral smear may not show any parasites. In such a situation, atleast 3 smears 6 h apart should be examined. At least 3 smears should be negative before excluding cerebral malaria.

3) The rapid diagnostic test (antigen detection test) and PCR may be helpful.

4) CSF examination is necessary to exclude other causes of febrile encephalopathy. CSF is generally normal in cerebral malaria, however, mild pleocytosis (10-50 cells/mm3) and protein rise up to 200 mg/dL may be seen.

5) CT and MRI are usually normal or show edema and cortical or subcortical infarcts in watershed zone in 15%-20% patients.

6) EEG shows nonspecific abnormalities, such as diffuse slowing, spike wave discharges, and burst suppression pattern.

Management

Cerebral malaria is a serious condition. If cerebral malaria is suspected admit the patient in a hospital immediately. Stabilize the patient and transfer the patient to a hospital.

In hospital management

1) Antimalarial therapy
2) Fluids and nutrition
3) Treatment of seizures
4) Respiratory status
5) Anaemia
6) Coagulopathy

Following are the dosages of antimalarials-

1) IV Chloroquine - initial dose 10mg/kg over a period of not less than 8 hours, preferable by slow intravenous infusion, Subsequent infusions of 5mg/kg should be administered every 8 hours until a total dose of 25mg/kg is given.

2) Artemether- adults and children over 6 months 3.2 mg/kg as a loading dose by Intrmuscular injection, followed by 1.6 mg/kg daily until the patient is able to tolerate oral medications for a maximum of 7 days.

3) Artesunate- A loading dose of 2mg/kg should be followed by 1mg/kg after 4 hours and 24 hours,thereafter a dose of 1mg/kg should be given daily until the patient is able to tolerate oral medications for a maximum of 7 days.

IV quinine is also used but it is associated with lot of side effects.

Supportive & Adjunctive Therapy:

- Comatose patient should be given meticulous nursing care.
- A Nasogastric tube should be inserted to aspirate the stomach contents
- Urethral catheter to be inserted and attached to a urobag which will measure output

  Fluid intake and output chart should be maintained.

  Level of coma should be monitored along with temperature, respiratory rate and depth, blood pressure and vital signs.
- Antipyretics - Paracetamol is effective in reducing fever.

- Anticonvulsants - It is crucial to control or prevent seizure, as they can cause neural damage and are associated with a fatal outcome. A slow Intravenous dose of 0.15mg /kg of Diazepam is effective in controlling convulsion and it can be repeated if required.
- Reduction of Intracranial Pressure - Raised ICP can cause death by transtentorial herniation or by compromising cerebral blood flow. Mannitol is used to reduce cerebral edema.
- Correction of Hypoglycaemia - This can be done by using hypertonic glucose.
- Anemia should be treated with blood transfusion.
- Acidosis - Correction of anaemia, dehydration and control of seizures reduces acidosis.
- Thrombocytopenia needs to be monitored and corrected.

  Exchange transfusion is justified when parasitemia exceeds 10% of circulating RBCs.

  Microcirculatory Flow - Pentoxifylline reduces red cell deformability, blood viscosity, systemic vascular resistance and platelet aggregation which improve microcirculatory flow.
- Desferroxamine - An iron chelator which reduces formation of reactive oxygen by reducing amount of free iron.

Post Infection Chronic Care

1) Tuberculosis- To monitor whether the patient is taking his medications regularly especially the AKT.
2) Compliance & monitoring for side effects is an important task of the physician
3) Improve the nutrition-which includes High protein diet with dietary advice is very important. Also multivitamins should be given as it may give extra nutrition which may be skipped from diet.
4) Rehabilitation- Physical and occupational therapy to improve weakness.
5) Post surgical care in case of surgery for eg- In Case of abscess, the wound needs to be checked for pus.

In bed ridden patients skin care, DVT prophylaxis needs to be monitored to prevent DVT, bedsores, also the ryle's tube,catheter tracheostomy care needs to be taken care of.

Summary

CNS infections are serious conditions which require hospitalization. Early diagnosis and treatment will prevent complications. The common CNS infections encountered are meningitis, abscess and cerebral malaria. Tuberculous meningitis needs long term treatment. Therefore, compliance to treatment needs to be monitored.

30. Neuromuscular Disorders

The brain controls the movements of skeletal (voluntary) muscles via specialised nerves. The combination of the nervous system and muscles, working together to permit movement, is known as the neuromuscular system. There are many separate diseases that are classified as neuromuscular disorders.

Some of the major diseases affecting the neuromuscular system are classified into three groups:

A. Disorders affecting primarily the muscles

1. Muscular dystrophies
2. Inflammatory myopathies
3. Toxic myopathy

B. Disorders affecting primarily the nerves

1. Motor neuron disease
2. Spinal muscle atrophy
3. Poliomyelitis
4. Guillian Barre syndrome

C. Disorders affecting primarily the neuromuscular junction

1. Myaesthenia gravis

Muscular Dystrophies

Muscular dystrophy is characterized by progressive muscle degeneration causing muscle weakness. Muscle degeneration occurs due to disruption of the cell wall of muscle cell. It is caused by a genetic abnormality that leads to faulty production or absence of the proteins essential for the structural integrity of the cell wall. Subnormal functioning of these walls therefore makes those more prone to damage even with forces of day to day muscle contraction. This leads to accelerated damage of the tissue which cannot be repaired by existing cells. As the difference between number of damaged cells and number of cells available for repair increases muscles grow weaker and weaker.

Various investigations are recommended for the diagnosis of muscular dystrophy.

Diagnosis of muscular dystrophy can be confirmed using following steps:

Diagnosis

Points to note from the history of the patient:

- History of progressive muscle weakness in the patient
- Weakness progressing in different regions of the body like UEs, LEs and Trunk
- History of progressive functional deficits
- History of consanguinity of parents
- Strong family history

Assessment and evaluation

- Manual muscle testing shows weakness of the muscles, the pattern of weakness changes as per the type of muscular dystrophy
- Tendon jerks are usually diminished or in early stage of the disease will be normal
- Tone of the muscles is normal however sometimes you may find hypotonia
- Posture and gait assessment will show compensatory mechanisms like increased lumbar lordosis, waddling and toe walking etc.
- Easy fatigability will be observed during assessment
- Some dyspnoea may be present depending on the involvement of cardiac and respiratory systems

Investigations

- Blood serum testing will show increased serum CPK levels
- Muscle biopsy will show histopathological changes in the muscles and soft tissues
- Electromyography - EMG shows difference in the muscle unit potentials of dystrophic muscles. It shows features of primary muscle disease.
- Musculoskeletal MRI -It possesses diagnostic capabilities similar to muscle biopsy and may be preferred over EMG and Biopsy due to its non-invasive nature. It may show muscle degeneration, necrosis and fibrosis.
- Genetic testing - Genetic testing is the gold standard test for confirming the type of muscular dystrophy. Patients should be encouraged to undergo genetic testing as well as counseling.

Common types of muscular dystrophies

Duchenne Muscular Dystrophy (DMD), Becker's Muscular Dystrophy (BMD) and

Limb Girdle muscular dystrophy (LGMD). The less common forms are FacioScapulo Humeral dystrophy (FSHD), Congenital muscular dystrophy (CMD), Myotonic muscular dystrophy, Occulopharyngeal muscular dystrophy, distal muscular dystrophy, Emery Dreiufuss muscular dystrophy.

1. **Duchenne muscular dystrophy** : This is the most common and the most severe type of muscular dystrophy with rapid progression of muscle weakness. This affects young boys only. It is an X- linked recessive disorder, which results in an absence of dystrophin. Deficiency of dystrophin leads to degeneration of the muscle fibers with resultant muscle weakness. The first symptoms are decreased motor skills, clumsy walking, calf pseudohypertrophy, lumbar lordosis. Hip extensions are often the first muscle group affected.

   Gower's maneuver positive - Gower's sign is when the patient makes use of his hands to climb up on his body while getting up from the floor. Frequent falls while walking, running or jumping, easy fatiguability, difficulty climbing stairs, poor balance, waddling gait, toe walking, etc.

   The patients gradually lose independent ambulation and are wheelchair bound and become bedridden later, owing to the resultant spinal deformity. Symptoms start by the age of 7 years and they become wheelchair bound by the age of 10-12 years. Later on cardiorespiratory complications develop which lead to early mortality by the age of 22 years.

2. **Becker muscular dystrophy:** It is an X linked recessive disorder involving genetic mutation which leads to abnormal dystrophin protein production (not completely absent dystrophin as in DMD). The disease progresses in the same stages as DMD. The muscle weakness, postural and structural deviations and compensations remain identical. The functional loss is also same as observed in DMD. However the rate of progression of the disease is much slower. The life expectancy is much more that in DMD.

3. **Limb girdle muscular dystrophy:** Limb Girdle muscular dystrophy (LGMD) is one of the slow progressive muscular dystrophies, where the muscles of the hip and shoulder region are involved earlier than other muscles. Slowly the muscles undergo thinning causing severe weakness in other parts of the body as well. The patient has difficulty in getting up from the floor without support, climbing up the stairs, walking, lifting arms, overhead activities and poor balance with frequent falls.

4. **Facioscapulohumeral dystrophy:** As the name suggests the disease affects the muscles of arms, shoulder, neck and face. In the later stages of the disease other muscles may also get involved and severely limit the function. The patient has asymmetric facial muscle weakness (eyelid drooping, inability to whistle, decreased facial expression), asymmetric shoulder muscle weakness, inability to chew and swallow, speak, difficulty breathing, etc.

5. **Myotonic muscular dystrophy:** The characteristic of the disease is Myotonia, which means delayed relaxation of the muscle after voluntary action or prolonged contraction. Along with myotonia and muscle weakness it presents with cataract, heart conduction defects, hormonal variations and mental retardation.
6. **Congenital muscular dystrophy:** It presents with muscle weakness at birth or during infancy. Children typically appear "floppy" due to low muscle tone and lack of spontaneous movement. Although muscle weakness can stabilize short term, it progresses with time. This leads to rigidity of spine, contractures and spinal deformities. In later stage respiratory complications may arise. These affect quality of life and life span.
7. **Emery-Dreifuss Muscular Dystrophy:** One of the characteristic features of the disease is involvement of the cardiovascular system by the third decade of life leading to cardiomyopathy along with generalized muscle weakness.

Management

The management of muscular dystrophy is multidisciplinary.

Medical management:

Muscular dystrophy is medically incurable at the moment. Various medicines and newer drugs are under investigation but none have given a conclusive finding.

Medical management aims to:

1) Completely halt or slow down the disease progression
2) Lengthen the period of independent walking
3) Symptomatic improvements
4) Functional improvements to ease activities of daily living
5) Prevent complications of contractures and deformities
6) Preserve cardio-respiratory functions

Gold standard medical therapy at the moment is steroid therapy

Corticosteroids and glucocorticoids are routinely used in the treatment of muscular dystrophy. Although it is not a mainstay of treatment in India, it is integral in the management of muscular dystrophies in western countries. However there are side effects of steroids which must be monitored.

Side effects of steroids: Weight gain, Behavioral changes- irritability, hyperactivity, euphoria, mood lability (mood swings), depression,Excessive hair growth,Growth failure with short stature, Cushingoid appearance- swollen puffy face,Acne,Hypertension,Hyperglycemia/ glycosuria,Hypokalemia (low potassium), stress ulcers, Cataracts, Osteoporosis- fractures

Rehabilitative management:

Due to the progressive and incurable nature of the disease, rehabilitation is the crux of the management of dystrophies. Clinicians must emphasize benefits of rehabilitation.

Rehabilitative management includes various disciplines like physiotherapy, aquatic therapy, occupational therapy, speech therapy, Diet and nutrition and psychological intervention. All these are equally important and the requirement may differ depending upon how advanced the disease is.

Physiotherapy - The aim of physiotherapy treatment is to prevent secondary musculoskeletal complications, training the muscles at a moderate intensity to slow down the process of fibrosis and muscle degeneration, to facilitate functional independence and to prevent secondary cardio-respiratory impairment.

Stretching and exercises are the key components of physiotherapy for muscular dystrophy. Physiotherapists will prescribe tailored exercises to all the patients and may prescribe assistive devices like knee and ankle braces, close contact braces to facilitate standing, walking and prevent scoliosis.

Aquatic therapy - The aim aquatic therapy is same as that of physiotherapy but with more emphasis on the cardio-respiratory endurance of the patients. Aquatic therapy refers to performing exercises in the water with a trained therapist. Exercises are tailor made according to the abilities of the patient.

Occupational Therapy - Occupational therapy aims to maintain the function of the patients and provide assistive devices or alternate techniques for activities of daily living and vocational activities.

Occupational therapists will also provide assistive devices that are key in improving independence in daily activities.

Speech therapy - Patients with muscular dystrophy may present with hypertrophy of tongue and in later stages dysarthria and dysphagia due to muscle weakness. Speech therapists will address these impairments and prevent further complications like aspiration and recurrent respiratory infections.

Diet and nutrition management - Due to lack of activity and sluggishness of bowel movements children and adults with muscular dystrophy may develop nutritional deficits and reduced intake. A proper diet and nutrition advice and timely monitoring and assessments are therefore key in their management.

Psychological counseling - Psychological counseling is required not only for the patients but also for the care givers. Patients develop negative emotional and behavioral problems as the disease progresses and need to taught and made aware of the strategies for the management of these. Some common psychological problems are emotional sensitivity, anger management, depression, anxiety, temper tantrums and learned helplessness. Care givers should also be made aware as to how to deal with such problems.

Surgical management :

Due to progressive muscle weakness and imbalance, children develop contractures of the muscles, and skeletal deformities.

Surgical corrections may be required for these deformities. Surgical corrections are mainly of three types tendon release surgeries to prevent contractures of the muscles , bony corrections in case of fixed contracture and scoliosis prevention surgeries and spinal fixation.

Surgical intervention is decided based on the functional improvement that the patient will gain after surgery and the severity of secondary complications that may develop in absence of surgical management.

Genetic Counselling:

Once diagnosed the patients should be sent for genetic counseling, wherein the nature, prognosis of the disease and possibilities and patterns of inheritance will be discussed with the patient. They will also be given further information about the management of the disease and prevention in subsequent generations.

Inflammatory Myopathy

These are autoimmune diseases in which the skeletal muscles are damaged by an inflammatory immune mechanism.

1) **Polymyositis -** Polymyositis is an idiopathic inflammatory myopathy that causes symmetrical, proximal muscle weakness; elevated skeletal muscle enzyme levels. Myalgias, arthralgias and dysphagia may also be associated. The patient has difficulty kneeling, climbing or descending stairs, raising arms, lifting objects, combing hair, holding the head up. Pelvic girdle involvement is usually greater than upper body involvement. Cardiac involvement may cause symptoms of pericarditis or cardiomyopathy.

Signs and symptoms:

- Fatigue
- Anorexia
- Morning stiffness
- Fever (associated with antisynthetase antibodies such as anti-Jo-1)
- eight loss
- On examination - muscle tenderness and nodular feel on palpation

2) **Dermatomyositis -** this myositis is associated with erythematous skin changes over extensor surfaces of the joints and a facial rash. The muscle weakness is similar to polymyositis

3) **Inclusion body myositis -** this type of myositis is seen after the age of 50 years and it involves the fingers, forearm flexors and leg extensors.Muscle biopsy shows inflammatory infiltrates,with characteristic rimmed inclusion vacuoles & amyloid deposits.

Fig. 30.1 :

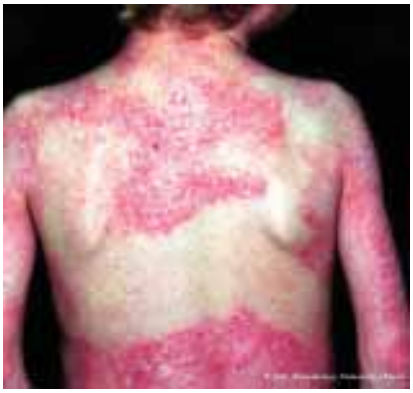


Fig. 30.2 : Dermatomyositis

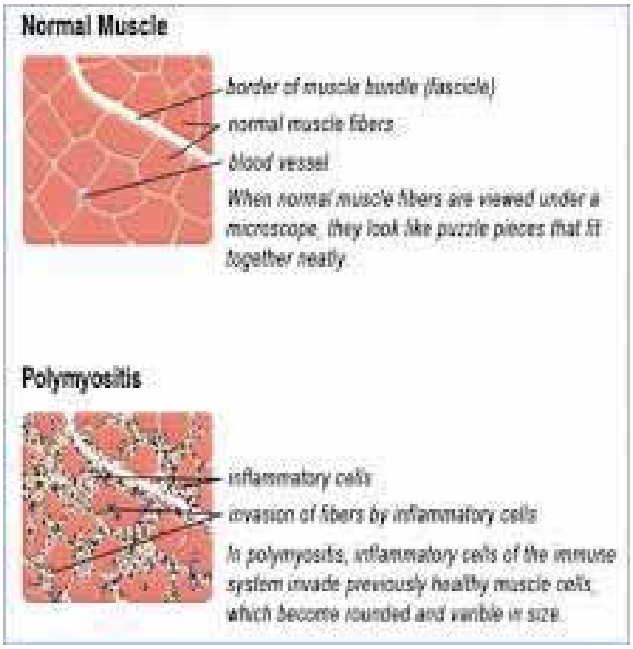


Fig. 30.3 : Muscle biopsy

Investigations

- Complete blood count (CBC) - May show leukocytosis or thrombocytosis; leukocytosis is present in more than 50% of patients
- Erythrocyte sedimentation rate or C-reactive protein level - Elevated in 50% of patients with polymyositis
- Elevated muscle enzyme levels
- Myoglobinuria
- Autoantibodies - Antinuclear antibody assay - Positive in polymyositis; Myositis-specific antibodies; anti-Jo-1 antibodies in polymyositis
- Positive rheumatoid factor results
- MRI scan: shows signal intensity abnormalities of muscle due to inflammation, edema, or scarring.
- Electromyography: It may show evidence of membrane irritability, increased insertional activity, fibrillation potentials, positive sharp waves at rest. The EMG may show a typical myopathic picture - decreased amplitude and duration; increased polyphasic potentials. Chronic changes such as evidence of denervation-reinnervation may also be seen.
- Muscle biopsy: It shows muscle fiber inflammation with focal endomysial infiltration by mononuclear cells, endothelial cell damage, and increased amounts of connective tissue. Later in the course of polymyositis it may show muscle fiber degeneration, fibrosis, and regeneration.

Treatment

Corticosteroids

Prednisone is the first-line treatment of choice for polymyositis.

Dosage 1 mg/kg/day, either as a single or divided dose. This high dose is continued for 4-8 weeks, until the creatine kinase level returns to normal. Taper the dose by 5-10 mg on a monthly basis until the lowest effective dose.

Immunosuppressants

Intravenous immunoglobulin (IVIG) is used for the short-term treatment of steroid-resistant cases of polymyositis.

Diet

Patients with polymyositis may benefit from a high-protein diet. Monitor patients to avoid excessive weight gain due to corticosteroid use.

Activity

Encourage patients to start an exercise program as early as possible. During the acute stage, passive range of motion exercises and splints are given to avoid contractures.

Once acute inflammation is under control, the rehabilitation program is started.

Toxic Myopathy

Major common causes are-

1) Steroid myopathy
2) Statin induced myopathy

These medicines are commonly encountered by a family physician. Any patient who is already on steroids or statins; develops muscular weakness which is non specific, generalized, and recent onset should raise a suspicion for side effect of this medicine. Statin should be held for few weeks and if the weakness reverses it is diagnostic. In case of steroids, one should taper the dose in consultation with a specialist physician.

Management

If detected early and if the medications are stopped, weakness may be reversed.

Motor Neuron Disease

Motor neuron disease (MND) is a neuromuscular disease caused due to selective degeneration of the motor neurons. The degeneration is progressively noted in the upper motor neuron (cortex) or lower motor neurons (Medulla and anterior horn cells) or both. It is characterized by progressive degeneration of neurons causing progressive muscle weakness. The cause is unknown. There are various types of MND, based on region affected, rate of progression of the disease and UMN or LMN involvement. The prognosis of each type differs significantly.

Types of Motor Neuron Disease

Type of Motor Neuron Disease	UMN Degeneration	LMN Degeneration
1. Amyotrophic lateral sclerosis (ALS)	Present	Present
2. Primary lateral sclerosis (PLS)	Present	Absent
3. Progressive bulbar palsy (PBP)	Absent	Present only in the bulbar region
4. Progressive spinal muscular atrophy (PMA)	Absent	Present

1. Amyotrophic lateral sclerosis:

ALS is the most common variant of MND. Disease manifests due to both UMN and LMN degeneration.

Symptoms are of UMN type like progressive muscle weakness, brisk reflexes, increased tone of the muscles, cramps, and LMN type like wasting, fasciculations, hypotonia, severe weakness in different regions of the body. There are two types- a) limb onset where the weakness begins in the upper limb or lower limb, b) bulbar onset where there is difficulty in speech, swallow and breathing at the onset.

The prognosis of this condition is the worst with life expectancy of up to 3 - 5 years from diagnosis. The weakness progresses all over the body and the patient becomes bed ridden and will need ventilator support.

2. Primary lateral sclerosis:

PLS is a relatively uncommon variant of MND. It manifests mainly in the form of UMN degeneration.

The symptoms are mainly the UMN signs in limb and bulbar region but with lesser wasting and weakness of the limbs as compared to ALS. The progression of the disease is slower than in ALS and the prognosis and life expectancy is more (6-7 years).

3. Progressive bulbar palsy:

Progressive bulbar palsy is also a rare variant of MND. It is caused by degeneration of lower motor neurons in bulbar region. It may develop into a bulbar onset ALS.

Symptoms include dysarthria (difficulty or slurring of speech) , dysphagia (difficulty or slowness of swallowing and chewing food), breathing difficulty, exertion dyspnoea and orthopnoea.

4. Progressive spinal muscular atrophy:

Progressive spinal muscular atrophy is also a rare variant of MND.

The progression is relatively slower and mainly exhibits lower motor neuron symptoms.

Diagnosis:

Diagnosis of MND is a diagnosis of exclusion.

There are set criteria, Revised Eorld federation of neurology El-escorial criteria for the diagnosis of Amyotrphic Lateral Sclerosis as this is the most common type of motor neuron disease. However the other types are differentiated and diagnosed using clinical features, physical assessment and electromyography.

ALS category	Requirements
Definite	UMN and LMN signs in 3 regions of the body
Definite Familial	UMN and LMN signs in 3 regions of the body and confirmed genetic involvement
Probable	UMN and LMN signs in two regions of the body
Probable (Lab supported)	LMN and UMN signs in 1 region of the body and evidence of acute denervation in 2 muscles of 2 limbs
Possible	UMN and LMN signs in only 1 region of the body

Investigations

1. Electromyography is the gold standard in the diagnosis of MND which shows anterior horn cell involvement.
2. MRI brain and spine screening: It helps to exclude any focal spinal or cerebral disease. MRI report will be normal in MND.
3. PET CT scan: It is done in patients where paraneoplastic syndrome is suspected. It rules out presence of malignancies anywhere in the body. PET CT scan will be normal in MND.
4. Lumbar puncture: It is done to rule out any other causes of muscular weakness. CSF study will be normal in MND.
5. Blood tests: Routine and heavy metal screening. Blood tests will be normal in MND.
6. Genetic testing: SOD1 gene abnormality may be detected.

Management

As the disease manifests in multiple body systems over a long period of time and affects quality of life of the patient, multidisciplinary management is the best approach.

Pharmacological management

1. Riluzole is the only approved medicine that has shown significant effect on the survival duration. Riluzole inhibits the glutamate release and modulates some of the post synaptic effects of glutamate. Dosage: 50 mg bd. Side effects: nausea, vomiting, vertigo, liver dysfunction, renal dysfunction, anemia. Monitoring: Monitor hemoglobin, LFT and serum creatinine levels.
2. Neuroprotective drugs: CoQ10, vitamin B12, Vitamins C, E, omega3 fatty acids. For details refer to Section E.
3. Antispastic drugs and muscle relaxants may be required for muscle spasticity and muscle cramps. Refer to Section E for more details.

Non Pharmacological management

Exercise: Regular moderate intensity physical exercise has several benefits in MND. It prevents rapid damage to the muscles and functional deterioration. Exercise also has an anti-inflammatory effect. Exercise also helps prolong respiratory insufficiency, dysphagia and dysarthria.

Multidisciplinary rehabilitation for MND consists of following disciplines:

1. Neurorehabilitation: Physiotherapy, Occupational Therapy, Speech therapy, Psychological counseling, Aquatic therapy
2. Diet and nutrition: High protein diet is recommended. In patients where swallowing is affected, dietitian and swallow therapist should be consulted to modify the diet consistency, regularity, food items, etc. Some patients may require nutritional supplements.
3. In late stages PEG (Percutaneous endoscopic gastrotomy) may be required. PEG is a surgical technique that has shown significant effect of the survival in MND by preventing dysphagia related complications. Refer to gastroenterologist for PEG.
4. Respiratory management: Artificial ventilator support in the later stages of the disease which has significantly prolonged the survival of MND patients. Chest physician should be involved in the care of MND patient to assess requirement for non invasive ventilation for eg. Bipap machine, etc.

Spinal Muscle Atrophy

The spinal muscular atrophies (SMAs) comprise a group of autosomal-recessive disorders which involve progressive weakness of the lower motor neurons.

Different types of spinal muscular atrophies have been described based on age of onset. The most common types are acute infantile (SMA type I, or Werdnig-Hoffman disease, present before 6 months of age), chronic infantile (SMA type II, present between the ages of 6 and 18 months), chronic juvenile (SMA type III or Kugelberg-Welander disease, appears after age 18 months), and adult onset (SMA type IV, Onset is typically in the mid 30s) forms.

The genetic defects associated with SMA types I-III are localized on chromosome 5q11.

Patients with spinal muscular atrophy present with weakness and muscle wasting in the limbs, respiratory, and bulbar or brainstem muscles. LMN signs are present i.e. decreased tone, diminished reflexes, atrophy. Patients with spinal muscular atrophy often have above-average intelligence quotients (IQs) and demonstrate high degrees of intelligence.

Investigations:

1. EMG and NCV: They are diagnostic and show anterior horn cells involvement.

2 MRI brain and spine are normal.

3. CSF study is normal.

4. Serum CPK level may be normal or slightly elevated.

5. Blood tests: Routine and heavy metal screening is normal.

6. Genetic testing reveals SMN1 gene abnormality.

Management:

Supportive treatment should be aimed at improving the patients' quality of life and minimizing disability, particularly in patients with slow progression. Refer to MND management.

Poliomyelitis

A viral infection which, at its worst destroys the anterior horn cells in the spinal cord and brain stem motor nuclei, causing paralysis. The disease can be mild, severely disabling, or fatal. A feature of polio is that normal sensation accompanies the muscle weakness. For details refer to Section A.

Guillain Barre Syndrome

Here the complaints begin with respiratory or gastric illness and progressive muscle weakness from hours to days.It involves limbs & may be associated with tingling,numbness in the arms.

On examination

Complaints start with progressive weakness of 2 or more limbs with neuropathy & areflexia

Types

Ascending-Weakness starts with lower limb & then progresses upwards to the trunk,upper limb,respiratory muscles.

Descending-Weakness will start in the cranial nerves or upper limb or bulbar muscles & then progress downwards involving the respiratory muscles.

Investigations

1. CSF-High protein without pleocytosis. CSF may be normal in early hours

2. GBS antibody (GM1)

3. Blood tests like electrolytes,LFT,CPK,ESR

4. EMG/NCV

5. PFT

Management

If you suspect GBS immediately hospitalize the patient. ICU management will be required in case of respiratory failure.

Immunoglobulins, corticosteroids, plasmapheresis will be needed.

Chronic care and Rehabilitation.

Myasthenia Gravis

It is a condition which is characterized by progressive weakness of facial,bulbar,neck,and ocular muscles.This occurs due to production of antibodies to the acetylcholine receptors on the post synaptic junction membrane, which block conduction across the neuromuscular junction. Myasthenia symptoms can be improved by inhibiting the acetylcholinesterase which normally removes the acetylcholine.

Here the patient may initially have ptosis, diplopia, weakness,fatigue which becomes worse by repeated activity and which is improved by rest.Also there may be difficulty in chewing,swallowing,breathing; combing hair, raising the arms above shoulder level. . Limb weakness is more in proximal muscles than distal muscles. There are no sensory nerve involvement, and the disorder is purely motor.

Bulbar muscle weakness is also common, along with weakness of head extension and flexion. Aspiration may occur if the cough is ineffective. Patients progress from mild to more severe disease over weeks to months. Weakness tends to spread from the ocular to facial to bulbar muscles and then to truncal and limb muscles. Exposure to bright sunlight, surgery, immunization, emotional stress, menstruation, and physical factors might trigger or worsen exacerbations. The symptoms can be quickly precipitated by various factors which is called 'myaesthenic crisis' and is a medical emergency.

Investigations:

Laboratory testing includes Anti-AChR radioimmunoassay-85% positive in generalized MG, 50% in ocular MG.

Anti musk antibody, anti striated muscle antibody

Single -fiber electromyography-blocking & jitter with normal fiber.

For ocular or cranial MG- exclude intracranial lesions by CT OR MRI.

Other tests for RA Factor & ANA & TSH to rule out other diseases.

D/D

Lambert syndrome (LEMS): Muscle weakness is similar to myasthenia but is associated with tumors. It can be differentiated from myasthenia by EMG findings.

Treatment

Pharmacology:

1. Anticholinesterase inhibitors - Pyridostigmine is used for long-term maintenance.
2. Immunosuppressants: Corticosteroids,
3. Immunomodulators: Immunoglobulin, azathioprine, cyclosporine
4. Plasmapheresis

Non pharmacology:

Chronic care is required for long term.
Rehabilitation is very important.
Diet advice is required if any difficulty in chewing.
Yoga helps in improving breathing capacity.

31. Neurodevelopmental Disorders

Any perinatal event (before,during,after the time of birth) could cause damage to the brain .This could lead to mental as well as physical disabilities.These group of disorders are known as neurodevelopmental disorders. These are sometimes noticed immediately after birth or later in early childhood as the parents notice that the child is not reaching the expected/appropriate milestones.

Neurodevelopmental disorders are a broad spectrum or an umbrella,which covers multiple conditions.Broadly,they can be divided as :

A) Cerebral palsy

B) Mental Retardation/Intellectual disability

C) Autism Spectrum disorders

D) Others; would include,genetic disorders,such as Downs syndrome,learning disability,ADHD,Slow learners

Symptoms

These disorders have a diverse clinical picture.Signs and symptoms vary depending on the type and severity of brain damage.However, a simple guideline or yard stick could be comparison with a normal/neurotypical child of the same age.

1. Motor milestones such as neck holding,sitting,standing and walking, either delayed or not achieved.child is either floppy,or very tight(spastic) or has uncontrolled movements(dystonia/choreoathetoid movements)
2. Speech delay :child not able to speak or can speak few words.This could also be accompanied with swallowing,chewing difficulties(oromotor dysfunction)
3. Not responding to being called or not tracking toys or light(hearing and vision defect,as comorbidities)
4. Cognitive impairment: has difficulty in understanding or learning new activities

Causes

Causes can be divided broadly into when the event has occurred:

a) Prenatal(before birth):

Abnormal development of the brain is seen if the mother has infections (TORCH) WHICH GETS TRANSMITTED INTRAUTERINE,NUTRITIONAL DEFICIENCY IN MOTHER,CONSUMPTION OF medicines/teratogens or hypoxia just before birth(cord around neck,meconium aspiration,prolonged labour) or genetic mutations.

b) Natal(at birth):

Prematurity,low birth weight,delayed cry (indicating hypoxia or lack of oxygen),multiple births(twins,triplets,etc),septicemia in mother or placental tissue/umbilical cord,injury at birth (such as which may happen during forceps/ suction assisted delivery)

c) Postnatal (after birth):

Birth asphyxia (lack of oxygen0 due to physical trauma,respiratory or cardiac disorders, pathological jaundice,seizures/epilepsy,or morphological abnormalities, such as hydrocephalous 9if uncorrected)

d) Early childhood;

Trauma to the head and brain, infections such as meningitis/encephalitis,seizures/ epilepsy

e) No obvious cause; sometimes, no cause can be identified

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B) Mental Retardation/Intellectual disability

C) Autism Spectrum disorders

D) Others; this would include,genetic disorders,such as Downs syndrome,learning disability,ADHD,Slow learners

Cerebral Palsy:

Cerebral palsy is a disorder causing inability to movements,incoordination,excessive tightness, due to damage to the brain during the developmental stage(around the time of birth and early childhood).This damage may also lead to impairments in understanding ,cognition,learning,intellect,behavior,communication,speech,hearing and vision.

Cerebral palsy is the leading cause of childhood disabilities in India.3 in every 100 births are diagnosed with cerebral palsy.

Types of cerebral palsy:

a) Based on part of the body impaired/affected;

Quadriplegic(all the four limbs affected)

Diplegic (both legs affected)

Hemiplegic (an arm and leg on one side affected)

Monoplegic (only anyone limb affected)

Triplegic (both legs and one arm affected)

b) Based on area of the brain damaged:

Spastic (increased stiffness in all muscles) - the cerebral cortex, especially, the motor cortex is affected

Dyskinetic (abnormal movements of the body) - the basal ganglia is affected(part of the brain controlling the voluntary movements)

Dystonic (fluctuating muscle tension) or athetoid(uncontrollable jerky movements)

Ataxic (clumsy movements and poor balance)- cerebellar affection

Hypotonic (Floppy muscles) - this is the opposite of spastic.muscles are loose here and may mimic muscle weakness. Injury to cerebellum may manifect as this or hypothyroidism is also a common reason.

Here child achieves most milestones, but very late and Needs support for most activities.

c) Mixed:

Two or more forms may coexist.

Investigations:

1. **MRI Brain +DTI(diffusion tensor imaging)** : this imaging will in most cases clarify ,where the problem, the extent and also give an indication whether there is a hypoxic injury.

   Typically, a MRI Brain of a child with CP would show periventricular leukomalacia (PVL),with a variation in degree and severity.

2. **EEG:** In a child with co morbid seizures/fits, it is important to do an EEG.Even otherwise, a routine EEG may give an indication of potential epileptogenic focus, which has not manifested yet.Caution about future possibility of seizure,can be exerted.

Treatment:

Conventional treatment consists of-

Surgical :

1) Correction of anamolies, such as hydrocephalous using surgical means(VP shunts, etc..)

2) Correction of deformities (tenotomies) or use of Botox to reduce spasticity

3) Correction of squint surgically

4) Cochlear implants for hearing deficit(if indicated)/hearing aids

Rehabilitation: which includes physiotherapy,occupational therapy,speech therapy,visual rehabilitation program,etc..

Medications: Medications are generally used to treat comorbid conditions, such as seizures,dystonia,hyperactivity/aggression

Antiepileptics drugs

(AEDS generally used in children are sodium valproate (20mg/kg/day in two divided doses),levicitram (20mg/kg/day in two divided doses).

In uncontrolled seizures, these are combined with Frisium,clobazam,etc..

Other antieplieptics, used are gardenal and tegretol (Carbemezepine)

Pacitane/Tizanidine is now used for control of dystonia/involuntary movements in gradually increasing doses,titrated to need.

Hyperactivity :

Resperidone or triimethyl phenydilate

Advances in treatment of CP:

1. **Stem cell therapy-** Over the years, various types of stem cells and cellular elements have been used, via various routes of administration to stimulate neurogenesis in the damaged brain, especially in children. This intervention holds more logical attraction, since adaptive responses would be expected to be permissive in a growing brain. Recent work in the field of stem cells is seeing an increasing trend towards the use of either: a) Allogenic/autologous cord blood derived cells b) Autologous bone marrow derived cells. The favoured route of transplantation, is biased towards safety, viz. either intravenous or intrathecal as opposed to direct stereotactic injection into the brain. (More details can be found in the chapter of "Stem cell therapy for Neurological Disorders"..in recent advances section)
2. **HBOT**

Mental retardation

MR is a developmental disability, where intellectual functioning of an individual is below average(as measured by standard intelligence tests).This results in significant limitations in the persons daily living skills (adaptive functioning). Such skills include,the ability to communicate,home living skills,self care,social skills,functional academic skills/scholastic performance and job related skills.In intellectual disability, the IQ(Intelligence quotient) is blow 70-75%.These children,in addition to intellectual

dysfunction,may also have comorbid seizures/convuslsions and aggressive behaviours.

Apart from the common causes of neurodevelopmental disorders mentioned earlier, MR/ID can also be caused by hereditary factors, such as genetic defect(Fragile X syndrome),single gene defects like Phenylketonuria(PKU).

Diagnosis:

Psychological assessment: To properly scale the IQ is mandatory.This helps in understanding the level of dysfunction and plan out rehabilitative measures accordingly.

Investigations:

The investigations for MR remain broadly similar to that in Cerebral Palsy,i.e.MRI Brain and EEG.

MRI Brain may not reveal any abnormality.Hence, PET CT Scan Brain is recommended.(PICS),which reveals the areas of the brain which are functioning less and thereby contributing to the intellectual disability./MR.

Genetic tests (Fragile X SYNDROME),tests for metabolic defects and inborn error of metabolism are optional.

Treatment:

Conventional treatment:

The treatment for MR/ID ,so far, conventionally, has been only rehabilitative.These children need to be trained in special schools, to be able to use their abilities to the optimum,to achieve some functional independence.

Medications:

Medications are used to treat comorbid conditions, such as seizures/ epilepsy,hyperactivity and aggression .

Newer advances:

Stem cell therapy- In case of intellectual disability, any damage to the brain is a permanent and irreversible damage as the neurons of the brain, once damaged, cannot repair themselves on their own. The underlying neuropathology of intellectual disability includes neuronal death along with disruption in neuronal networks, cell migration, cell multiplication, axon growth, brain plasticity, synaptogenesis, etc. Studies have shown that major defects are recorded in hippocampus and cerebral cortex areas of the brain which further lead to faulty information processing and consecutively affect the cognition and adaptive behavior. To reverse the damage caused to the central nervous system, only a neurorestorative therapy like stem cell therapy would be beneficial. Stem cells have a unique property of migrating towards

the damaged areas on administration. They survive, migrate, proliferate and differentiate into the required cell types. They not only replace the dead cells but also stimulate the endogenous cells and prevent further damage. Their paracrine activities such as secretion of growth factors, angiogenesis, neurogenesis, immunomodulation, decreasing inflammation, etc also help in the repair process. This could help repair the disrupted neuronal networks in ID and hence improve the information processing. (More details can be found in the chapter of "Stem cell therapy for Neurological Disorders"..in recent advances section)

Autism and Autism spectrum disorders

Autism is a neurodevelopmental disorder characterized by impairments or delays in social interaction,communication and language,as well as ,, by repitive routines and behaviours.

They are called spectrum disorders because of wide range and severity of symptoms.The prevalence of autism has increased radically over the few decades.Currently, the figures are 1 in 68 children in USA and 1 in 250 in India.

This expotential rise, could partly be attributed to increasing awareness and diagnosis of this disorder. Traditionally, till very recently, these children were misdiagnosed as Mental retardation,which in turn lead to lack of intervention and bad prognostication.

Like other neurodevelopmental disorders, the cause of autism is multifactorial,hence no specific diagnostic blood investigations/biomarkers are available.

The diagnosis, is mostly clinical,based on analysis of behavioral symptoms.

Apart from the causes common to other neurodevelopmental disorders,increasing association with some genetic causes is being seen,such as Fragile X syndrome,maternal duplication 0f 15q1-q13,and deletions and duplications of 16p11.

Clinical symptoms:

Clinical symptoms , typically, consist of the triad of symptoms: Lack of communication, social interaction and abstract thinking.

These lead to other secondary characteristics, like, hyperactivity, no eye contact, low attention span, no verbalization or repetition of speech(echolalia),inability to concentrate and learn.

Pathophysiology

Brain hypoperfusion and immune dysfunctions have been characterized as the two main brain pathologic alterations in autism cases. Research on animal brain to study the etiology of autism has shown that a major dysfunction of the autistic brain resides in neural mechanisms of the structures in the medial temporal lobe, and, perhaps, more specifically the amygdaloid complex. Distinct patterns of memory losses and

socioemotional abnormalities emerge as a result of extent of damage to the medial temporal lobe structures.

Diagnosis and investigations

Diagnosis of autism is traditionally done by a developmental pediatrician with inputs from psychologists.Clinical assessment scales, based on an array of questions asked to the parents, forms the basis of diagnosis.

These scales are DSM V, CARS, ISAA.

Investigations

1. EEG: Routinely only EEG is carried out by neurologists,to rule out potential epiletiform activity,which is associated with a subset of autistic children.
2. MRI Brain: grossly,MRI Brain is expected to be normal.However, it is important to be carried out, in order to rule out correctable causes,such as brain tumor or know the possible underlying cause, such as coexisting neurofibromatosis,corpus callosum agenesis,hypoxia related injury,etc.

Treatment:

Conventional therapies:

Rehabilitation : Early intensive behavioral intervention -designed to facilitate development and learning, promoting socialization, self awareness, reducing maladaptive behaviors and educating and supporting families.

Occupational therapy,sensory integration techniques, speech therapy help in overall development of the child

Nutritional interventions restrict allergy associated dietary components, as well as to supplement minerals or vitamins which may be lacking. Autistic children tend to have problems with digestion, including food sensitivity - particularly to casein and gluten in dairy and wheat products.

Medical interventions usually treat specific activities associated with autism. Serotonin reuptake inhibitors (SSRI's) such as fluoxetine, fluvoxamine, sertraline, and clomipramine, are used for treatment of anxiety and depressionThey may also have the added benefit of increasing social interaction and inhibiting repetitive behavior.

Antipsychotic drugs such as thioridazine, fluphenazine, chlorpromazine, and haloperidol have been showed to decrease behavioral abnormalities in autism.

Atypical antipsychotics such as risperidone, olanzapine and ziprasidone have also demonstrated beneficial effect at ameliorating behavioral problems.

Autism associated seizures are mainly treated by administration of anticonvulsants such as carbamazepine, lamotrigine, topiramate, and valproic acid.

Attention deficient/hyperactivity is treated by agents such as methylphenidate.

Other treatments include psychiatric care, neurodevelopmental therapies, and treatment for co-occurring medical conditions.

Recent advances;

Stem cell therapy:

The potential of stem cells for the treatment of autism is being studied extensively. These proposals are in view of the stem cells having strong angiogenic potential which could facilitate processes of improving perfusion by angiogenesis and balancing inflammation by immune regulation would exhibit beneficial clinical effects in patients with autism. Other contributing effects of the stem cells, which have been proposed are, strong immunosuppressive activities as well as paracrine effects to stimulate neuronal function via growth factors, such as BDNF, VEGF,NGF AND PDGF. (More details can be found in the chapter of "Stem cell therapy for Neurological Disorders"..in recent advances section)

Other upcoming treatments include, Hyperbaric Oxygen therapy (HBOT), Relationship Development Intervention (RDI),Water Therapy or Aquatic Therapy, Floortime or Developmental Individual Difference Relationship Model (DIR Model), Hippotherapy, The Handle Method, Neurofeedback, etc.

Summary

Neurodevelopmental disorders cause delayed development of the child in motor, sensory, speech, intellectual, and social domains. The causes can be prenatal, perinatal or postnatal. The detection of these disorders may be missed at birth. Therefore, family physician should carefully examine children for developmental delay. At the earliest sign one should refer the patient to a pediatrician. Rehabilitation at early age can accelerate development of these children. Though there is no cure for these conditions, the patient's family should be educated about various options like specialized rehabilitation centres, vocational rehabilitation centres, support groups, special schools, etc. Care of caregivers is also essential.

Section D

Management of Neurological Emergencies

32. Acute Stroke

Strokes can be either ischemic or hemorrhagic. In an ischemic stroke, the blood supply to part of the brain is cut off because a vessel is blocked due to either atherosclerosis or a blood clot. Past medical history helps in diagnosing strokelike a history of prior stroke, diabetes mellitus, hypertension, and atrial fibrillation.

What to Examine ?

Ask for age, as it is more prevalent in over 50, history of hypertension, Diabetes, smoking, and TIA in the last month.

Look for -

- Loss of sensations in an arm, leg or one side of the body
- Weakness or paralysis
- Partial loss of vision or hearing
- Double vision
- Dizziness
- Slurred speech
- Confused state
- Imbalance and falling

Neurological Examination and GCS scoring should be done to establish the diagnosis.

Investigations-

- CT brain and MRI
- Blood glucose
- Oxygen saturation
- Serum electrolytes/renal function tests
- Complete blood count
- Prothrombin time/INR
- PTT
- ECG

- Liver function tests
- ABG
- Chest X-ray

How to manage?

Airway, Breathing and Circulation to be established. Elevate head end by 30 degrees.

Acute management of stroke

Blood glucose

- Treat hyperglycemia with insulin if serum glucose >200 mg/dL
- Treat hypoglycemia with D50

Blood pressure

Continuous cardiac monitoring for ischemic changes or atrial fibrillation

Intravenous fluids

- Avoid D5W and excessive fluid administration
- IV isotonic sodium chloride solution at 50 mL/h unless otherwise indicated

Stop oral intake

Oxygen

- Start O2 if Saturation less than 94%

Temperature

- Control temperature to avoid high fever

Refer to the hospital at the earliest.

33. Delirium

Delirium is a common clinical syndrome characterized by disturbed consciousness, confusion and decreased awareness.

Delirium may occur due to dementia, old age, fever and acute infection, particularly in children. Poor nutrition or dehydration, severe, chronic or terminal illness, alcohol or drug abuse or alcohol withdrawals are some of the causes for delirium.

A number of medications like analgesics or sedatives or combinations of medications can trigger delirium. Medications for mood disorders, such as anxiety and depression and Parkinson's disease medications can also cause delirium.

WHAT TO EXAMINE?

Physical and neurological examination

Look for

- Dehydration
- Infection
- Alcohol withdrawal

A neurological exam - check vision, balance, coordination and reflexes to rule out stroke.

Investigations

- CT brain and MRI
- Blood glucose
- Oxygen saturation
- Serum electrolytes/renal function tests
- Complete blood count
- Prothrombin time/INR
- PTT
- ECG
- Liver function tests

- Thyroid function tests
- Serum vitamin B12 and folate levels.
- Chest X-ray

HOW TO MANAGE?

Identify and manage the underlying cause or combination of causes.

In case the patient appears confused and violent-

- Give clear, brief, assertive instructions and attempt to establish a rapport
- Avoiding threat and appear reassuring, caonfident with eye contact and allowing greater space around the patient than normal

Look for dementia, Alzheimer's or Parkinsonism and treat appropriately

Communicate and provide reassurance.

Haloperidol can be started for a short duration

Refer to psychiatrist

34. Status Epilepticus

Check ABC
Check airway

⇓

Insert IV

Start IV line and administer 50ml 50%Dextrose and Thiamin 100mg

tart anti- convulsant

⇓

Lab Tests

Blood Tests	Blood Sugar	Liver and	ABG	Anti convulsant
CBC, S electrolytes, Serum Calcium, Magnesium		Renal Function Tests		level in a k/c/o epilepsy

⇓

Administer Diazepam (0.15mg/kg) IV over 5 mins

⇓

Phenytoin (18-20mg/kg) over 20 mins in normal saline

⇓

Monitor Oxygen Saturation
Intubate if required

⇓

Insert Urinary Catheter
Urine Routine

⇓

Monitor Temperature
Control fever

⇓

If Seizure continues after 20 mins
Additional Phenytoin (10mg/kg) IV

⇓

If seizures continue after 20 mins

⇓

Phenobarbital (15mg/kg)IV

⇓

Consider General Anaesthesia if seizures continue


In children:
Maintain Airway, Breathing and Circulation
High Temperature (Indicates Febrile seizure)
Yes
Drowsy, neck stiffness, petechiae, bulging fontanelle in case of infants
No
Yes
No
Anti pyretics
Treat as Meningitis until proven otherwise.
Investigations:
CBC, ESR, Serum Electrolytes, Blood Sugar
Treatment:
IV Antibiotics
Previous history of seizures
Yes
Level of anticonvulsants or compliance should be checked.
No
History and Examination including visual problems, headaches, milestones, head injury.
Investigations:
EEG, CT scan, Blood investigations.

	Management in Adults	
0-5 minutes	Airway Breathing and Circulation **(ABC)**	
	Monitor Vital signs	
	Establish IV access and send blood for investigations	
	Blood glucose to be checked	Treat Metabolic imbalances and hypoglycemia as quickly as possible
	Treatment: Lorazepam 0.1 mg/kg/dose upto 4mg maximum IV/IMover 2-4 minutes	
	OR Diazepam 0.5mg/kg/dose maximum upto 20mg/dose IM or rectally	
10-15 minutes	IF SEIZURES PERSIST	
	Repeat Lorazepam	
	Monitor for hypotension, tachycardia, bradycardia	
	Phenytoin 20mg/kg/dose	
15-20 minutes	IF SEIZURES PERSIST	
	Phenobarbital 20mg/kg/dose IV	
	Monitor for respiratory depression	
20-30 minutes	IF SEIZURES PERSIST	
	Repeat Phenytoin	

35. Unconsciousness

Unconsciousness or altered state of consciousness:When patient is unable to respond appropriately to stimuli or is drowsy and confused.

Potential Causes - "AEIOU TIPS"

- A - Alcohol (Drugs & Toxin
- E - Endocrine, Exocrine, Electrolyte
- I - Insulin
- O - Opiates, Overdose
- U - Uremia
- T - Trauma, Temperature
- I - Infection
- P - Psychiatric disorder
- S - Seizure , Stroke, Shock, Space occupying lesion

What to Examine?

Attempt to get full history.

Smell the breath - ketones or alcohol,

Look for abnormal posturing like decorticate (flexion of UE with extension of LE) or decerebrate (extension of all limbs)

- Look for cyanosis, jaundice
- Look for signs of trauma
- Look for respiratory rate and patterns (Cheyne-Stokes)
- Temperature
- Heart rate; Blood pressure; Auscultation and examination of the heart (cardiovascular)
- Abdomen for trauma
- Neck Stiffness

- Fundal examination
- Glasgow Coma Scale
  - Eye opening
  - Motor response
  - Verbal response
- Brain stem function
  - Pupillary reactions
  - Corneal responses
  - Spontaneous eye movements
  - Oculocephalic responses
  - Oculovestibular responses
  - Respiratory pattern
- Motor function
  - Motor response
  - Muscle tone
  - Tendon reflexes
  - Seizures

How to Manage?

Always assess & stabilize ABC first

- A-Airway
- B-Breathing
- C-Circulation

Especially airway with Cervical Spine immobilization / protection in case of trauma.

- Start Oxygen
- IV line: IV Fluids, Thiamine 100mg IV, 1 amp D 50
- Complete history and physical exam after stabilization
- Check X-ray cervical spine for spinal cord injury

Investigations:

- ECG
- Blood sugar
- Serum Electrolyte
- Liver function tests

- Urinalysis
- Thyroid function tests
- CT Head
- Lumbar Puncture
- USG Abdomen

Quickly manage

- Low glucose level - IV dextrose
- Hypoxia - give oxygen
- Pinpoint pupils not breathing - IVnalaxone
- Seizure -IV Lorazepam
- Hypothermia - warm up
- Infection- IV antibiotic

36. Head Trauma

What To Ask?

- Loss of Consciousness
- Vomiting
- Amnesia
- Seizures
- Disorientation and confusion

What To Examine?

Neurological examination:

First rate the head injury by Glasgow Coma Scale (GCS)

Glasgow Coma Scale

Eye Opening

Score	1 Year or Older	0-1 Year
4	Spontaneously	Spontaneously
3	To verbal command	To shout
2	To pain	To pain
1	No response	No response

Best Motor Response

Score	1 Year or Older	0-1 Year
6	Obeys command	
5	Localizes pain	Localizes pain
4	Flexion withdrawal	Flexion withdrawal
3	Flexes upper limbs extends lower limbs (decorticate)	Flexes upper limbs extends lower limbs (decorticate)
2	Extension (decerebrate)	Extension (decerebrate)
1	No response	No response

Best Verbal Response

Score	>5 Years	2-5 Years	0-2 Years
5	Oriented and converses	Appropriate words	Cries appropriately
4	Disoriented and converses	Inappropriate words	Cries
3	Inappropriate words; cries	Screams	Inappropriate crying/ screaming
2	Incomprehensible sounds	Grunts	Grunts
1	No response	No response	No response

Definition of mild, moderate and severe head injury by GCS score

Degree of head injury	GCS score
Mild	13-15
Moderate	9-12
Severe	8 or less

Neurological Examination should include

Neck and cervical spine

- Deformity
- Tenderness
- Muscle spasm

Head

- Scalp bruising
- Lacerations
- Swelling
- Tenderness

Raccoon eyes-Refer to nearest hospital

Bruising behind the ear (Battledore sign) -Refer to nearest hospital

Eyes

- Pupil size
- Equality
- Reactivity

Fundoscopy for retinal haemorrhage

Ears

- Blood behind the ear drum-Refer to nearest hospital
- CSF leak-Refer to nearest hospital

Nose

- Deformity
- Swelling
- Bleeding
- CSF leak-Refer to nearest hospital

Mouth

- Dental trauma
- Soft tissue injuries

Face

- Focal tenderness
- Crepitus-Refer to nearest hospital

Motor function

- Reflexes present

How To Manage?

No history of loss of consciousness, no vomiting or amnesia, a normal and minimal if any subgaleal swelling	Normal Neurological Examination	No CT scan. Monitoring at home. Parace-tamol for headache.	Give a warning sign list to the caregiver
Brief loss of consciousness, post-traumatic amnesia, a single episode of vomiting or significant subgaleal swelling	Normal Neurological Examination	CT Scan Monitor for a few hours if CT scan normal. If CT scan not available then X-ray Skull and look for fracture CTscan required if there is a fracture on X-ray. If X-ray normal, monitor for few hours and then monitor at home.	Give a warning signs list to the caregiver for monitoring at home
Loss of consciousness, repeated episodes of vomiting, blood from the ear, CSF from the ear, CSF from the nose, seizures, penetrating or	Neurological Deficits	CT scan compulsory Admit patient to a hospital for monitoring for 48 hours.	Antibiotics and analgesics as indicated. No sedatives should be given. Watch for warning signs.

perforating wounds, non-cooperative patient, patients who have undergone previous brain surgery, patient who has been on anticoagulant therapy, epileptic or alcoholic patients			
Unconscious patients	Neurological Deficits, Decorticate or Decerebrate response	Resuscitation. CT scan compulsory. Refer to an emergency care hospital	Apply oxygen 10 l/min by face mask.Establish intravenous access. Transfer patient preferably on spinal board and with neck collar in place.

Most minor head injuries make a full recovery within a short period and just cause bruising and pain for a short while. Scalp injuries generally require suturing asw they tend to bleed a lot. In case of closed injuries with swelling on the scalp application of ice to the injured area to helps reduce the swelling.

Headache - Give paracetamol 6hrly to relieve pain.

Warning signs list to be handed to patient caregivers to bring the patient back to the doctor-

- Vomiting
- Headache not relieved after a few hours
- Drowsiness
- Irritability
- Seizure
- Unusual or confused behaviour
- Bleeding or discharge from the ear or nose
- Weakness or numbness in arm or leg
- Altered vision

37. Spine Trauma

Post traumatic spinal cord injury is often seen in road traffic accidents and construction sites-

On receiving the patient assess for

- Airway/Breathing: Intubation may be required but it would need sedation (Lorazepam 1-2 mg IV) with constant monitoring
- Circulation: Start IV access to begin IV Fluids, preferably Normal Saline
- Immobilize the spine

What to examine?

- Neurological assessment
- Note the sensory level
- Assess the motor function
- Use the Glasgow coma score to assess the sensorium

Autonomic Control

Vital signs can be quite abnormal following spinal cord injury due to loss of autonomic control which occurs particularly in cervical or thoracic spine injuries-

- Note the heart rate - watch for bradycardia, the physician can use atropine if it is not contraindicated by a head injury.
- Note blood pressure and watch out for hypotension to rule out neurogenic shock. Patient may need intravenous fluids to maintain BP
- Loss of temperature control - watch for hypothermia
- Respiratory difficulty depends on injury level and should be monitored by asking the patient to cough and monitoring oxygen saturation
- Watch abdomen for distension

Investigation

- Plain X-ray of the entire cervical, thoracic and lumbar spines
- MRI spine can be planned once the patient is stable

- CBC ABG Serum Electrolytes

How to manage?

First 24 hours

- Confirm ABC
- Immobilize the neck spine with neck collar. If a neck collar is not available then plastic IV fluid bottles can be secured on either side of the head with a tape, so that there is no movement of the cervical spine.
- In case the patient needs to be resuscitated, the spinal immobilization should be maintained. To move the patient log roll should be used
- Take care with water temperature for washes, and use of hot or cold devices against skin in case ofspinal cord injury patients
- Bladder function depends on the level of spinal cord injury. It is better to catheterize the patient to avoid neurogenic bladder where the loss of bladder function is obvious in the initial stages
- Refer to a neurosurgeon.

"It is important to note that injection methyl prednisolone if started within 8 hrs. of spine cord injury has a significantly beneficial effect on the overall recovery. It is therefore, important to shift a spine injured patient as soon as possible to a specialized trauma hospital. if there is likely to be delay in transfer then injection methyl prednisolone may be started as 30 mg/ kg may be given over 30 mins. and then 5.4 mg/kg per hour, continued till the patient is shifted to a specialized center."

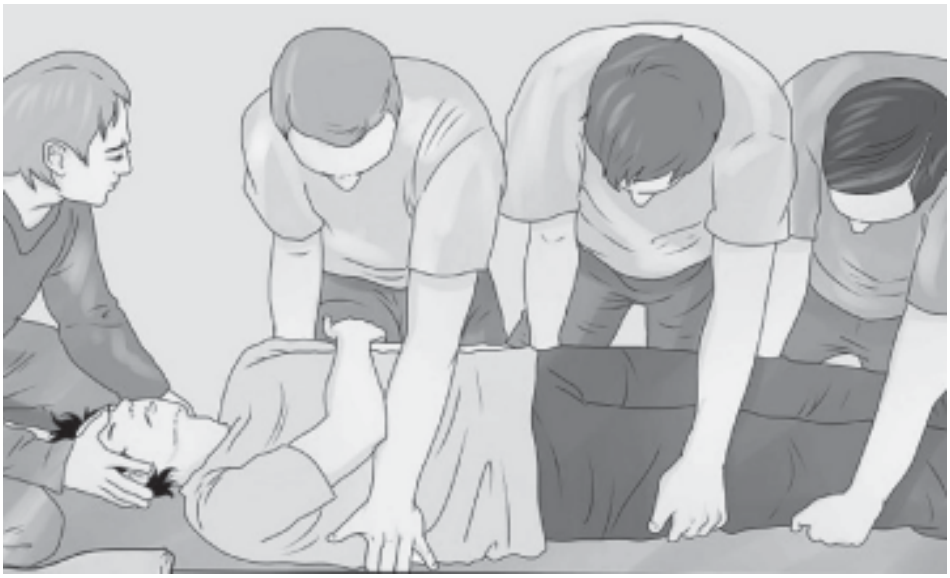


Fig .37.1: Log Roll a patient of spinal cord injury

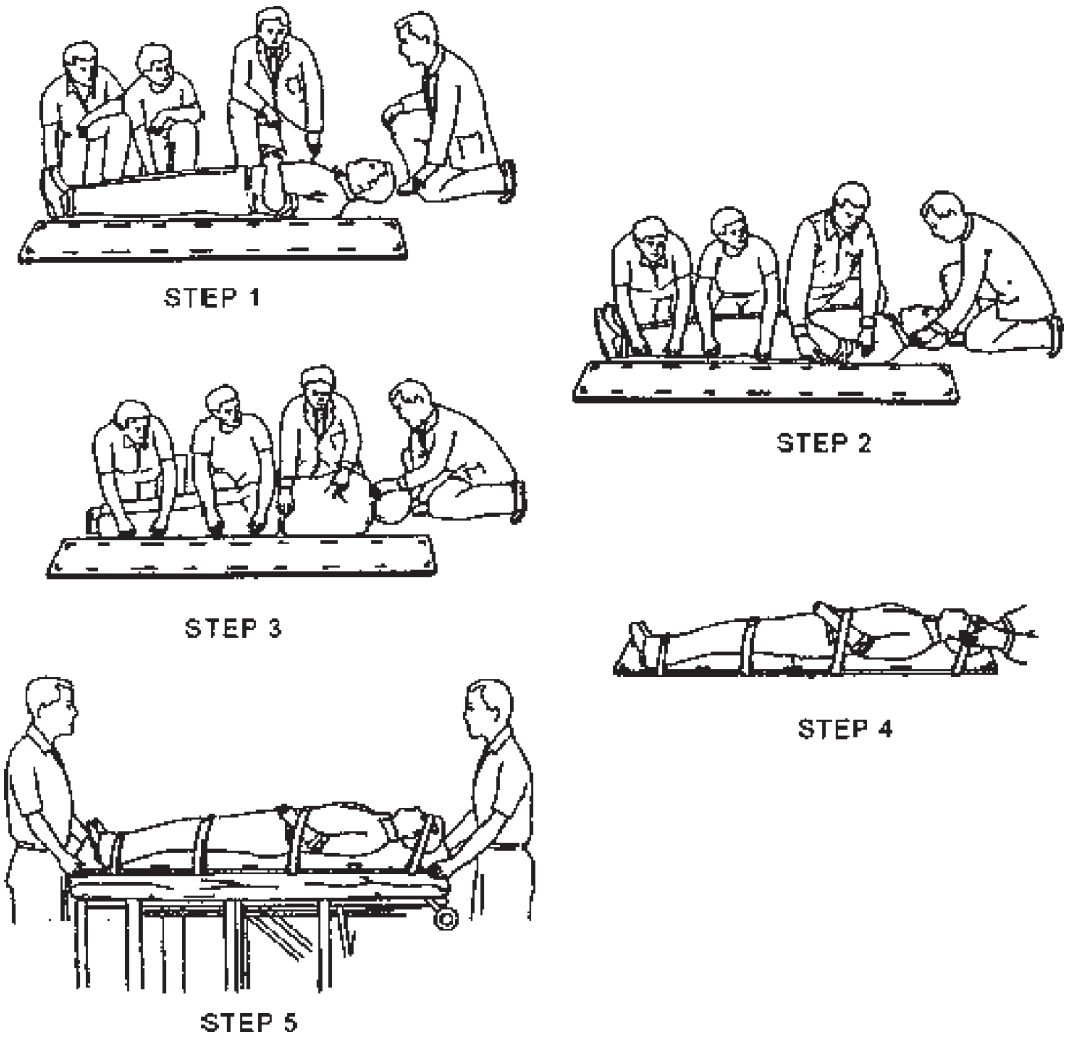


Fig. 37.2:

Step 1 : Four persons to help. The person at the head end calls out the instructions.

Step2 : Secure and hold the patients neck with both forearms as shown.

Step 3 : Turn the patient as called out by the head end togather.

Step 4 : Roll the patient back on to a spinal board.

Section E
Neuropharmacology

38. Anti Convulsants

The anticonvulsants, sometimes also called antiepileptics, belong to a diverse group of drugs used in prevention of the occurrence of epileptic seizures. The goal of an anticonvulsant is to suppress the rapid and excessive firing of neurons that start a seizure. A good anticonvulsant would prevent the spread of the seizure within the brain.

Many anticonvulsants block sodium (Na+) channels, calcium (Ca2+) channels, ampa receptors or nmda receptors. Some anticonvulsants inhibit the metabolism of gaba or increase its release.

Classification:

Classical

Phenytoin

Phenobarbital

Primidone

Carbamazepine

Ethosuximide

Valproate (valproic acid)

Newer

Levetiracetam

Fosphenytoin

lamotrigine

Topiramate

Gabapentin

Tiagabine

Vigabatrin

Oxycarbazepine

Felbamate

Benzodiazepines

The benzodiazepines are a class of drugs with anticonvulsant, hypnotic, anxiolytic, amnestic and muscle relaxant properties. Long-term use can be problematic due to the development of tolerance and dependency

Mechanism of action

Benzodiazepines act by increasing neuronal membrane permeability to Cl ions by binding to stereospecific benzodiazepine receptors on the postsynaptic GABA neuron within the CNS and enhancing the GABA inhibitory effects, which in turn result in hyperpolarisation and stabilisation.

Contraindications: Severe hepatic impairment; respiratory depression; acute narrow-angle glaucoma; pregnancy and lactation.

Special Precautions need to be taken in cases of hepatic and renal dysfunction; pulmonary insufficiency; and myasthenia gravis. These drugs may impair the ability to drive or operate machinery.

Adverse Drug Reactions: Drowsiness, headache, dizziness, confusion; blurred vision; weakness; unsteadiness. Respiratory depression is a serious complication.

Drug Interactions: Potentiation of CNS depression produced by alcohol; general anaesthetics; narcotic analgesics; TCAs; MAOIs; phenothiazines; antipsychotics; barbiturates; scopolamine

The following benzodiazepines are used to treat status epilepticus:

Diazepam

It is preffered in acute panic states & anxiety associated with organic disease

Onset of action: Almost immediate (IV); rapid (oral).

Duration: IV: 20-30 min.

Absorption: Time to peak plasma concentration: Approx 30-90 min (oral); approx 10-30 min (rectal).

Distribution: Plasma protein binding: 98-99%.

Metabolism: Extensively hepatic via CYP3A4 and CYP2C19 isoenzymes to desmethyldiazepam (active metabolite).

Excretion: Via urine (as free or conjugated metabolites). Biphasic half-life: Rapid (initial), 1 or 2 days (terminal), 2-5 days (desmethyldiazepam).

Indications : anxiety, tension, muscle spasm, psychosomatic & behaviour disorders

Contraindications : acute narrow angle glaucoma, hypersentivity to benzodiazepines. myasthenia gravis.

Special precautions to be taken in hepatic & renal impairment patients

Side effects : drowsiness,altered activeness,vertigo,increased appetite & weight gain

Dosage

Parenteral

Seizures

Adult: Initially, 5-10 mg IV repeated at 10- to 15-min intervals up to max 30 mg. On stoppage of seizures, appropriate maintenance therapy to be started. Initial dose at 2-4 hr interval may be started. IM administration could be done if IV is not possible.

Child: 30 days to 5 yr: Initially, 0.1-0.5 mg IV, may be repeated every 2-5 min up to max 5-10 mg;

>5 yr Initially, 1 mg, may be repeated every 2-5 min up to max 10 mg. Followed by maintenance treatment.

Elderly: dosage should not exceed half the adult dose.

Dose reduction may be required in hepatic impairment.

Lorazepam

Adult: 4 mg injected slowly, may be repeated once after 10 minutes if seizures recur. Dose should be given at a rate not >2 mg/minute into a large vein.

Child: Neonates and children up to 12 yr: 0.1 mg/kg (max: 4 mg) as a single dose, may be repeated once after 10 minutes if needed

Lorazepam is a short acting benzodiazepine. Lorazepam enhances the inhibitory effect of GABA on neuronal excitability by modulating GABA receptors.

Onset of action: Hypnosis: anticonvulsant: 5 min (IV), 30-60 min (oral).

Duration: 6-8 hr.

Absorption: peak plasma concentrations after 2 hr.

Distribution: Crosses the placenta and blood-brain barrier; enters breast milk. Protein-binding: 85%.

Metabolism: Hepatic; converted to inactive metabolites.

Excretion: Urine and faeces; 10-20 hr (elimination half-life).

Indications: anxiety, status epilepticus, sedation

Containdications: Severe hepatic impairment; respiratory depression; acute narrow-angle glaucoma; pregnancy and lactation.

Midazolam

Midazolam is a short-acting benzodiazepine.

Absorption: Rapidly absorbed (any route); peak plasma concentrations after 20-60 min (depending on route).

Distribution: Protein-binding: 96%

Metabolism: Extensively hepatic via CYP3A4 isoenzyme; converted to hydroxymethylmidazolam.

Excretion: Urine (as glucuronide conjugates); 2 hr (elimination half-life), prolonged in neonates, elderly and hepatic impairment

Indications: The midazolam nasal spray is only used when an epileptic seizure lasts more than ten minutes. Seizures that last this long can cause status epilepticus. Midazolam nasal sprays are also used to stop the seizures as soon as possible.

Dosage

The midazolam nasal spray is very easy to use, even for someone that has never used it before. For new sprays a few pumps are required to clear the spray of air. During epileptic seizures, generally one spray per nostril is sufficient for the patient to recover from it. As each spray contains 2,5 mg midazolam, this sums up to a total dosage of 5 mg. For some patients 10 mg of midazolam is used.

Alprazolam

It is a triazolo analogue of benzodiazepine,which is indicated in antianxiety

Mechanism of action:

Alprazolam has anxiolytic, muscle-relaxant, anticonvulsant, antidepressant and sleep-modifying effects. It binds to the ? aminobutyric acid (GABA)-specific sites throughout the CNS, leading to an increase in the inhibitory effect of GABA on neuronal excitability.

Absorption: peak plasma concentrations after 1-2 hrs.

Distribution: Protein-binding: 70-80%

Metabolism: Hepatic; converted to ?-hydroxyalprazolam and benzophenone.

Excretion: Urine (as unchanged drug and metabolites); 11-15 hrs (elimination half-life).

Indications-anxiety disorders,anxiety associated depression, sedation (mild)

Dosage

Oral

Short-term management of anxiety

Adult: 0.25-0.5 mg tid, increased to 3-4 mg daily if necessary.

Elderly: Initially, 0.25 mg bid/tid.

Hepatic impairment: Avoid in severe impairment.

Oral

Panic attacks

Adult: Up to 10 mg daily.

Contraindications : acute narrow angle glaucoma, hypersentivity to benzodiazepines, acute pulmonary insufficiency or sleep apnoea, severe hepatic impairment; pregnancy, lactation. CNS depressants are not recommended in children.

Side effects : drowiness, psychological and physical dependence, withdrawal seizures, anorexia, musculoskeletal weakness, ataxia, dizziness, confusion and depression. Blood dyscrasias being a serious adverse effect.

Drug Interactions: Potentiates action of alcohol and CNS depressants. Reduced conc with cigarette smoking by 50%.

Zolpidem

This is a non benzodiazepine sedative belonging to imidazopyridine class.

Dosage

Oral

Short-term management of insomnia

Adult: As immediate release tab: 5-10 mg immediately before bedtime; Max: 10 mg/day. As extended release tab: 6.25-12.5 mg immediately before bedtime; Max: 12.5 mg/day. Max duration of treatment: 4 weeks which includes tapering.

Elderly: As immediate release tab: 5 mg immediately before bedtime. As extended release tab: 6.25 mg immediately before bedtime. Max duration of treatment: 4 weeks including tapering.

Hepatic impairment: As immediate release tab: 5 mg immediately before bedtime. As extended release tab: 6.25 mg immediately before bedtime. Max duration of treatment: 4 weeks including tapering.

Indications : short term treatment for insomnia.

Contraindication : obstructive sleep apnoea, myasthenia, severe hepatic insufficiency,acute pulmonary insufficiency.

Special precaution to be taken in neonates, nursing mothers, pregnancy and depression

Patients should be adviced not to drive after taking medication.

Side effects

Atypical thinking and behaviour, hallucination, nightmare, somnolence, headache, dizziness, vertigo, drowsiness, asthenia, ataxia, rebound insomnia, amnesia, upper and lower respiratory tract infection, fatigue, visual disturbances, increased ALT serum concentrations; while Hepatitis, anaphylactic reactions, angioedema are serious complications of adverse effects.

Hydantoins

Phenytoin

Phenytoin is available at a relatively low cost, making it one of the most affordable seizure control medications. It is available in extended release capsules and injectable forms.

Mechanism of action

Phenytoin acts as an anticonvulsant by increasing efflux or decreasing influx of sodium ions across cell membranes in the motor cortex, thus stabilising neuronal membranes and decreasing seizure activity.

Distribution: Widely distributed. Protein-binding: 90%.

Metabolism: Extensively hepatic; converted to inactive metabolites.

Excretion: Via urine as hydroxylated metabolite; elimination half life at steady state: 22 hr.

Dosage

Oral

Epilepsy

Adult: Initially, 3-4 mg/kg daily as single dose or in divided doses. Alternatively, 150-300 mg daily increased gradually to 600 mg daily if necessary. Maintenance: 200-500 mg daily.

Child: Initially, 5 mg/kg daily in 2-3 divided doses. Maintenance: 4-8 mg/kg daily in divided doses. Max dose: 300 mg daily.

Intravenous

Tonic-clonic status epilepticus

Adult: Adjunctive therapy with a benzodiazepine (e.g. diazepam): 10-15 mg/kg by slow inj or intermittent infusion at a max rate of 50 mg/min. Maintenance: 100 mg IV (or orally) given every 6-8 hr.

Child: Neonates: 20 mg/kg as a loading dose, then 2.5-5 mg/kg bid; 1 mth-12 yr: 18 mg/kg as a loading dose, then 2.5-5 mg/kg bid; >12 yr: 18 mg/kg as a loading dose, then up to 100 mg 3-4 times daily.

Phenytoin has a narrow therapeutic window. Hence, a fine balance must be maintained between its efficacy and dose-related side effects. Phenytoin demonstrates non-linear pharmacokinetics, which causes the enzyme system involved to become saturated with phenytoin, even with a small change in dose and can lead to a large change in phenytoin levels.Thus, monitoring phenytoin plasma levels regularly is necessary to decide the next appropriate dosage. Target plasma rangeof phenytoin: 10-20 mg/L

Indications: epilepsy, status epilepticus, migraine,trigeminal neuralgia

Contraindications : Pregnancy, IV administration in sinus bradycardia, heart block, or Stokes-Adams syndrome.

Special precautions - Precautions should be taken while administering intravenously in patients with hypotension, heart failure, Patient's BP and ECG should be monitored during therapy. IV must be given slowly (too rapid admin may cause hypotension, CNS depression, cardiac arrhythmias and impaired heart conduction). Therapy should not be discontinued abruptly as it may increase seizure frequency.

Side effects- headache, dizziness, tremor, insomnia, tenderness and hyperplasia of the gums, acne, hirsutism, osteomalacia. Phenytoin toxicity is manifested as a syndrome of cerebellar, vestibular, ocular effects, notably nystagmus, diplopia, slurred speech, and ataxia; also with mental confusion, dyskinesias, exacerbations of seizure frequency, hyperglycaemia. Prolonged use may affect mental function and cognition in children. Toxic epidermal necrolysis, Stevens-Johnson syndrome could occur in serious adverse events.

Fosphenytoin

Mechanism of action

Fosphenytoin is converted to phenytoin in the body. It modulates voltage-dependent Na channels of neurons.

Absorption: Plasma concentrations peak after 30 minutes (IM).

Distribution: Displaces phenytoin from binding sites. Protein-binding: 95-99%.

Metabolism: Complete; hydrolysed to phenytoin, phosphate and formaldehyde.

Excretion: Urine (as inactive metabolites).

Dosage:

Parenteral

Tonic-clonic status epilepticus

Adult: As Phenytoin sodium equivalents (PSE): Loading dose: 15 mg/kg, given via IV infusion at a rate of 100-150 mg/minute. Maintenance: Initially, 4-5 mg PSE/kg/day by IM inj or IV infusion at a rate of 50-100 mg PSE/minute; subsequent doses depend on patient's response and trough-plasma phenytoin levels.

Child: As Phenytoin sodium equivalents (PSE): Loading dose: 15 mg/kg, given via IV infusion at a rate of 2-3 mg/kg/minute. Maintenance: Initially, 4-5 mg/kg/day by IM inj or IV infusion at a rate of 1-2 mg/kg/minute; subsequent doses depend on patient's response and trough-plasma phenytoin levels.

Hepatic impairment: Dose reduction or slower infusion may be needed.

Parenteral

Seizures

Adult: Except status epilepticus: As Phenytoin sodium equivalents (PSE): Loading dose: 10-15 mg/kg, given via IM inj or IV infusion at a rate of 50-100 mg/minute. Maintenance: Initially, 4-5 mg/kg/day by IM inj or IV infusion at a rate of 50-100 mg/minute; subsequent doses depend on patient's response and trough-plasma phenytoin levels.

Child: ?5 yr: As Phenytoin sodium equivalents (PSE): Loading dose: 10-15 mg/kg, given via IM inj or IV infusion at a rate of 1-2 mg/kg/minute. Maintenance: Initially, 4-5 mg/kg/day by IM inj or IV infusion at a rate of 1-2 mg/kg/minute; subsequent doses depend on patient's response and trough-plasma phenytoin levels.

Hepatic impairment: Dose reduction or slower infusion may be needed.

Indications: status epilepticus, as a substitute for phenytoin

Contraindications: Porphyria; sinus bradycardia; SA block; 2nd- and 3rd-degree heart block; Stokes-Adams syndrome; pregnancy, lactation.

Special Precautions: Hepatic or renal impairment; elderly; patients requiring phosphate restriction. Monitor ECG, BP and respiratory function during infusion; observe patient for at least 30 minutes after infusion. IV infusion rate should not exceed 150 mg PSE/minute in adults or 3 mg PSE/kg/minute in children ?5 yr.

Side effects: Burning, itching and paraesthesia in the groin area following IV administration; asystole, ventricular fibrillation, hypotension, bradycardia, heart block which could be fatal.

Fatty acids

The valproates - valproic acid, sodium valproate, and divalproex sodium are anticonvulsant and mood-stabilizing drugs

Mechanism of Action:

Valproate is a carboxylic acid anticonvulsant which increases levels of ?-aminobutyric acid (GABA) in the brain.

Absorption: Time to peak plasma concentration: Oral: Approx 4 hr; extended release: 4-17 hr.

Distribution: Plasma protein binding (concentration dependent): 80-90%; free fraction: Increases from approx 10% at 40 mcg/mL to approx 18.5% at 130 mcg/mL; decreases in the elderly and patients w/ hepatic or renal impairment. Crosses the placenta; enters breast milk.

Metabolism: Valpromide is almost completely and rapidly metabolised in the liver to valproic acid. Valproic acid is extensively metabolised by liver, via glucuronidation and mitochondrial ?-oxidation.

Excretion: Excreted in urine (30-50% as glucuronide conjugate; <3% as unchanged drug), small amounts in faeces and expired air. Elimination half-life: Adult: 5-20 hr;

>2 mth: 7-13 hr.

Sodium valproate

It is a broad spectrum anticonvulsant producing little sedation

Oral

Complex partial seizures

Adult: Given as valproic acid or valproate semisodium: ?10 yr Initially 10-15 mg/kg/day in 2-4 divided doses, increased by 5-10 mg/kg/wk. Max: 60 mg/kg/day. Given as sodium valproate: 600 mg/day in 2 divided doses, increased by 150-300 mg every 3 days. Usual range: 1-2 g/day (20-30 mg/kg/day). Max: 2.5 g/day.

Child: Given as sodium valproate: >20 kg: 400 mg/day in 2 divided doses, increased gradually until control is achieved. Usual range: 20-30 mg/kg/day. Max: 35 mg/kg/day. <20 kg: 20 mg/kg/day in 2 divided doses, increased to 40 mg/kg/day.

Elderly: Initiate at lower dose and increase slowly.

Hepatic impairment: Contraindicated.

Oral

Simple and complex absence seizures

Adult: As monotherapy, conversion to monotherapy or adjunctive therapy. Given as valproic acid or valproate semisodium: ?10 yr Initially 15 mg/kg/day in 2-4 divided doses, increased by 5-10 mg/kg/wk. Max: 60 mg/kg/day.

Child: Given as sodium valproate: >20 kg: 400 mg/day in 2 divided doses, increased gradually until control is achieved. Usual range: 20-30 mg/kg/day. Max: 35 mg/kg/day. <20 kg: 20 mg/kg/day in 2 divided doses, increased to 40 mg/kg/day.

Elderly: Initiate at lower dose and increase slowly.

Hepatic impairment: Contraindicated.

Oral

Bipolar disorder

Adult: As valpromide: 600-1800 mg/day in 2 divided doses. Usual dose: 1200 mg/day. Initiate at required dose or dosage may be increased every 2-3 days to reach optimal dose in 2 wk w/ simultaneous and progressive dose reduction of concurrent psychotropic drugs.

Intravenous

Complex partial seizures

Adult: As monotherapy, conversion to monotherapy or adjunctive therapy. Given as sodium valproate: ?10 yr Initially 10-15 mg/kg/day in 2-4 divided doses, increased by 5-10 mg/kg/wk. Usual dose: 20-30 mg/kg/day. Each dose to be given as slow IV inj over 3-5 min or by infusion in 0.9% saline, 5% dextrose or lactated ringer's inj over 60 min (Max rate: 20 mg/min). Max: 2.5 g/day.

Child: As monotherapy, conversion to monotherapy or adjunctive therapy. Given as sodium valproate: Initially 10 mg/kg/day in 2-4 divided doses, increased until control is achieved. Usual range: 20-30 mg/kg/day. Max: 40 mg/kg/day w/ plasma valproic acid levels monitoring.

Elderly: Initiate at lower dose and increase slowly.

Hepatic impairment: Contraindicated.

Intravenous

Simple and complex absence seizures

Adult: As monotherapy, conversion to monotherapy or adjunctive therapy. Given as sodium valproate: ?10 yr Initially 10-15 mg/kg/day in 2-4 divided doses, increased by 5-10 mg/kg/wk. Usual dose: 20-30 mg/kg/day. Each dose to be given as slow IV inj over 3-5 min or by infusion in 0.9% saline, 5% dextrose or lactated ringer's inj over 60 min (Max rate: 20 mg/min). Max: 2.5 g/day.

Child: As monotherapy, conversion to monotherapy or adjunctive therapy. Given as sodium valproate: Initially 10 mg/kg/day in 2-4 divided doses, increased until control is achieved. Usual range: 20-30 mg/kg/day. Max: 40 mg/kg/day w/ plasma valproic acid levels monitoring.

Elderly: Initiate at lower dose and increase slowly.

Hepatic impairment: Contraindicated.

Monitoring sodium valproate plasma levels regularly is necessary to decide the next appropriate dosage. Target plasma rangeof sodium valproate: 50-100 mg/L

Indications: epilepsy and bipolar disorder, migraine, schizophrenia, treatment of status epilepticus alternatively to phenytoin.

Contraindications - liver impairment, concurrent administration of clonazepam, active liver disease, porphyria; mitochondrial and urea cycle disorders, pregnancy

Special precautions need to be taken in mentally retarded children with epilepsy. Dose should be reduced in children.

Side effects-anorexia, drowsiness,ataxia,tremor, nystagmus, somnolence, dizziness, fatigue, hyperammonaemic encephalopathy, hypothermia, hallucinations, pancreatitis, blood dyscrasias. Fatal hepatotoxicity could occur in children. .

Divalproex

Dosage

Oral

Primary generalised seizures

Adult: Initially, 10-15 mg/kg/day in 2-4 divided doses, if necessary, increase at 5-10 mg/kg/wk. Max: 60 mg/kg/day.

Child: 10 yr: Initially, 10-15 mg/kg/day in 2-4 divided doses, if necessary, increase at 5-10 mg/kg/wk. Max: 60 mg/kg/day.

Oral

Partial seizures

Adult: Initially, 10-15 mg/kg/day in 2-4 divided doses, if necessary, increase at 5-10 mg/kg/wk. Max: 60 mg/kg/day.

Child: 10 yr: Initially, 10-15 mg/kg/day in 2-4 divided doses, if necessary, increase at 5-10 mg/kg/wk. Max: 60 mg/kg/day.

Oral

Prophylaxis of migraine

Adult: 500 mg once daily for 1 wk, may increase to 1000 mg once daily.

Indications: Petit mal epilepsy,alternative/adjuvant drug for grand mal,psychomotor,myoclonic & temporal lobe epilepsy

Contraindications : liver impairment,concurrent administration with clonazepam

Special precaution : major surgery,mental retarded children with epilepsy,pregnancy

Side effects : anorexia,drowsiness,ataxia, tremor, hairloss, hyperammonaemia; pancreatitis, thrombocytopenia, weight gain

Barbiturates

Barbiturates are drugs that act as central nervous system (CNS) depressants, and bring about mild sedation to anesthesia. The following are classified as anticonvulsants:

Phenobarbital - it is the most widely used anticonvulsant. It also has sedative and hypnotic properties.

Mechanism of action:

Phenobarbitone is a short-acting barbiturate. It depresses the sensory cortex, reduces motor activity, changes cerebellar function, and produces drowsiness, sedation and hypnosis. Its anticonvulsant property is exhibited at high doses.

Onset: Hypnosis: Oral: 20-60 min; IV: Approx 5 min.

Duration: Oral: 6-10 hr; IV: 4-10 hr.

Absorption: peak plasma concentrations in about 2 hr (oral), and within 4 hr (IM).

Distribution: Crosses the placenta; enters breast milk. Protein-binding: 45-60%.

Metabolism: Partly hepatic.

Excretion: Via urine (as unchanged drug). Plasma half-life: 75-120 hr (adult), greatly prolonged (neonates), 21-75 hr (children).

Dosage

Oral

Partial seizures

Adult: 60-180 mg daily taken at night. Titrate dose according to patient's needs to achieve adequate control of seizures. Plasma concentrations of 15-40 mcg/ml (65-170 micromol/l) are usually required.

Child: 1 mth-12 yr: Initially, 1-1.5 mg/kg bid. Increase by 2 mg/kg daily, as required, to a maintenance dose of 2.5-4 mg/kg once or bid. 12-18 yr: Initially, 60-180 mg bid. Maintenance: 60-180 mg once daily.

Renal impairment: CrCl: <10 ml/min- Administer every 12-16 hr.

Hepatic impairment: Severe: Monitor plasma levels and adjust dose as necessary.

Oral

Generalised tonic-clonic seizures

Adult: 60-180 mg daily taken at night. Titrate dose according to patient's needs to achieve adequate control of seizures. Plasma concentrations of 15-40 mcg/ml (65-170 micromol/l) are usually required.

Child: 1 mth-12 yr: Initially, 1-1.5 mg/kg bid. Increase by 2 mg/kg daily, as required, to a maintenance dose of 2.5-4 mg/kg once or bid. 12-18 yr: Initially, 60-180 mg bid. Maintenance: 60-180 mg once daily.

Renal impairment: CrCl: <10 ml/min- Administer every 12-16 hr

Hepatic impairment: Severe: Monitor plasma levels and adjust dose as necessary.

Oral

Intravenous

Status epilepticus

Adult: Doses of 10 mg/kg to a max of 1 g.

Child: As sodium: Neonates and children up to 12 yr: Initially, 20 mg/kg by slow IV inj then 2.5-5 mg/kg once or bid. 12-18 yr: Initially 20 mg/kg (max 1 g) by slow IV inj then 300 mg bid.

Intravenous

Generalised tonic-clonic seizures

Child: As sodium: Neonates: Loading dose is 20 mg/kg by slow IV inj followed by 2.5-5 mg/kg once daily either by slow IV inj or orally.

Intravenous

Partial seizures

Child: As sodium: Neonates: Loading dose is 20 mg/kg by slow IV inj followed by 2.5-5 mg/kg once daily either by slow IV inj or orally.

Intramuscular

Sedation

Adult: As sodium: 30-120 mg/day in 2-3 divided doses.

Renal impairment: CrCl: <10 ml/min- Administer every 12-16 hr.

Hepatic impairment: Severe: Monitor plasma levels and adjust dose as necessary

Indications-mania, delirium, insomnia, anti convulsant. Phenobarbital sodium injection can be used to stop acute convulsions or status epilepticus.

Contraindications-concurrent administration with CNS deppresants,renal & hepatic impairment, pulmonary insufficiency, porphyria, pregnancy.

Side effects: Bradycardia, hypotension, syncope; drowsiness, lethargy, impaired judgement, hangover effect, confusion, somnolence, agitation, hyperkinesia, ataxia, nervousness, headache, insomnia, nightmares, hallucinations, anxiety, dizziness; agranulocytosis, thrombocytopenia, megaloblastic anaemia; thrombophlebitis (IV); respiratory depression. Long term administration may produce behavioral abnormalities, megaloblastic anemia, hyperactivity in children.

Carboxamides

Carbamazepine

Mechanism of Action

Carbamazepine reduces polysynaptic responses and blocks post-tetanic potentiation

Distribution: Crosses the placenta; enters breast milk. Protein-binding: 75%. Well distributed in the body.

Metabolism: Hepatic; converted to its metabolites.

Excretion: Urine (as metabolites), faeces; 5-26 hr (elimination half-life).

Dosage

Oral

Epilepsy

Adult: Initially, 100-200 mg once or bid gradually increased by increments of 100-200 mg every 2 wk. Maintenance: 0.8-1.2 g daily in divided doses. Max dose: 2 g daily.

Child: 1 yr: 100-200 mg daily, 1-5 yr: 200-400 mg daily, 5-10 yr: 400-600 mg daily, 10-15 yr: 0.6-1 g daily. Alternatively, 10-20 mg/kg daily in divided doses.

Rectal

Epilepsy

Adult: 250 mg every 6 hr for patients incapable of oral treatment.

Oral

Carbamazepine level should be considered if toxicity is suspected (>12mg/L) or in presence of possible noncompliance. The therapeutic reference range of carbamazepine is 4-12 mg/L. The minimum toxic level is 10 mg/kg.

Indications: epilepsy, partial seizures, primary epilepsy or secondary generalised forms of seizure with a tonic clonic component.

Contraindications : AVblock, bone marrow depression; porphyria, pregnancy, hepatic and renal impairment.

Side effects - leucopenia, proteinuria, renal failure, heart failure and hyponatraemia loss of appetite, dry mouth, headache, dizziness, ataxia

Levetiracetam

Mechanism of action

The drug binds to a synaptic vesicle glycoprotein, SV2A and inhibits presynaptic calcium channels reducing neurotransmitter release. This impedes impulse conduction across synapses.

Onset: 1 hr

Distribution: Not significantly protein bound (<10%). Distributed in breast milk.

Metabolism: Not extensively metabolised (24% into inactive metabolite); primarily by enzymatic hydrolysis.

Excretion: Excreted in the urine as both unchanged drug (66%) and metabolites. Plasma half life of 6-8 hr.

Dosage

Oral

Adjunct in partial seizures

Adult: Initially, 500 mg bid on the 1st day, increase in steps of 1 g at 2-4 wk intervals until effective antiepileptic control is achieved. Max: 3 g/day.

Child: 4-15 yr (<50 kg): Initially 10 mg/kg bid. May be increased by 10 mg/kg bid at 2-wk intervals. Adolescents ?16 yr or 50 kg initially 500 mg bid. May be increased by 500 mg bid at 2-4 wk intervals. Max: 60 mg/kg/day.

Renal impairment: Suitable total daily dose (given as 2 divided doses) based on CrCl.

Cr Cl: 50-79ml/min: 1-2 g, 30-49 ml/min: 500 mg - 1.5 g, <30 ml/min: 500 mg - 1 g

Oral

Monotherapy for partial seizures with or without secondary generalisation

Adult: Initially 500 mg daily, increased after 2 wk to 1 g daily. May further increase in steps of 500 mg at 2 wk intervals. Max: 3 g/day.

Renal impairment: Suitable total daily dose (given as 2 divided doses) based on CrCl.

Cr Cl: 50-79ml/min: 1-2 g, 30-49 ml/min: 500 mg - 1.5 g, <30 ml/min: 500 mg - 1 g

Intravenous

Adjunct in partial seizures

Adult: Initially, 500 mg bid on the 1st day. May increase in steps of 1 g at 2-4 wk intervals until effective antiepileptic control is achieved. Max: 3 g/day. No safety and efficacy data for IV usage >4 days.

Child: 4-15 yr (<50 kg): Initially 10 mg/kg bid via IV infusion over 15 min. May be increased by 10 mg/kg bid at 2-wk intervals. Adolescents ?16 yr or 50 kg initially 500mg bid via IV infusion over 15 min. May be increased by 500 mg bid at 2-4 wk intervals. Max: 60 mg/kg/day.

Renal impairment: Suitable total daily dose (given as 2 divided doses) based on CrCl.

Cr Cl: 50-79ml/min: 1-2 g, 30-49 ml/min: 500 mg - 1.5 g, <30 ml/min: 500 mg - 1 g

Intravenous

Monotherapy for partial seizures with or without secondary generalisation.

Adult: Initially 500 mg daily, increased after 2 wk to 1 g daily. May further increase in steps of 500 mg at 2 wk intervals. Max: 3 g/day. No safety and efficacy data for IV usage >4 days.

Renal impairment: Suitable total daily dose (given as 2 divided doses) based on CrCl.

Cr Cl: 50-79ml/min: 1-2 g, 30-49 ml/min: 500 mg - 1.5 g, <30 ml/min: 500 mg - 1 g

Indications - partial onset seizures,myoclonic seizures,primary tonic-clonic seizures

Contraindications : pregnancy,lactation

Special precautions should be taken in patients with renal and hepatic impairment; patients undergoing haemodialysis. If psychotic symptoms (eg hallucination) and behavioural symptoms (eg agitation, anxiety) occur, reduce dosage. Abrupt withdrawal may result in increased seizure frequency. May impair ability to drive or operate machinery during initial therapy.

Side effects : somnolence, dizziness, vertigo, ataxia,hairloss,depression, tremor, amnesia, headache, diplopia.

Topiramate

This is used for seizures including refractory seizures,simple & complex partial seizures.

Mechanism of Action

Topiramate is a sulfamate-substituted monosaccharide. It acts by blocking voltage-dependent sodium channels; augmenting the activity of ?-aminobutyric acid (GABA) at GABA-A receptor; antagonising AMPA glutamate receptors; and inhibiting carbonic anhydrase.

Absorption: peak plasma concentrations after 2 hr. Bioavailability unaffected by food.

Distribution: Protein-binding: 9-17%. Volume of distribution in man is double that in woman. Crosses the placenta, distributed into breast milk.

Metabolism: Not extensively metabolised.

Excretion: Excreted by urine (as unchanged drug and metabolites); elimination half-life: 21 hr. Children has a higher clearance and shorter elimination half-life than adults.

Dosage

Oral

Adjunct for seizures associated with the Lennox-gastaut syndrome

Adult: Initially, 25 mg at night for 1 wk, thereafter increase in steps of 25-50 mg at intervals of 1-2 wk until effective dose is achieved. Doses >25 mg/day should be taken in 2 divided doses. Usual dose: 200-400 mg daily. Max: 800 mg daily.

Child: 2-16 yr: Initially, 25 mg nightly for the 1st wk increased at intervals of 1-2 wk by increments of 1-3 mg/kg daily according to response. Daily doses of >25 mg should be taken in 2 divided doses. Usual dose: 5-9 mg/kg daily. Max: 30 mg/kg/day.

Hepatic impairment: Dosage adjustment may be needed.

Oral

Epilepsy

Adult: Monotherapy: Initially, 25 mg at night for 1 wk, thereafter increase in steps of 25-50 mg at intervals of 1-2 wk. Doses >25 mg/day should be taken in 2 divided doses. Usual dose: 100-400 mg daily. Max: 400 mg daily. Adjunctive treatment: Initially, 25 mg at night for 1 wk, thereafter increase in steps of 25-50 mg at intervals of 1-2 wk until effective dose is achieved. Doses >25 mg/day should be taken in 2 divided doses. Usual dose: 200-400 mg daily. Max: 800 mg daily.

Child: 10-16 yr: Initially, 0.5-1 mg/kg at night for the 1st wk, increased at intervals of 1-2 wk by increments of 0.5 to 1 mg/kg daily. Usual dose: 3-6 mg/kg daily. Daily doses >25 mg should be taken in 2 divided doses. Max: 16 mg/kg/day.

Hepatic impairment: Dosage adjustment may be needed.

Oral

Indications-adjunctive treatment of partial seizures,with or without secondary generalisation.primary generalised tonic clonic seizures.

Contraindications : lactation

Special precautions should be taken in cases of renal or hepatic impairment, pregnancy. Drug may impair ability to drive or operate machinery. Adequate hydration should be maintained to reduce the risk of renal calculi especially in predisposed patients. Abrupt withdrawal should be avoided; decrease dose by 100 mg daily at weekly intervals.

Side effects : weight los,impaired cognition & memory,confusion,mood disorders, dizziness, drowsiness, fatigue, migraine, visual disturbances, oligohidrosis, hyperthermia and hyperammonaemic encephalopathy.

GABA analogs

Gabapentin- used as an adjunctive medication to control partial seizures (effective when added to other antiseizure drugs). Gabapentin is well tolerated in most patients, has a relatively mild side-effect profile, and passes through the body unmetabolized.

Mechanism of Action

Gabapentin is structurally related to the neurotransmitter GABA but is neither a GABA agonist nor antagonist. High affinity gabapentin binding sites are located throughout the brain. These sites correspond to the presence of voltage-gated Ca channels particularly controlling the ?-2/?-1 subunit. This channel appears to be located presynaptically and may modulate the release of excitatory neurotransmitters which participate in epileptogenesis and nociception.

Absorption: Absorbed from the GI tract. Bioavailability may be increased w/ food esp high-fat meals. Time to peak plasma concentration: W/in 2-3 hr; 5 hr in fasting state and 7.3 hr (as enacarbil).

Distribution: Enters breast milk. Volume of distribution: 58 ± 6 L. Plasma protein binding: <3%.

Metabolism: As enacarbil: Undergoes extensive first-pass metabolism mainly in enterocytes and liver (to a lesser extent) to form gabapentin, CO2, acetaldehyde and isobutyric acid.

Excretion: Via urine (as unchanged drug) and the remainder in the faeces. Elimination half-life: Approx 5-7 hr.

Dosage

Oral

Epilepsy

Adult: Initially, 300 mg on the 1st day, 300 mg bid on the 2nd day and 300 mg tid on the 3rd day. Thereafter, may increase dose until effective antiepileptic control is achieved. Usual maintenance range: 0.9-3.6 g daily; daily dose to be taken in 3 equally divided doses and max dosing interval: 12 hr. Max: 4.8 g daily.

Child: 6 yr Initially, 10-15 mg/kg daily, titrated over a period of approx 3 days until effective antiepileptic control is achieved, usually w/in 25-35 mg/kg daily in 3 divided doses w/ max interval of 12 hr. Max: 50 mg/kg daily.

Renal impairment: Haemodialysis: Loading dose: 300-400 mg followed by 200-300 mg after each 4 hr of haemodialysis.

CrCl (ml/min): <15: 300 mg on alternate days to 300 mg daily, 15-29: 300 mg on alternate days to 600 mg daily, 30-49: 300-900 mg daily, 50-79: 600-1,800 mg daily.

Oral

Indications: epilepsy, neuropathic pain

Special precautions should be taken in patients with mixed seizures including absences, renal impairment undergoing haemodialysis, children, pregnancy and lactation. To discontinue therapy if acute pancreatitis develops. Abrupt withdrawal may cause rebound seizures. Drug impairs the ability to drive or operate machinery.

Side effects

Somnolence/sedation, blood glucose fluctuation, , elevated creatine kinase and LFTs, jaundice, fever, hyponatraemia, movement disorder, Stevens-Johnson syndrome, pneumonia, viral and respiratory infection, otitis media, leucopenia, anorexia, behavioral disturbances; dizziness, ataxia, convulsions, hyperkinesias, dysarthria, amnesia, tremor, insomnia, headache, amblyopia, diplopia, vertigo, dry mouth or throat, flatulence, dental abnormalities, hypersensitivity, musculoskeletal pain, twitching, impotence, decreased WBC.

Succinimides

Ethosuximide

It is a succinimide anticonvulsant, used mainly in absence seizures. It is sold by pfizer under the name zarontin.

Mechanism of action

It binds to T-type voltage sensitive calcium channels and blocks them.

Distribution : Widely distributed throughout the body, but not significantly bound to plasma proteins.

Metabolism : Extensively hydroxylated in the liver to its principal metabolite which is inactive.

Excretion : Excreted in the urine mainly as metabolite, either free or conjugated.

Dosage

Oral

Absence seizures

Adult: Initially, 500 mg daily, may increase in steps of 250 mg at intervals of 4-7 days. Usual dose: 1-1.5 g daily. Optimum plasma concentration: 40-100 mg/L (300-700 micromol/L). Max: Up to 2 g in some patients. Strict supervision is recommended if dose >1.5 g daily.

Child: <6 yr: Initially, 250 mg daily, may increase gradually to usual dose of 20 mg/kg daily. 6 yr: Initially, 500 mg daily, may increase in steps of 250 mg at intervals of 4-7 days. Usual dose: 1-1.5 g daily. Max: <6 yr: Up to 1 g/day and ?6 yr: 2 g/day .

Max Dosage:

Indications: absence (petite mal) seizures; ineffective in partial seizures with complex symptomatology or tonic-clonic seizures.

Contraindications: Hypersensitivity, pregnancy and lactation.

Side effects: Blood toxicities and disorders; headache, fatigue, lethargy, drowsiness, dizziness, ataxia, hiccup and mild euphoria; more rarely, psychotic states, rashes, hepatic and renal changes, SLE, erythema multiforme. Gum hypertrophy, irritability, hyperactivity, sleep disturbances, night terrors, inability to concentrate, aggressiveness, increased libido, myopia.

Special Precautions: Hepatic or renal impairment, porphyria. Complete blood cell count, liver function tests, and urinalysis should be performed periodically. Drug increase the risk of grand mal seizures when used alone in mixed types of epilepsy. Avoid sudden withdrawal. May impair ability to drive or operate machinery.

Clobazam

Mechanism of action

Clobazam binds to one or more specific GABA receptors at several sites within the CNS. Increased permeability of neuronal membrane to chloride ions results in GABA's inhibitory effect leading to hyperpolarisation and stabilisation.

Absorption: peak plasma concentrations after 1-4 hr.

Distribution: Rapidly crosses the blood-brain barrier. Protein-binding: 85%.

Metabolism: Hepatic by demethylation and hydroxylation.

Excretion: Urine (as unchanged drug and metabolites); 18-42 hr (elimination half-life).

Dosage

Oral

Short-term management of anxiety, Adjunct in epilepsy

Adult: 20-30 mg as a single dose at night or as daily divided doses, increased to 60 mg/day in severe conditions.

Child: 3-12 yr: 125 mcg/kg bid increased every 5 days. Usual maintenance dose: 250 mcg/kg bid. Max: 500 mcg/kg bid.

Elderly: or debilitated patients: 10-20 mg daily.

Hepatic impairment: Dose adjustment may be needed.

Indications-typical or atypical absence seizures,in those who have myoclonic jerks and secondary generalised tonic/clonic seizure

Contraindications: Hypersensitivity; history of drug dependence; myasthaenia gravis; pregnancy (1st trimester), lactation; serious liver damage; sleep apnoea syndrome; impaired respiratory function.

Side effects: dizziness, fine tremors; worsening of respiratory symptoms in predisposed individuals; ataxia, drowsiness, headache, confusion; loss of libido, motor dysfunction; dependence; visual disturbances and weight gain.

39. Analgesics

An analgesic (commonly known as a painkiller) is any member of the diverse group of drugs used to relieve pain. Analgesic drugs act in various ways on the peripheral and central nervous system; they include paracetamol (acetaminophen), the nonsteroidal anti-inflammatory drugs (nsaids) such as the salicylates, narcotic drugs such as morphine, synthetic drugs with narcotic properties such as tramadol, and various others. Some other classes of drugs not normally considered analgesics are used to treat neuropathic pain syndromes; these include tricyclic antidepressants and anticonvulsants.

Paracetamol

Mechanism of action

Paracetamol exhibits analgesic action by peripheral blockage of pain impulse generation. IIts weak anti-inflammatory activity is related to inhibition of prostaglandin synthesis in the CNS.

Onset: Oral: <1 hr. IV: 5-10 min (analgesia); w/in 30 min (antipyretic).

Duration: 4-6 hr (analgesia). IV: 6 hr (antipyretic).

Absorption: Time to peak plasma concentration: Approx 10-60 min (oral).

Distribution: Distributed into most body tissues; crosses the placenta and enters breast milk. Plasma protein binding: Approx 25%.

Metabolism: Hepatic via glucuronic and sulfuric acid conjugation. N-acetyl-p-benzoquinoneimine (minor hydroxylated metabolite), is usually produced in very small amounts by CYP2E1 and CYP3A4 isoenzymes in the liver and kidneys.

Excretion: Mainly via urine (as glucuronide and sulfate conjugates, <5% as unchanged drug). Elimination half-life: Approx 1-3 hr.

Dosage

Oral

Mild to moderate pain and fever

Adult: 0.5-1 g 4-6 hrly. Max: 4 g daily.

Child: 3 to <6 mth 60 mg; 6 mth to <2 yr 120 mg; 2 to <4 yr 180 mg; 4 to <6 yr 240 mg; 6 to <8 yr 240 or 250 mg; 8 to <10 yr 360 or 375 mg; 10 to <12 yr 480 or 500 mg; 12-16 yr 480 or 750 mg. Given 4-6 hrly if necessary. Max: 4 doses in 24 hr.

Intravenous

Mild to moderate pain and fever

Adult: 33-50 kg: 15 mg/kg as a single dose, at least 4 hrly. Max: 60 mg/kg (up to 3 g) daily; >50 kg: 1 g as a single dose, at least 4 hrly. Max: 4 g daily. Admin by infusion over 15 min.

Child: <10 kg: 7.5 mg/kg as a single dose, at least 4 hrly. Max: 30 mg/kg daily; 10-33 kg: 15 mg/kg as a single dose, at least 4 hrly. Max: 60 mg/kg (up to 2 g) daily; >33-50 kg: 15 mg/kg as a single dose, at least 4 hrly. Max: 60 mg/kg (up to 3 g) daily. Admin by infusion over 15 min.

Renal impairment: CrCl (ml/min);- ≤30: Increase dosing interval to 6 hrly

Hepatic impairment : Max: 3 g/day.

Rectal

Mild to moderate pain and fever

Adult: As supp: 0.5-1 g 4-6 hrly. Max: 4 g daily.

Child: 3 mth to <1 yr 60-125 mg; 1 to <5 yr 125-250 mg; 5-<12 yr 250-500 mg. Given 4-6 hrly if necessary, up to 4 times daily.

Side effects: thrombocytopenia, leucopenia, pancytopenia, neutropenia, agranulocytosis, rarely, hypotension and tachycardia.

Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalised exanthematous pustulosis, acute renal tubular necrosis and hepatotoxicity could be fatal complications.

NSAIDS

Mechanism of action

NSAIDS inhibit cyclooxygenase, leading to a decrease in prostaglandin production; this reduces pain and inflammation.

Diclofenac Sodium

Dosage:100-150mg daily in 2-3 divided doses

Indications: headache, migraine

Contraindications: active or recurrent peptic ulcers,hypersensitivity,asthama

Special precaution: patients having history of GI bleeding,haematemesis,or malena,ulcerative colitis, retension of fluid

Side effects : epigastric pain

Aceclofenac

Dosage : 100mg orally bd,dosages reduction to be considered in hepatic impairment

Indications : for pain relief and inflammation

Contraindications : moderate to severe renal impairment; pregnancy (3rd trimester); history of peptic ulceration or GI bleed; patients with infections.

Special precautions : Cautiously administer to patients with GI disease, ulcerative colitis, Crohn's disease, haematological abnormalities, hepatic porphyria; history of bronchial asthma; history of heart failure or hypertension; mild renal, hepatic or cardiac impairment. May impair ability to drive or operate machinery.

Side effects : dizziness, nephrotoxicity; blood dyscrasias could be fatal.

Opiates and Morphinomimetics

Morphine, the archetypal opioid, and various other substances (e.g. Codeine, oxycodone, hydrocodone, diamorphine, pethidine) all exert a similar influence on the cerebral opioid receptor system. Tramadol and buprenorphine are thought to be partial agonists of the opioid receptors. Dosing of all opioids may be limited by opioid toxicity (confusion, myoclonic jerks and pinpoint pupils), but there is no dose ceiling in patients who tolerate this.

Mechanism of action

Morphine is a phenanthrene derivative which acts mainly on the CNS and smooth muscles. It binds to opiate receptors in the CNS altering pain perception and response. Analgesia isthought to be due to its action at the mu-1 receptors

Onset: Approx 30 min (conventional tab); 5-10 min (IV).

Duration: 4 hr (conventional tab); 8-24 hr (extended-release tab/cap).

Distribution: Distributed throughout the body mainly in the kidneys, liver, lungs and spleen, w/ lower concentrations in the brain and muscles. Crosses the blood-brain barrier and placenta; enters breast milk. Volume of distribution: 1-6 L/kg. Plasma protein binding: Approx 35%.

Metabolism: Metabolised in the liver and gut via glucuronidation to produce morphine-3-glucoronide and morphine-6-glucoronide; undergoes extensive first-pass metabolism.

Excretion: Via urine (approx 90%) and through the bile into the faeces (10%) mainly as conjugates. Mean plasma elimination half-life: Approx 2 hr (morphine); 2.4-6.7 hr (morphine-3-glucoronide).

Dosage

Oral

Moderate to severe pain

Adult : 5-20 mg 4 hrly. Extended-release: 5-20 mg 12 hrly. Dosage is dependent on the severity of pain.

Child : 3-5 yr 5 mg 4 hrly; 6-12 yr 5-10 mg 4 hrly.

Hepatic impairment : Dosage may need to be reduced.

Parenteral

Moderate to severe pain

Adult: IM/SC: 5-20 mg; 2.5-10 mg via slow IV inj over 4-5 min w/ patient in recumbent position or a starting dose of 1-2 mg/hr via continuous IV infusion (max: 100 mg/day; 4 g/day in cancer patients). Doses may be adjusted according to severity of pain and patient's response.

Hepatic impairment: Dosage may need to be reduced.

Rectal

Severe pain

Adult : 10-20 mg 4 hrly. Dosage may be increased as required.

Intraspinal or intrathecal administration could be done in cases of severe pain. This should be done by a pain management specialist, a neurosurgeon or a anaesthesiologist.

Contraindications: Respiratory depression, obstructive airway disease, delayed gastric emptying, heart failure, chronic lung disease, known or suspected paralytic ileus, phaeochromocytoma. Concurrent administration with MAOI or within 2 weeks after treatment.

Side-effects : anorexia, taste disturbance, dyspepsia, respiratory depression, sedation, dizziness, confusion, insomnia, headache, somnolence, involuntary muscle contractions, hyperhidrosis, asthenic conditions, HTN, bronchospasm, seizures, amenorrhoea, rhabdomyolysis, nystagmus.

Gradual tapering of the dose is required to avoid withdrawal symptoms.

Specific agents

In patients with chronic or neuropathic pain, various other substances may have analgesic properties. Tricyclic antidepressants, especially amitriptyline, have been shown to improve pain in what appears to be a central manner. The exact mechanism of carbamazepine, gabapentin and pregabalin is similarly unclear, but these anticonvulsants are used to treat neuropathic pain.

Amitriptyline

Mechanism of action

Amitriptyline is a dibenzocycloheptadiene tricyclic antidepressant. It increases synaptic

concentration of serotonin and/or norepinephrine in the CNS by blocking the neuronal reuptake of norepinephrine and serotonin.

Absorption: Time to peak plasma concentration: Approx 6 hr.

Distribution: Crosses the placenta and is distributed into breast milk. Volume of distribution: Approx 18-22 L/kg. Extensively bound to plasma protein.

Metabolism: Undergoes extensive first-pass metabolism and is demethylated hepatically by CYP3A4, CYP2C9 and CYP2D6 isoenzymes to nortriptyline (active metabolite). Other paths involve hydroxylation by CYP2D6 and N-oxidation.

Excretion: Via urine (mainly as metabolites, either free or conjugated). Elimination half-life: Approx 9-25 hr.

Dosage

Oral

Adult: Initially, 50-75 mg/day as a single dose (at bedtime) or in divided doses, may increase gradually to 150 mg/day. Max: 300 mg/day in severe depression.

Child: Adolescent: Initially, 25-50 mg/day as a single dose (at bedtime) or in divided doses.

Elderly: Initially, 25-50 mg/day as a single dose (at bedtime) or in divided doses.

Contraindications: Recent MI, arrhythmias (particularly heart block), mania. Concomitant use with MAOI or within 14 days of discontinuing the MAOI; linezolid, IV methylene blue.

Side effects

Hypotension, HTN, tachycardia, palpitation, MI, arrhythmias, heart block, stroke, changes in AV conduction and ECG, confusion, paraesthesia; incoordination, dysarthria, extrapyramidal symptoms (e.g. tardive dyskinesia); seizures; tinnitus, dry mouth, blurred vision, paralytic ileus, hyperpyrexia, urinary retention, bone-marrow depression including agranulocytosis, eosinophilia, leucopenia, thrombocytopenia, fatigue, headache, parotid swelling, alopecia. Gynaecomastia and galactorrhoea, impotence and altered liver function.

Pregabalin

Mechanism of action

Pregabalin is an analog of the neurotransmitter GABA. It binds to the ?2-? subunit resulting in modulation of Calcium channels and reduction in the release of several neurotransmitters, including glutamate, norepinephrine, serotonin, dopamine, calcitonin gene-related peptide and substance P.

Absorption: Time to peak plasma concentration: W/in 1.5 hr.

Distribution: Volume of distribution: 0.5 L/kg. Not bound to plasma protein.

Metabolism: Negligible metabolism.

Excretion: Via urine (approx 98%) as unchanged drug). Elimination half-life: 6.3 hr.

Dosage

Oral

Neuropathic pain

Adult: Initially, 150 mg/day, may increase to 300 mg/day after 3-7 days. Max: 600 mg/day after a 7-day interval. All doses to be given in 2 or 3 divided doses.

Renal impairment: Dose adjustment required in renal impairment

CrCl (ml/min): - 30 to <60: 75 mg/day. Max: 300 mg/day. All doses to be given in 2 or 3 divided doses,

15 to <30: Initially, 25-50 mg/day. Max: 150 mg/day. All doses to be given as a single dose or in 2 divided doses, <15: Initially, 25 mg/day. Max: 75 mg/day. All doses to be given as a single dose.

Side effects: Somnolence, dizziness,blurred vision, muscle cramp, insomnia, amnesia, paraesthesia, increased appetite, wt gain, euphoria, confusion, reduced libido, erectile dysfunction; attention, memory, coordination and gait disturbances; fall, feeling drunk, abnormal feeling. Rarely, Stevens-Johnson syndrome, rhabdomyolysis, breast enlargement, gynaecomastia.

Potentially Fatal : Angioedema.

Carbamazepine is also used in treatment of Trigeminal neuralgia

Dosage

Adult: Initially, 100 mg once or bid gradually increased as necessary. Maintenance: 400-800 mg daily in 2-4 divided doses. Max: 1.2 g daily.

Gabapentin

Neuropathic pain

Adult: Initially, 300 mg on the 1st day, 300 mg bid on the 2nd day and 300 mg tid on the 3rd day; alternatively, 900 mg daily in 3 divided doses. Dose may increase in increments of 300 mg every 2-3 days. Max: 3,600 mg daily.

Renal impairment: Haemodialysis: Loading dose: 300-400 mg followed by 200-300 mg after each 4 hr of haemodialysis.

CrCl (ml/min): <15: 300 mg on alternate days to 300 mg daily, 15-29: 300 mg on alternate days to 600 mg daily, 30-49: 300-900 mg daily, 50-79: 600-1,800 mg daily.

Oral

Postherpetic neuralgia

Adult: As gabapentin enacarbil: Modified-release preparation: Initially, 600 mg in the morning for 3 days, then increased to 600 mg bid.

Renal impairment: As gabapentin enacarbil: Modified-release preparation: Haemodialysis: 300 mg after each dialysis session, may increase to 600 mg if needed.

CrCl (ml/min): - <15: 300 mg in the morning on alternate days, may increase to 300 mg daily in the morning., 15-29: 300 mg in the morning on days 1 and 3 followed by 300 mg daily in the morning, may increase to 300 mg bid., 30-59: 300 mg in the morning for the 1st 3 days followed by 300 mg bid, may increase to 600 mg bid.

Combinations

Analgesics are frequently used in combination, such as the paracetamol and codeine preparations found in many non-prescription pain relievers. They can also be found in combination with vasoconstrictor drugs such as pseudoephedrine for sinus-related patients.the use of paracetamol, as well as aspirin, ibuprofen, naproxen, and other nsaids concurrently with weak to mid-range opiates has been shown to have beneficial effects.

Topical

Topical analgesia is generally recommended to avoid systemic side-effects. Painful joints, for example, may be treated with an ibuprofen- or diclofenac-containing gel. Lidocaine and steroids may be injected into painful joints for longer-term pain relief.

Atypical and/or adjuvant analgesics

Orphenadrine, cyclobenzaprine, scopolamine, atropine, gabapentin, first-generation antidepressants and other drugs possessing anticholinergic and/or antispasmodic properties are used in many cases along with analgesics to potentiate centrally acting analgesics such as opioids when used against pain especially of neuropathic origin and to and modulate the effects of many other types of analgesics by action in the parasympathetic nervous system.

Ibuprofen, naproxen

Indication : analgesic, antipyretic, musculo skeletal disorder

Dosage : ibuprofen 200-600 mg thrice daily naproxen-250 mg twice daily

Contraindication : pregnancy, active peptic ulcer, gi bleeding, lactation

Special precaution : asthama, bleeding tendencies, cardiovascular disorder

Side effect : jaundice,thrombocytopenia

40. Migraine Drugs

Migraine treatment depends on the duration and severity of pain, associated symptoms, degree of disability, and initial response to therapy. Drugs can be used to decrease the frequency/ intensity of migraine. Many of these have actions in the serotonergic system.

Propanolol

Mechanism of action

Propranolol inhibits the norepinephrine transporter and stimulates norepinephrine release.It causes vasodilation, leading to improved blood supply to the brain and relief of headache and migraine.

Dosage

Prophylaxis of migraine

Adult: As conventional tab or oral soln: Initially, 40 mg bid or tid. Usual range: 120-240 mg/day. As extended release cap: 80 mg once daily, may be increased to 160 mg once daily. Max: 240 mg/day.

Child: As conventional tab or oral soln: ?12 yr 10-20 mg bid or tid. >12 yr Initially, 40 mg bid or tid increased to wkly intervals up to 160 mg/day. Max: 240 mg/day.

Hepatic impairment: Severe: 20 mg tid.

Contraindications :

Sinus bradycardia, cardiogenic shock, sick sinus syndrome, Raynaud's syndrome, 2nd and 3rd degree heart block, overt CHF, bronchial asthma, COPD, untreated phaeochromocytoma, Prinzmetal's angina; severe peripheral arterial disease, metabolic acidosis. Concomitant use with thioridazine.

Side effects :

Bradycardia, hypotension, syncope, shock, angina pectoris. giddiness, ataxia, dizziness, irritability, sleepiness, hearing loss, and visual disturbances to vivid dreams, hallucinations, and confusion. Hypoglycaemia, transient eosinophilia, thrombocytopenic and nonthrombocytopenic purpura; elevated levels of K, transaminases, and BUN. Rarely, Peyronie's disease and dry eyes.

Flunarizine

Mechanism of action:

Flunarizine has H1-receptor blocking action and calcium-channel blocking effect.

Distribution: Highly lipophilic. Protein-binding: >90%.

Metabolism: Extensive.

Excretion: Via bile (as metabolites); 18 days (elimination half-life).

Dosage

Oral

Adult: 5-10 mg daily at bedtime.

Contraindications: Pregnancy, lactation, GI or urinary tract obstruction, acute porphyrias.

Side effects : Drowsiness, headache, depression, insomnia, extrapyramidal reactions, galactorrhoea.

Prophylaxis treatment:

Beta-adrenergic blockers: propronolol- starting with 40 mg bd may be increased to 160mg if required.

Calcium channel blockers: verapamil, flunarizine 5rmg od

Treatment of acute attack:

For mild to moderate migraine attacks or severe attacks that have been responsive in the past to similar agents, use the following options:

NSAIDS (oral)

Combination analgesics containing caffeine

Isometheptene combinations

For moderate to severe migraine or mild to moderate migraines that respond poorly to nsaids, use:

Migraine-specific drugs (i.e., triptans [naratriptan, rizatriptan, sumatriptan, zolmitriptan], dhe)

Or

Combination drug therapy (e.g., aspirin plus acetaminophen* plus caffeine)

Or

Other drugs such as ergotamine

For migraine accompanied by nausea or vomiting, use a non-oral route of administration.

Sumatriptan

Mechanism of action

Sumatriptan is a selective serotonin agonist that acts at 5-HT1 receptors. It causes vasoconstriction of cranial arteries and inhibition of neurogenic inflammatory processes in the CNS.

Onset: Oral: 30 min; Intranasal: 15 min; subcutaneous: 10-15 min.

Absorption: peak plasma concentrations reached in 2 hr (oral), 25 min (subcutaneous), 1.5 hr (intranasal).

Distribution: Enters breast milk. Protein-binding: 14-21%

Metabolism: Extensive first-pass metabolism by MAO type A

Excretion: Mainly via urine (as inactive indole acetic acid derivative and its glucuronide), via faeces (as unchanged drug and metabolites). Elimination half-life: 2hr.

Dosage

Oral

Migraine

Adult: >18 yr: 50-100 mg repeated at 2-hr intervals if migraine recurs. Max: 300 mg/24 hr.

Hepatic impairment: Max single dose: 50 mg.

Nasal

Migraine

Adult: 12-17 yr: 10 mg into 1 nostril, repeated at least 2 hr after the 1st dose if symptoms recur. Max: 20 mg/24 hr. >18 yr: 20 mg into 1 nostril, repeated at least 2 hr after the 1st dose if symptoms recur. Max: 40 mg/24 hr.

Hepatic impairment: Dose reduction needed.

Subcutaneous

Migraine

Adult: >18 yr: 6 mg as a single dose inj, repeated at least 1 hr after the 1st dose if symptoms persist. Max: 12 mg/24 hr.

Hepatic impairment: Dose reduction needed.

Subcutaneous

Cluster headache

Adult: >18 yr: 6 mg as a single dose inj, repeated at least 1 hr after the 1st dose if symptoms persist. Max: 12 mg/24 hr.

Hepatic impairment: Dose reduction needed.

Indications-migraine, cluster headache.

Contraindications - Not to be used prophylactically and in patients with basilar or hemiplegic or ophthalmoplegic migraine. History of MI or stroke, severe hepatic impairment, ischaemic heart disease, uncontrolled hypertension, peripheral vascular disease, hypersensitivity to sulfonamides.

Special precaution-paediatrics,pregnancy,lactation not recommended,IHD ,hepatic impairment

Side effects - Transient hypertension, hypotension, dizziness, flushing, fatigue, drowsiness, weakness, seizures, heat, tightness in any part of body, paraesthesia, seizures, irritation of nasal mucosa and epistaxis. Rebound headache with frequent use.

Potentially Fatal: Cardiac arrhythmias, MI.\

Sodium valproate

Dosage

Oral

Prophylaxis of migraine

Adult: Initially, 250 mg bid. Max: 1 g/day; extended release: 500 mg once daily for 7 days then increase to 1 g once daily. Usual range: 500-1000 mg/day.

Elderly: Initiate at lower dose and increase slowly.

Hepatic impairment: Contraindicated

Topiramate

Prophylaxis of migraine

Adult: >16 yr: Initially 25 mg daily at night for 1 wk, increased in steps of 25-mg at wkly intervals. Usual dose: 50-100 mg daily in 2 divided doses. Daily doses >25 mg should be taken in 2 divided doses.

Hepatic impairment: Dosage adjustment may be needed.

41. Stroke Drugs

Aspirin

It is acetylsalic acid

Mechanism of action

It inhibits cyclooxygenase, which is responsible for the synthesis of prostaglandin and thromboxane. It also inhibits platelet aggregation.

Duration: 4-6 hr.

Absorption: Peak plasma concentrations after 1-2 hr.

Distribution: Widely distributed; crosses the placenta; enters breast milk. Protein-binding: 80-90%.

Metabolism: Hepatic; converted to metabolites.

Excretion: Via urine by glomerular filtration, active renal tubular secretion and passive tubular reabsorption (as unchanged drug); via haemodialysis; 15-20 minutes (elimination half-life, parent drug).

Dosage - post stoke patients-50 mg, 75 mg, 150 mg or 300mg daily depending upon the age.

Contraindications - peptic ulcer, liver disease, bleeding tendencies, pregnancy (3rd trimester), children <12 yr, patients with haemophilia or haemorrhagic disorders, gout, severe renal or hepatic impairment, lactation.

Side effects - tinnitus,vertigo, impairment of hearing & vision, excitement & mental confusion, electrolyte imbalance. Reye's syndrome (children <12 yr). Hepatotoxicity; CNS depression which may lead to coma; CV collapse and respiratory failure; paroxysmal bronchospasm and dyspnoea.

Clopidogrel

Mechanism of action

Clopidogrel inhibits adenosine diphosphate (ADP) from binding to its receptor sites on the platelets and subsequent activation of glycoprotein GP IIb/IIIa complex thus preventing fibrinogen binding, platelet adhesion and aggregation.

Distribution: Protein-binding: Extensive.

Metabolism: Hepatic: Extensive; converted to inactive carboxylic acid derivative and thiol derivative (active).

Excretion: Via urine and faeces (as metabolites and unchanged drug).

Dosage - prophylaxis of thromboembolic events 75 mg once daily.

Contraindications - Active pathological bleeding. Administration within 7 days after MI and ischaemic stroke, coagulation disorders, lactation

Precautions - patients at risk of increased bleeding from trauma, surgery, or other pathological conditions; ulcer; renal and hepatic impairment; history of bleeding or haemostatic disorders.

Side effects - paraesthesia, vertigo, headache, dizziness

Potentially Fatal: Bleeding disorders including GI and intracranial haemorrhage. Blood dyscrasias.

Statins

These are dyslipidemic drugs which are administered for controlling of cholestrol, rosuvasatin and atorvastatin are commonly being used.

Atorvastatin

Mechanism of action

Atorvastatin inhibits HMG - CoA reductase, the enzyme that catalyses the conversion of HMG-CoA to mevalonate. This results in the induction of the LDL receptors and stimulation of LDL catabolism, leading to lowered LDL-cholesterol levels.

Distribution : Volume of distribution: Approx 381 L. Plasma protein binding: 98%.

Metabolism: Metabolised by CYP3A4 isoenzyme to active ortho- and parahydroxylated derivates and an inactive ?-oxidation product.

Excretion: Via faeces (as metabolites); urine (<2% as unchanged drug). Elimination half-life: Approx 14 hr.

Dosage - 20 mg- 80 mg daily

Contraindications: Active liver disease or unexplained persistent elevations of serum transaminases. Concomitant use w/ciclosporin, gemfibrozil, telaprevir, tipranavir. Pregnancy and lactation.

Side effects - Headache, anorexia. Pain in extremity, musculoskeletal and pharyngolaryngeal; myopathy, muscle spasms, myalgia, arthralgia, nasopharyngitis, insomnia, UTI. Increased serum aminotransferase, glycosylated haemoglobin and fasting serum glucose levels.

Potentially Fatal: Severe rhabdomyolysis w/ acute renal failure. Hepatitis, pancreatitis. Rarely, Stevens-Johnson syndrome, anaphylaxis, toxic epidermal necrolysis.

Rosuvastatin

Mechanism of action

Rosuvastatin is a selective and competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme in cholesterol synthesis. It increases the number of hepatic LDL receptors on the cell surface, enhancing uptake and catabolism of LDL. It also decreases apolipoprotein B, triglycerides and increases HDL.

Absorption: Time to peak plasma concentration: Approx 5 hr.

Distribution: Volume of distribution: 134 L. Plasma protein binding: Approx 90%.

Metabolism: Limited metabolism via CYP2C9 isoenzyme.

Excretion: Via faeces (approx 90%); urine (approx 5% as unchanged drug). Elimination half-life: Approx 19 hr.

Dosage - 20 mg- 80 mg daily

Contraindications: Active liver disease or unexplained persistent elevated serum transaminases. Severe renal impairment. Concomitant use w/ ciclosporin and gemfibrozil. Pregnancy and lactation.

Side effects - Headache, dizziness, myalgia, chest pain, peripheral oedema, depression, insomnia, rash, paraesthesia, asthenia, abnormal LFT, elevated serum transaminase levels.

Potentially Fatal: Severe rhabdomyolysis w/ acute renal failure. Hepatitis, pancreatitis. Rare: Stevens-Johnson syndrome, anaphylaxis, toxic epidermal necrolysis.

Anticoagulants

Coumarins (Warfarin)

These are anticoagulants, antiplatelets & fibrinolytics (thrombolytics)

Mechanism of action – Warfarin inhibits synthesis of vit K-dependent coagulation factors VII, IX, X and II and anticoagulant protein C and its cofactor protein S. Extension of the clot can be prevented. Secondary embolic phenomena are avoided.

Onset: 24 hr

Duration: 2-5 days.

Absorption: Peak plasma concentration: within first 4 hr.

Distribution: Protein binding: Extensive (99%) to albumin. Crosses placenta.

Metabolism: Hepatic;

Excretion: Via urine (as metabolites after reabsorption from the bile); 37 hr (elimination half-life).

Dosage

Oral

Treatment and prophylaxis of venous thromboembolism

Adult: Initially, 5 mg daily. Rapid anti-coagulation: Initially, 10 mg daily for 2 days. Adjust subsequent doses based on PT/INR. Usual maintenance dose: 2-10 mg daily.

Elderly: Lower initial dose.

Hepatic impairment: Severe: Avoid.

Containdications - haemorrhagic tendencies; recent surgery; peptic ulcer; severe hypertension; senility; aneurysms; alcoholism; severe renal and hepatic impairment; pregnancy.

Side effects - drop in haematocrit, purple toes syndrome, skin necrosis, hepatic dysfunction, pancreatitis

Potentially Fatal : Haemorrhage (narrow therapeutic index).

Low molecular weight heparin

Enoxaparin

Enoxaparin is a low molecular weight heparin w/ anticoagulant properties.

Mechanism of action

It acts by enhancing the inhibition rate of activated clotting factors including thrombin and factor Xa through its action on antithrombin III.

Onset: 3-5 hr.

Duration: Approx 12 hr.

Absorption: Peak plasma concentrations: 1-5 hr.

Distribution: Volume of distribution: 4.3 L. Plasma protein binding: Does not bind to heparin binding proteins.

Metabolism: Hepatically metabolised.

Excretion: Via urine (40% as unchanged drug; 10% as active metabolites). Elimination half-life: Approx 4-5 hr.

Dosage

Acute stroke

1 mg/kg subcutaneously bid

Contraindications: Patients with active major bleeding, acute bacterial endocarditis, recent haemorrhagic stroke, active gastric or duodenal ulceration, thrombocytopenia

Side effects : Haemorrhage (including at the inj site), peripheral or unspecified oedema, anaemia, haematuria, ecchymosis, fever, confusion.

Potentially Fatal: Major haemorrhagic complications (e.g. retroperitoneal and intracranial bleeding)

42. Muscle Relaxants and Antispastic Drugs

Muscle Relaxants

Muscle relaxants are drugs which affect skeletal muscle function and decrease the muscle tone. They are used to alleviate symptoms such as muscle spasms, pain, and hyperreflexia.

Some commonly used muscle relaxants are:

Chlorsoxazone

Mechanism of action

Chlorsoxazone inhibits multisynaptic areas at the level of the spinal cord and subcortical areas of the brain. These areas are involved in producing and maintaining skeletal muscle spasm of varied etiology. Thus it helps in relieving painful muscle spasms.

Onset: 1 hr.

Duration: 3-4 hr.

Absorption: peak plasma concentrations after 1-2 hr.

Metabolism: Hepatic; yielding 6-hydroxychlorzoxazone.

Excretion: Via urine (mainly as glucuronide); 1 hr (elimination half-life).

Dosage

Oral

Painful muscle spasm associated with musculoskeletal conditions

Adult: Initially, 500 mg 3-4 times daily, may subsequently reduce to 250 mg 3-4 times daily. Max: 750 mg 3-4 times daily.

Indications: painful muscle spasms associated with musculoskeletal or neuromuscular problems.

Contraindications: Liver disease. Porphyria. Lactation.

Special Precautions: Pregnancy. Tasks requiring mental alertness may be impaired. Monitor liver function while administering the drug.

Side effects: Drowsiness, dizziness, lightheadedness, headache, excitement, restlessness, irritability, Jaundice, liver damage.

Serious side effects: Anaphylactoid reactions, angioedema, fatal hepatocellular toxicity.

Methocarbamol

Methocarbamol is a centrally acting skeletal muscle relaxant.

Mechanism of action

Methocarbamol is involved in the inhibition of carbonic anhydrase and it is known to cause general depression of the central nervous system. It is also known to prolong muscle refractory period. Absorption: Peak plasma concentration in 1-2 hr (oral).

Metabolism: Metabolised by dealkylation and hydroxylation.

Excretion: Via urine as metabolites and unchanged drug. 1-2 hr (elimination half-life).

Dosage

Oral

Painful muscle spasm associated with musculoskeletal conditions

Adult: Initially: 1.5 g 4 times daily, reduced according to response after 2-3 days. Maintenance: 2.25-4 g daily in divided doses. Max dose 8 g daily.

Elderly: Dose may need to be reduced by half.

Intravenous

Painful muscle spasm associated with musculoskeletal conditions

Adult: 1 g administered by slow inj or infusion at a rate not faster than 300 mg/min. In cases where patients are not able to continue with oral therapy, additional doses of 1 g every 8 hr may be used for up to 3 consecutive days. Max 3 g daily.

Elderly: Dose may need to be reduced by half.

Intramuscular

Painful muscle spasm associated with musculoskeletal conditions

Adult : Up to 500 mg into each gluteal region at intervals of 8 hr. In cases where patients are not able to continue with oral therapy, additional doses of 1 g every 8 hr may be used for up to consecutive 3 days. Max 3 g daily.

Elderly: Dose may need to be reduced by half.

Intravenous

Tetanus

Adult: Initial total dose: 3 g with 1-2 g via direct inj at a rate of 300 mg/minute and the remainder 1-2 g may be administered via infusion. Repeat infusion of 1-2 g every 6 hr until a nasogastric tube can be inserted. Tablets may be crushed and suspended in water or saline solutions and administered through the nasogastric tube. Total oral dosage of up to 24 g daily may be needed.

Child: 15 mg/kg or 500 mg/m2 given by IV inj (suggested rate 180 mg/m2/min). Dose may be repeated every 6 hr if necessary by IV inj or infusion. Max dose 1.8 g/m2 daily for 3 consecutive days.

Indications: painful muscle spasms associated with musculoskeletal or neuromuscular problems.

Contraindications: Coma or pre-coma states, brain damage, myasthenia gravis. Do not admin parenteral solutions in patients with renal impairment, epilepsy or history of epilepsy.

Special Precautions: Renal or hepatic impairment; acidosis. Pregnancy and lactation. May impair ability to drive or operate machinery. Children ?12 yr.

Side effects: anorexia, lassitude, drowsiness, dizziness, restlesness, anxiety, confusion, fever, headache, blurred vision, convulsions; Parenteral: Flushing and a metallic taste; incoordination, diplopia, nystagmus, vertigo; sloughing and thrombophloebitis at the site of inj.

Serious side effects: Parenteral: Syncope, hypotension, bradycardia, anaphylaxis.

Antispastic drugs

Antispastic drugs aid in improving muscle hypertonicity and involuntary jerks.

Following are commonly used antispastic drugs:

Baclofen

Baclofen is a -aminobutyric acid derivative.

Mechanism of action

It inhibits both monosynaptic and polysynaptic reflexes at spinal level.

Absorption: peak plasma conc after 1-3 hr.

Distribution: Blood-brain barrier, CSF (equivalent to 12% conc found in plasma). Protein-binding: 30%.

Metabolism: Hepatic (15% of the dose).

Excretion: Via urine (70-80% as unchanged drug); elimination half-life (Via urine (70-

80% as unchanged drug); elimination half-life (t1/2): 3-4 hr (plasma), 5 hr (CSF). 3-4 hr (plasma), 5 hr (CSF).

Dosage

Oral

Severe chronic spasticity

Adult: Initially, 5 mg tid for 3 days increased to 10 mg tid for 3 days, then in similar increments and intervals until either 20 mg tid is reached or until desired effect is obtained. Max: 100 mg daily.

Child: 0.75-2 mg/kg daily. May initiate with 2.5 mg 4 times daily, increased gradually every 3 days until desired effect is obtained. Maintenance: 6-10 yr: 30-60 mg daily; 2-6 yr: 20-30 mg daily; 12 mth-2 yr: 10-20 mg daily. Max: >10 yr: 2.5 mg/kg daily.

Elderly: Initiate with lower doses.

Intrathecal administration may be done by a neurosurgeon or pain management specialist in severe chronic spasticity

Contraindications: Active peptic ulcer disease.

Special Precautions: Cerebrovascular disorders, epilepsy, severe psychotic disorders, confusional states, history of peptic ulcer, respiratory depression, diabetes (DM), hepatic or renal impairment, elderly, pregnancy. Avoid sudden withdrawal.

Side effects: Sedation, drowsiness, ataxia, dizziness, headache, confusion, hallucinations, enuresis.

Serious side effects: Respiratory or CV depression, seizures.

Tolperisone

Tolperisone is a centrally acting muscle relaxant.

Mechanism of action

It acts at the reticular formation in the brain stem by blocking voltage-gated sodium and calcium channels.

Dosage

Oral

Spasticity, Muscle spasms

Adult : 50-150 mg tid.

Child : <6 yr: 5 mg/kg daily in 3 divided doses; 6-14 yr: 2-4 mg/kg daily in 3 divided doses.

Contraindications : Myasthenia gravis.

Side effects : Muscular weakness, headache, hypotension.

Tizanidine

Tizanidine is a centrally acting 2-agonist.

Mechanism of action

It exerts its antispastic effect by causing presynaptic inhibition of motor neuron hyperactivity.

Absorption: peak plasma concentrations in 1-2 hr.

Distribution: Protein-binding: 30%. Elimination half-life: 2-4 hr.

Metabolism: Extensive hepatic first-pass metabolism mainly via the cytochrome P450 isoenzyme CYP1A2.

Excretion: Via urine (mainly as inactive metabolites).

Dosage

Oral

Spasticity

Adult: >18 yr: Initially, 2 mg once daily increased according to response by 2-mg increments at intervals of at least 3-4 days up to 24 mg daily in 3-4 divided doses. Max: 8 mg/dose. Max: 24 mg/day.

Elderly: Not recommended.

Renal impairment: Depending on creatine clearance- CrCl: <25 (ml/min)- Initially, 2 mg once daily, gradually increasing the dose before increasing the frequency of admin

Hepatic impairment: Avoid or use with extreme caution.

Contraindications: Severe hepatic dysfunction.

Special Precautions: Hepatic or renal insufficiency. Children, elderly, pregnancy and lactation. Monitor LFT regularly. Stop treatment if liver enzymes are raised persistently >3 times upper limit of normal range. Avoid abrupt withdrawal of therapy.

Side effects: Drowsiness, fatigue, dizziness, insomnia, headache, anxiety, hypotension, bradycardia, muscle pain and weakness, transient increase in serum transaminases, hallucinations.

Serious side effects : Hepatitis.

Botox

Botulinum toxin is a protein and neurotoxin produced by the bacterium Clostridium botulinum.

Botulinum toxin Type A (BTX-A) is a common treatment for muscles affected by the upper motor neuron syndrome which causes spasticity in a group of muscles. Botox injections inhibit muscle spasticity by weakening or paralyzing certain muscles or by blocking the nerves involved in hypertonicity.

Mechanism of action

BTX-A inhibits the release of acetylcholine (the neurotransmitter that activates muscles). Botox paralyzes muscle by stopping acetylcholine release. BTX-A reduces both voluntary and involuntary motor activity of the muscles.

Indications:

- Severe spascticity in a muscle or muscle groups due to UMN lesions.
- Spasticity not improved by antispastic drugs and other measures.
- Cervical dystonia (spasmodic torticollis)
- Local intradermal injection of BTX-A in chronic focal neuropathies.
- Idiopathic and neurogenic detrusor overactivity
- Pediatric incontinence, incontinence due to overactive bladder, and incontinence due to neurogenic bladder
- Movement disorders associated with stroke, multiple sclerosis, Parkinson's disease, or cerebral palsy
- Focal dystonias affecting the limbs, face, jaw, or vocal cords

Contraindications: pregnancy, lactation

Side effects : paralysis of the wrong muscle group and allergic reaction, pain, swelling, or bruising at the injection site, flu-like symptoms, headache.

Advantages : The advantage of Botox is its ease of administration. The effects of Botox last for about three to twelve months. Botox injection can be given to a single muscle or muscle group; where focal a action is required. Local injections act locally, and thus, a widespread action is prevented.

Disadvantages : Injections have to be repeated every six months. Botox paralyzes both voluntary and involuntary muscle activity. The weakness due to botox may contribute to further dysfunction in patients who anticipate to use the muscles. The side-effects and the development of immune responses to the toxin are significant drawbacks of repeated injections. It is not suitable for treatment of widespread spasticity, spasms, and other abnormal activity affecting many muscle groups.

Alternatives to Botox injections are available and used when injections of Botox are contraindicated or may cause serious adverse effects. These are surgical methods, such as lengthening of tendons of spastic and shortened muscles, denervation of the spastic muscles, etc.

43. Antiparkinson and Other Drugs

Drugs controlling tremors

Levodopa

Levodopa is a dopaminergic agent which is used in the treatment of parkinson's disease.

Mechanism of action

Levodopa increases dopamine levels in the brain leading to the stimulation of dopamine receptors.

Absorption: Peak plasma concentrations within 2 hr.

Distribution: Protein-binding: 10-30%. Penetrates the blood-brain barrier; crosses the placenta; distributed into breast milk.

Metabolism: Metabolised in the gut, liver and kidney; decarboxylated by L-aminodecarboxylase to dihydrophenylacetic acid (DOPAC) and homovanillic acid (HVA). Other routes: O-methylation, transamination, oxidation.

Excretion: Via urine within 24 hr (80% as metabolites); via faeces (minimal amounts). 30-60 min (elimination half-life).

Dosage

Oral

Parkinsonism

Adult: Initially, 125 mg bid; increase gradually every 3-7 days according to response. Max dose: 8 g daily in divided doses.

Contraindication-acute narrow angle glaucoma, severe pyschosis, history of malignant ,melanoma

Special precaution - elderly,ihd,psychiatric,endocrine,hepatic & renal impairment

Side effect - Orthostatic hypotension, cardiac arrhythmias. Psychiatric symptoms (especially the elderly). Abnormal involuntary movements or dyskinesias, delirium, hallucinations. Slight elevation of liver enzymes, BUN and uric acid. Transient leucopenia and thrombocytopenia.

Levodopa and Carbidopa

Levodopa, a precursor of dopamine, crosses the blood-brain barrier and gets converted to dopamine in the basal ganglia while carbidopa is a dopa-decarboxylase inhibitor. The latter prevents conversion of L-dopa to dopamine outside the brain and minimises side effects.

Dosage

Oral

As monotherapy in Parkinson's disease

Adult: Per tablet contains L-dopa 100 mg and carbidopa 25 mg. Initially, 1 tab tid. Increase by 1 tab/day every 1-2 days up to a max. of 8 tabs of any strength/day. If the patient has been taking L-dopa alone, the combination should be started after a gap of at least 8 hr after stopping L-dopa.

Levodopa and Benserazide

Levodopa is the metabolic precursor of dopamine. Only a small amount of administered Levodopa enters blood-brain barrier unaltered and the remainder is converted peripherally to dopamine by dopa-decarboxylase. Benserazide is a peripheral decarboxylase inhibitor that reduces the peripheral conversion of Levodopa; concurrent admin enables dosage of Levodopa to be reduced and may diminish peripheral side effects such as nausea and vomiting.

Dosage

Oral

Parkinson's disease

Adult: Standard forms or Dispersible form Available in Levodopa (mg)/Benserazide (mg) formulations 50/12.5, 100/25, 200/50. Doses expressed as Levodopa: Initially 50 mg 3 or 4 times daily (100 mg tid in advance stage disease); gradually increase by 100 mg daily once or twice wkly. Effective dose range: 400-800 mg daily in divided doses; most require < 600 mg daily. Patients previously on levodopa monotherapy: Initiate with 10-15% of the usual dose previously taken. Patient previously on other levodopa/dopa-decarboxylase combination therapy: Withdraw previous therapy for 12 hr before initiating therapy at 50 mg 3 or 4 times daily.

Controlled - release form As Levodopa (mg)/Benserazide (mg) 100/25 cap: Initially 1 cap tid. Max initial dose: 6 caps/day. Patients previously on immediate-release Levodopa/Benserazide preparations: Initially dose should substitute every 100 mg of Levodopa with 1 controlled-release cap, given at same dosage frequency as before. Increase every 2-3 day

Elderly: Standard forms or Dispersible form Doses expressed as Levodopa: Initially 50 mg once or twice daily, gradually increase by 50 mg every 3-4 days according to response.

Donepezil

Mechanism of action

Donepezil reversibly and noncompetitively inhibits centrally-active acetylcholinesterase. It is used for the symptomatic treatment of Alzheimer's disease.

Absorption: Plasma levels peak within 3-4 hr after oral admin.

Distribution: Protein binding: About 95% (mainly albumin).

Metabolism: Partially metabolised in the liver mainly by CYP3A4 to 4 major metabolites.

Excretion: Elimination half-life: About 70 hr. Steady-state concentrations are achieved within 3 wk of treatment initiation.

Dosage

Oral

Mild to moderately severe dementia in Alzheimer's disease

Adult: Initially, 5 mg daily at bedtime, increase if necessary up to 10 mg once daily at bedtime after 4-6 wk.

Elderly: Initially, 5 mg daily at bedtime, increase if necessary up to 10 mg once daily at bedtime after 4-6 wk.

Side effects: anorexia, wt loss, insomnia, fatigue, muscle cramps; headache and dizziness; syncope, bradycardia; convulsions; increased liver transaminases; hallucinations, agitation and aggressive behavior; urine retention.

Immunoglobulins

IVIG

Dosage : The initial dose of IVIg for MG and other neuromuscular diseases is usually 2 g/kg. This is generally administered over 2 to 5 days. Slower rates of infusion are preferable in older patients and those with renal insufficiency or congestive heart failure. Intravenous immunoglobulin is often used for treatment of MG outpatients refractory to other immunomodulating therapies.

Side effects : adverse effects are related to the rate of infusion and include headache, light-headedness, and chills. Other side effects include nephrotoxicity, hypertension, thrombotic events, myocardial infarction and stroke.

44. Neuroprotective Agents

Neuroprotective Drugs

Neuroprotective agents are used in an attempt to save ischemic neurons in the brain from irreversible injury. Studies in animals indicate a period of at least 4 hours after onset of complete ischemia in which many potentially viable neurons exist in the ischemic penumbra (ie, the rim of the infarct). In humans, the ischemia may be less complete, and the time window may be longer, but human patients also tend to be older, with comorbidities that may limit benefit.

2 types of neuroprotective agents, one that prevents early ischemic injury and another that prevents reperfusion injury.

I. Prevention of early ishemic injury

N-methyl-D-aspartate receptor antagonists

By preventing excitatory neurotransmitter release, neuroprotective agents may reduce deleterious effects of ischemia on cells.

A. Memantine

Memantine, a derivative of amantadine, is a noncompetitive N-methyl-D-aspartate (NMDA)-receptor antagonist. It affects transmission of glutamate, the primary excitatory neurotransmitter in the CNS. Glutamate may contribute to the pathogenesis of Alzheimer's disease by overstimulating various glutamate receptors resulting in excitotoxicity and neuronal cell death.

Dosage

Oral

Moderate to severe dementia in Alzheimer's disease

Adult: As hydrochloride: Initially, 5 mg daily in the morning for the 1st wk; increase dose wkly in steps of 5 mg. Max: 20 mg daily. Wait for at least 1 wk between dose changes. Doses ?10 mg/day should be given in 2 divided doses. Suggested titration: 5 mg daily for ?1 wk; 5 mg bid for ?1 wk; 15 mg daily given in 5- and 10-mg separated doses for ?1 wk; then 10 mg bid.

Renal impairment : Depending on creatine clearance; 40-60 ml/min: Max dose: 10 mg/day

Side effects : Dizziness, confusion, headache, somnolence, hallucinations, tiredness, anxiety, abnormal gait, hypertonia, cystitis and increased libido.

B. Magnesium

Magnesium is another agent with actions on the NMDA receptor and a low incidence of adverse effects. It may reduce ischemic injury by increasing regional blood flow, antagonizing voltage-sensitive calcium channels, and blocking the NMDA receptor. In myocardial infarction and small stroke studies, patients tolerated the drug.

Dosage : 400 to 800 mg orally once a day.

II. Prevention of reperfusion injury

Citicoline

Citicoline is an exogenous form of cytidine-5'-diphosphocholine (CDP-choline) used in membrane biosynthesis. Citicoline may reduce ischemic injury by stabilizing membranes and decreasing free radical formation. Citicoline increases blood flow and O2 consumption in the brain. It is also involved in the biosynthesis of lecithin.

Dosage

Oral

Adult: 200-600 mg daily in divided doses.

Piracetam

It is a nootrophic agent and used as a cognitive enhancer.

Indication - cerebral vascular accidents and cerebral insufficiency,ischemic or even haemorrhagic acute accidents,mental retardation in children,behaviour & psychotic problems

Dosage - adult-800 mg 3 times a day.

Children - 50mg/kg body weight

Contraindication - severe renal impairment or hepatic functions and Cerebral haemorrhage.

Special precaution - impaired renal or hepatic functions,cardiac disorders.

Side effects: Hyperkinesia, nervousness, depression, CNS stimulation, sleep disturbances, dizziness, excitement, wt gain.

Ginkgo biloba

Indication - cerebral impairment due to organic degeneration of cortex,multiple vascular infarcts, headache, sleep disturbances, dizziness, tinnitus

Dosages - 40 mg 3 times a day.

Contraindication - acute phase of cerebrovascular accidents, acute myocardial infarction, hypotension, pregnancy & hypersensitivity to ingrediants.

Special precautions - nausea, gi, upsets, heart, palpitation

Vitamins

Vitamins like vitamin B1, B6, B12 and folate are also used for neuroprotection.

Vitamin B6 (Pyridoxine)

It is a water soluble vitamin, important for metabolism of carbohydrates, proteins and fats. It helps in GABA synthesis in the CNS and release of glycogen stored in muscles.

Dosage : 150 mg daily

Vitamin B12

Vitamin B12 plays a significant role in the synthesis and maintenance of myelin. The neurological problems caused by vitamin B12 deficiency are due to the damage caused to the myelin sheath.

Thus, Vit B12 medications and supplements are given in the treatment of peripheral neuropathy, diabetic neuropathy and to prevent neurological disturbances. Methylcobalamin is known to help repair the damage caused by diabetic neuropathy by modulating the protein kinase C signaling pathway or activating chemical signals. Vitamin B12 also helps protect against brain atrophy or shrinkage associated with Alzheimer's disease and impaired cognitive function.

Dosage : 1500 mcg/day

Vitamin C

Vitamin C is one of many antioxidants. Antioxidants are nutrients that Prevent damage caused from free radicals. Intracellular ascorbate in the CNS provides antioxidant protection, peptide amidation, myelin formation, synaptic potentiation, and protection against glutamate toxicity. Thus, it protects neurons from the oxidant damage associated with neurodegenerative diseases such as Alzheimer's, Parkinson's, and Huntington's disease.

Dosage : 500mg/day

Vitamin E

Vit E is important for the maintenance of the integrity and stability of biological membranes, and for the protection of the phospholipids of biological membranes from peroxidation. Vit E deficiency has been known to cause degeneration and loss of sensory axons in the posterior columns, sensory roots, and peripheral nerves. This

degeneration results from axonal membrane injury and then develops as an axonopathy.

Dosage : 400 mg/day

Folate

Folic acid is known to have some roles in the production of neurotransmitters necessary for nerve conduction. Folate deficiency may lead to cognitive impairment, dementia, depression, peripheral neuropathy and subacute combined degeneration of the spinal cord.

Dosage : 1.5 mg/day

Vitamin B1 (Thiamine)

Thiamine is a water soluble vitamin. It is an essential coenzyme in carbohydrate metabolism.

Dosage : As a prophylaxis: 10-25 mg daily

In Thiamine deficiency: 300 mg daily

Wernicke - Korsakoff syndrome: 100 mg by slow IV over 10 minutes; then 50-100 mg/day IM or IV until he can take oral

CoQ10 or Ubiquinone

CoQ10 acts as an antioxidant and membrane stabilizer. It is also involved in the electron transport chain, and is an important component for production of ATPs (energy) for cell functions. It is used in the treatment of mitochondrial cytopathies, Huntington's disease, Parkinson's disease, muscular dystrophies, migraine headaches and myopathies.

CoQ10 is used as a cardioprotective agent in cases of muscular dystrophy. In multiple studies, CoQ10 was found to be safe and well tolerated up to 1200 mg/day.

Dosage :

Adult: 300 mg bid, maximum 1200 mg/day

Children : 300 mg once a day

Ubiquinol

Ubiquinol is an oxidized form of CoQ10 and acts as an antioxidant.It is the most common form of CoQ10 and accounts for more than 80% of the total ubiquinol and ubiquinone pool in human plasma. It is used in neurodegenerative disorders, for e.g. Parkinson's disease, dementia, etc. Indications of ubiquinol use are same as of CoQ10. The bioavailability of ubiquinol is higher than CoQ10.

Dosage : Adults: 100 mg bid

Children: 50 mg bid or 100 mg od

Omega 3 fatty acids

These are essential fatty acids which act as antioxidants. They decrease inflammation and boost the immunity of the individual. There are three types: EPA, DHA (found in fish oil) and ALA (found in plants). Omega 3 fatty acids are used in neurodegenerative, cognitive disorders, ADHD, etc. for neuroprotection.

Dosage: 1 tablet three times a day

Section F

Modern Developments in the Treatment of Neurological Disorders

45. Use of tPA in Acute Ischemic Stroke

Stroke most often occurs as a result of acute vascular occlusion, and therefore acute revascularization is crucial. Prompt revascularization to restore perfusion minimizes the extent of infarction and improves neurologic outcome.

Importance of tPA

Intravenous administration of rtPA is a valuable treatment of patients with acute ischemic stroke. tPA use has shown improved outcomes in patients who can be treated within 3 hours of symptom onset. Earlier treatment results in better outcomes.

Inclusion and Exclusion Characteristics of Patients With Ischemic Stroke Who Could Be Treated With IV rtPA Within 3 Hours From Symptom Onset

Inclusion criteria

1. Diagnosis of ischemic stroke causing measurable neurological deficit
2. Onset of symptoms <3 hours before beginning treatment
3. Age more than 18 years

Exclusion criteria

1. Significant head trauma or prior stroke in previous 3 months
2. Symptoms suggest subarachnoid hemorrhage
3. Arterial puncture at noncompressible site in previous 7 days
4. History of previous intracranial hemorrhage
5. Intracranial neoplasm, arteriovenous malformation, or aneurysm
6. Recent intracranial or intraspinal surgery
7. Elevated blood pressure (systolic >185 mmHg or diastolic >110 mmHg)
8. Active internal bleeding
9. Acute bleeding diathesis, including but not limited to

10. Platelet count <100 000/mm³
11. Heparin received within 48 hours, resulting in abnormally elevated aPTT greater than the upper limit of normal
12. Current use of anticoagulant with INR >1.7 or PT >15 seconds
13. Current use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated sensitive laboratory tests (such as aPTT, INR, platelet count, and
14. ECT; TT; or appropriate factor Xa activity assays)
15. Blood glucose concentration <50 mg/dL (2.7 mmol/L)
16. CT demonstrates multilobar infarction (hypodensity >1/3 cerebral hemisphere)

Relative exclusion criteria

1. Only minor or rapidly improving stroke symptoms (clearing spontaneously)
2. Pregnancy
3. Seizure at onset with postictal residual neurological impairments
4. Major surgery or serious trauma within previous 14 days
5. Recent gastrointestinal or urinary tract hemorrhage (within previous 21 days)
6. Recent acute myocardial infarction (within previous 3 months)

Consider risk to benefit of IV rtPA administration carefully in any of above cases.

Additional Inclusion and Exclusion Characteristics of Patients With Acute Ischemic Stroke Who Could Be Treated With IV rtPA Within 3 to 4.5 Hours From Symptom Onset

Inclusion criteria

1. Diagnosis of ischemic stroke causing measurable neurological deficit
2. Onset of symptoms within 3 to 4.5 hours before beginning treatment

Relative exclusion criteria

1. Aged >80 years
2. Severe stroke (NIHSS>25)
3. Taking an oral anticoagulant regardless of INR
4. History of both diabetes and prior ischemic stroke

Mechanism of Action

Recombinant human tissue-type plasminogen activator (t-PA) produces local fibrinolysis and promotes thrombolysis by converting plasminogen to plasmin which degrades fibrin and fibrinogen.

Absorption: Onset: Coronary thrombolysis occurs in 30 min; reaches peak response at 60 min

Peak plasma time: 20-40 min

Metabolism : Rapidly cleared from circulation by liver

Elimination: Initial half-life: 5 minutes (free, unbound form), Terminal half-life: 72 minutes, Total body clearance: 34.3-38.4 mL/hr, Excretion: Urine

Dosage: Acute Ischemic Stroke

0.9 mg/kg IV infused over 1 hour

100 kg: Administer 10% of total dose as initial bolus over 1 minute; THEN 0.81 mg/kg as continuous infusion over 60 min; not to exceed total dose of 90 mg

>100 kg: Administer 9 mg (10% of 90 mg) as IV bolus over 1 min; THEN 81 mg as a continuous infusion over 60 min

Dosing considerations

- Treatment should be initiated only within 3 hours after onset of stroke symptoms
- Exclude intracranial hemorrhage by cranial computerized tomography (CT) scan or other diagnostic imaging method sensitive for the presence of hemorrhage

Side effects: Accelerated idioventricular rhythm, Pulmonary edema, Arterial embolism,Bruising,Bleeding,DVT,Hypotension,Intracranial hemorrhage,GI/GU hemorrhage,Pulmonary embolism,Fever/chills,Nausea/vomiting,Sensitivity reaction,Sepsis,Shock

Recommendations

1. Intravenous rtPA (0.9 mg/kg, maximum dose 90 mg) is recommended for selected patients who may be treated within 3 hours of onset of ischemic stroke.
2. In patients eligible for intravenous rtPA, benefit of therapy is time dependent, and treatment should be initiated as quickly as possible. The door-to-needle time (time of bolus administration) should be within 60 minutes from hospital arrival
3. Intravenous rtPA is reasonable in patients whose blood pressure can be lowered safely (to below 185/110 mmHg) with antihypertensive agents, with the physician assessing the stability of the blood pressure before starting intravenous rtPA.
4. In patients undergoing fibrinolytic therapy, physicians should be aware of and prepared to emergently treat potential side effects, including bleeding complications and angioedema that may cause partial airway obstruction
5. Use of intravenous fibrinolysis in patients with conditions of mild stroke deficits, rapidly improving stroke symptoms, major surgery in the preceding 3 months, and recent myocardial infarction may be considered, and potential increased risk should be weighed against the anticipated benefits

6. The intravenous administration of streptokinase for treatment of stroke is not recommended

Monitoring of the patient

Admit the patient to an intensive care or stroke unit for monitoring.

If the patient develops severe headache, acute hypertension, nausea, or vomiting or has a worsening neurological examination, discontinue the infusion (if IV rtPA is being administered) and obtain emergent CT scan.

Measure blood pressure and perform neurological assessments every 15 minutes during and after IV rtPA infusion for 2 hours, then every 30 minutes for 6 hours, then hourly until 24 hours after IV rtPA treatment.

Increase the frequency of blood pressure measurements if systolic blood pressure is >180 mmHg or if diastolic blood pressure is >105 mmHg; administer antihypertensive medications to maintain blood pressure at or below these levels

Delay placement of nasogastric tubes, indwelling bladder catheters, or intraarterial pressure catheters if the patient can be safely managed without them.

Obtain a follow-up CT or MRI scan at 24 hours after IV rtPA before starting anticoagulants or antiplatelet agents.

46. Role of Hyperbaric Oxygen Therapy in Neurological Disorders

Hyperbaric oxygen therapy (HBOT) is a medical treatment which enhances the body's natural healing process by inhalation of 100% oxygen in a total body chamber, where atmospheric pressure is increased and controlled. It is used for a wide variety of treatments usually as a part of an overall medical care plan.

Under normal circumstances, oxygen is transported throughout the body only by red blood cells. With HBOT, oxygen is dissolved into all of the body's fluids, the plasma, the central nervous system fluids, the lymph, and the bone and can be carried to areas where circulation is diminished or blocked. In this way, extra oxygen can reach all of the damaged tissues and the body can support its own healing process. The increased oxygen greatly enhances the ability of white blood cells to kill bacteria, reduces swelling and allows new blood vessels to grow more rapidly into the affected areas. It is a simple, non-invasive and painless treatment.

Indications:

FDA has approved HBOT for treatment of brain abscess and acute traumatic ischemia.

Off label indications for neurological disorders are:

Brain injury
Autism
Cerebral palsy
Migraine
Alzheimer's disease
Attention deficit hyperactive disorder
Multiple sclerosis
Motor neuron disease
Neuropathies
Dementia
Depression
Coma

Parkinson's disease
Epilepsy/Seizure disorders
Encephalomyelitis
Spinal cord injury
Stroke

Process or Procedure:

The patient is on a table that slides into the transparent chamber which is about 7 feet long.

The pressure inside the chamber is increased slowly. Children can be accompanied with a parent and can play or drink inside the chamber. One can see and talk to the technician at all times. The chamber is sealed and filled with 100% oxygen and pressure is increased to 1.5 to 2.5 times the normal air pressure which may cause some ear popping or mild discomfort. Pure, 100 percent oxygen is continuously maintained and circulated throughout the chamber during the treatment .The session will last anywhere from 45 minutes to one hour. At the end slow decompression of the chamber is carried out to avoid decompression sickness. Usually, 40 hourly sessions are conducted.

Benefits :

Healing in most areas of the body requires appropriate oxygen levels in the tissue. Most illnesses and injuries occur, and often linger, at the cellular or tissue level. In many cases, such as: circulatory problems; non-healing wounds; and strokes, adequate oxygen cannot reach the damaged area and the body's natural healing ability is unable to function properly. Hyperbaric oxygen therapy provides this extra oxygen naturally and with minimal side effects.

Hyperbaric oxygen therapy improves the quality of life of the patient in many areas when standard medicine is not working. Many conditions such as stroke, cerebral palsy, head injuries, and chronic fatigue have been reported to respond favorably to HBOT.

Hyperbaric oxygen is used to treat all conditions which benefit from increased tissue oxygen availability either as the primary therapy, or in conjunction with other drugs.

HBOT in brain injury or stroke:

Following an injury to the brain, either from trauma or lack of oxygen, cellular plasma leaks out into surrounding brain tissue causing swelling and reducing blood flow. The pressure on these cells,hampers their normal function,due to inadequate oxygenation.HBOT facilitates increase in the oxygen carrying capacity of the blood / plasma, making oxygen available to heal damaged capillary walls, preventing plasma leakage and reducing swelling. As the swelling decreases, blood flow can be restored to the dormant tissue (neovascularization) and these cells then have the potential to function again.

A clinical trial, aimed to evaluate whether increasing the level of dissolved oxygen by Hyperbaric Oxygen Therapy (HBOT) could activate neuroplasticity in patients with chronic neurologic deficiencies due to stroke was carried out and published in 2013 by Shai Efrati,,et al.,from Israel.The results indicate that HBOT can lead to significant neurological improvements in post stroke patients even at chronic late stages. The observed clinical improvements implied that neuroplasticity can still be activated long after damage onset in regions where there is a brain SPECT/CT (anatomy/physiology) mismatch.

HBOT in a child with cerebral palsy (CP)

In CP patients, some of the injured brain tissues may be "dormant" and non-functioning. HBOT can stimulate these "dormant" tissues and return them to more normal function. In young children, cognitive function and spasticity can be improved.

Hyperbaric oxygen therapy, used in conjunction with other therapies, ensures the best recovery possible for children with cerebral palsy and traumatic brain injury.

HBOT In autism:

the pathogenetic mechanisms postulated are cerebral hypoperfusion, inflammation, oxidative stress, and immune dysregulation. Studies have shown that children with autism may have decreased blood flow through the social brain (mesial temporal, amygdala, etc). Less blood flow results in decreased oxygen supply to these areas. The chances of the hypoxic tissue to receive more oxygen increases by enhanced supply. HBOT not only increases the oxygen in the blood but also allows the oxygen to effortlessly cross cell membranes and enter all of the other body's fluid systems. This cumulatively improves the transport of oxygen in the body. It stimulates angiogenesis, reduces oxidative stress by stimulating superoxide dismutase, reduces inflammation and stimulates local stem cells. This improves the neuronal functions. HBOT thus reverses the neurological abnormalities. Clinically, this leads to improvement in cognition, socialization, language, behavior, eye contact, etc in children with autism.

Contraindications: (for children and their parents): Absolute: pneumothorax and severe congestive heart failure. Relative: History of seizures, febrile illness (lower threshold for seizures and prolonged removal time due to slow decompression incase of an event), recent ear surgery, chronic sinusitis, active upper respiratory infection, (due to inability to equalize the ear pressure). Asthma, emphysema (lung barotrauma), congenital spherocytosis (fragile RBCs), claustrophobia (anxiety), optic neuritis (blindness), active cancer, pacemaker and pregnancy.

Possible Complications: One should be vigilant for possible complications of HBOT, that includes barotrauma injury (to middle ear, nasal sinuses, inner ear, lung, teeth), oxygen toxicity (central nervous system, lung), confinement anxiety, and ocular effects (myopia, cataract growth) and seizures.

47. Comprehensive Neurorehabilitation

Neurorehabilitation is the clinical subspecialty that is devoted to the restoration and maximization of functions that have been lost due to impairments caused by injury or disease of nervous system. The goal of neurorehabilitation is to help patients with impairments and disabilities and to make them functionally independent, which requires team of rehabilitation specialists, such as nurses, physical therapists, occupational therapists, speech therapist, psychologist and others.

Fig. 49.1: A pediatric Rehabilitation centre

Importance of Rehabilitation:

The rehabilitation team has a role to set short term goals (generally considered to be two to three weeks) and long term goals (longer than 3 weeks) which should be

objective, measureable and time limited. Neurorehabilitation team has an understanding of neural regulation of movement patterns. A framework for typical motor behaviour is necessary to understand how motor behaviour is altered in persons with neurological dysfunction and how plastic properties of nervous system interact to produce change. Motor control is the study of how an individual controls movements already acquired. Neuroplasticity is defined as brain's ability to adapt or use cellular adaptations to learn or relearn functions which are previously lost as result of cellular death by trauma or disease at any age. Neuronal sprouting is thought to be primary mechanism, allowing injured neurons, to reconnect in new ways and allowing intact undamaged neurons to form new connection and to enhance function. Motor learning will continue throughout life as long as environment asks for change and CNS has pliability and desire to learn. The rehabilitation team promotes this learning and facilitates neural plasticity.

The philosophic foundation of rehabilitation team is to promote purposeful activity thereby preventing dysfunction and eliciting maximum adaptation. These goal-oriented activities are meant to be culturally meaningful and important to the needs of patient and their families. Activities include daily life and work skills, exercise, recreation and crafts. Exercise tasks in animal models, have shown that specifically skilled type of exercises lead to increased angiogenesis in damaged cortical areas whereas unskilled activities did not show this positive change. It is believed that in humans too rehabilitation techniques would enhance neuroplastic changes.

How rehabilitation augments the effects of stem cell therapy

The concept of Neuro Regenerative Rehabilitation Therapy (NRRT) at NeuroGen promotes a multidisciplinary and holistic approach to bring about recovery of neural function with a close integration of Neuro regenerative (including stem cell therapy), Neuro protective (medications) and neurorehabilitative therapies (physical / occupational / speech/ psychological). Thus, it combines the best neurobiological repair technologies and neurorestorative techniques. The rehabilitation protocol is then individualized to the specific requirements of each patient emphasizing on functional recovery and independence in ADL. The rehabilitation team sets up goals and the injected stem cells from within the body help in achieving those goals. Studies have shown that exercise induces mobility in the injected stem cells, thereby enhancing the achievable outcomes. Hence, neurorehabilitation appears to work complimentarily with stem cells therapy.

Studies have suggested that the combination of bone marrow stem cell therapy and exercise training result in significant functional improvement in neurological disorders.

Neurorehabilitation facilitates neural plasticity and improves neural connectivity. It stimulates neurons to function at their optimum capacity. It also activates the local resident stem cells to help repair the damaged areas. Similarly exercise also stimulates the injected stem cells and guides them towards their targeted functions. It helps the regenerated cells to gain maximum function. Neurorehabilitation has also been

postulated to release growth factors, improve oxygenation and increase blood supply. Thus, the synergistic effect of stem cell therapy and neurorehabilitation brings about maximum benefits.

Physical therapy

As an important member of rehabilitation team a, physical therapist has a crucial role to play which includes, bed mobility, ambulation and transfer activities like ,transfers from bed to chair or from chair to commode or from wheelchair to car and so on. Their assessments emphasize measures of voluntary movement, sensory appreciation, ROM, strength, balance, fatigability, mobility, gait and functional status.

Practices in Physical Therapy includes:

1. Therapeutic exercise and re-education.
2. Neurofacilitation techniques.
    i) Proprioceptive neuromuscular facilitation
    ii) Bobath
    iii) Brunnstrom
    iv) Rood
3. Motor skills learning.
4. Task-oriented practice.
5. Forced use.
6. Massed Practice.
7. Biofeedback.
8. Virtual environment training.
9. Musculoskeletal techniques.
10. Electromyogram-triggered neuromuscular stimulation.
11. Orthosis and assistive devices.

Fig. 49.2: Rolling exercise

Fig. 49.3: Standing using assistive devices

Occupational Therapy

Occupational Therapists bring expertise to the rehabilitation team in enhancing the independence and personal satisfaction of patients in their activities of daily living (ADL), community and leisure activities, social integration, and work performance. They play integral part in evaluating the need for a range of assistive devices and training patients to make them independent in eating, dressing, bathing combing and other ADL.

In the patient's home and workplace, the therapist provide grab bars, rails, ramps, environmental controls, computer interfaces, architectural changes such as widening a doorway to allow wheelchair access and emergency remote-control calling systems. Along with the physical and recreational therapist, occupational therapist seek out the environmental, personal, and activity-specific equipment and technologies that enhance the quality of life of patients

Success in retraining during rehabilitation depends on diverse variables that include the characteristics of a task, changing contexts and environments when performing a task, psychological reinforcements including positive contextual factors like motivation, attention, memory for carryover of what is taught and negative contextual factors like environmental distractions, anxiety, sleep deprivation and family support play a significant role.

Fig. 49.4: Deep Pressure

Fig. 49.5

Psychology

The word psychology is derived from the Greek words Psyche (which means soul) and logos (which means study). Hence, psychology could be defined as a "study of the soul". However, today it is defined as the scientific study of the behaviour of individuals and their mental processes (American Psychological Association). Neuropsychological testing and evaluation is to identify the pattern of cognitive, behavioural, and emotional strengths and weaknesses and to provide specific treatment recommendations or clarify diagnostic questions. The domains and tests specified

Fig. 49.6: Cognitive rehabilitation

Psychological Counseling:

The purpose of counseling is to broadly empower the client to cope with life situations, to reduce emotional stress, to engage in growth producing activity, to have meaningful interpersonal relationships and to make effective decisions. Counseling increases the control over present circumstances and enhances present and future opportunities.

There are several main broad systems of psychotherapy:

i) **Psychoanalytic:** It encourages the verbalization of all the patient's thoughts, including free associations, fantasies, and dreams, from which the analyst formulates the nature of the unconscious conflicts which are causing the patient's symptoms and character problems.

ii) **Behaviour Therapy:** This focuses on changing maladaptive patterns of behavior to improve emotional responses, cognitions, and interactions with others.

iii) **Cognitive Behavioural Therapy:** Seeks to identify maladaptive cognition, appraisal, beliefs and reactions with the aim of influencing destructive negative emotions and problematic dysfunctional behaviours.

iv) **Psychodynamic:** Primary focus is to reveal the unconscious content of a client's psyche in an effort to alleviate psychic tension.

v) **Existential Therapy:** This is based on the existential belief that human beings are alone in the world. This isolation leads to feelings of meaninglessness, which can be overcome only by creating one's own values and meanings.

vi) **Humanistic:** The task of Humanistic therapy is to create a relational environment where this the self-actualizing tendency might flourish.

vii) **Transpersonal Therapy:** Addresses the client in the context of a spiritual understanding of consciousness.

ix) **Body Psychotherapy:** Addresses problems of the mind as being closely correlated with bodily phenomena, including a person's sexuality, musculature, breathing

habits, physiology etc. This therapy may involve massage and other body exercises as well as talking.

Play Therapy, Gestalt Therapy, Rational Emotive Behaviour Therapy, Solution based therapies and Reality Therapy some other forms of psychotherapy.

Speech therapy:

Speech therapy focuses on receptive language, or the ability to understand words spoken and expressive language or the ability to express. It also deals with the mechanics of producing words, such as articulation, fluency and voice. Speech therapy also deals with rehabilitation of language in children who do not speak congenitally due to hearing impairment, mental retardation, autism or attention deficit hyperactivity disorder.

Speech and language therapy is beneficial in neurogenic disorders of non - progressive and progressive origin.

i) **Aphasia:** Aphasia is defined as loss of reception or expression of language as a result of brain stroke. It can be classified as Broca's aphasia (patient presents with intact comprehension with affected expression), Wernicke's (patient presents with affected comprehension with jargon speech), Anomia or nominal aphasia (patient presents with naming difficulties).

   Recovery from aphasia depends on many prognostic factors like age, site and extent of lesion, concomitant problems and time lapsed between the stroke and initiation of therapy. Rehabilitation in aphasia focuses on the following:

   a) Improving auditory comprehension using pointing tasks "point to the spoon".
   b) Encouraging verbal utterances voluntarily.
   c) Improving sentence formation.
   d) Improving naming

   A study done on aphasics concluded that combination of two inout channels - auditory plus visual, auditory plus gestural may facilitate better comprehension and performance by the patient

   Many of the cases of do not improve with traditional speech and language. In such cases, nonverbal modalities can be used to augment or alternate patient's communication. The most commonly used AAC are communication boards, gestures and use of written modality.

   According to Collins (1986), severly aphasic patient may rely more on pictures for basic need that cannot be readily expressed by pointing or natural gesturing (as cited in Davis,2000) (5)

ii) **Dysarthria:** The literal definition of dysarthria is disordered utterance (dys means disordered or abnormal; arthria means to utter distinctly). A more comprehensive definition is that dysarthria is the impaired production of speech because of

disturbances in the muscular control of the speech mechanism (as cited in Freed, 2000). Dysarthria can be classified as spastic dysarthria (due to upper motor neuron lesion), flaccid dysarthria (due to lower motor neuron involvement), ataxic dysarthria (due to cerebellar involvement), hypokinetic and hyperkinetic dysarthria (due to basal ganglionic involvement) and mixed dysarthria.

Common causes of dysarthria are stroke, motor neuron disorder, multiple sclerosis, head injury and Parkinson's disease to name a few.

Most of the patients with dysarthria present with inability to produce sounds clearly, reduced loudness and monotonous or robotic speech. In cases of flaccid and spastic dysarthria, oro - motor structures and functions are restricted.

Treatment of dysarthria depends on the severity of speech problem. Speech and language pathologist aim to improve speech intelligibility (overall clarity of speech) by:

a) PNF (proprioceptive and neuromuscular facilitation).
b) Improving loudness levels.
c) Improving articulatory precision by using exaggerated consonants.

iii) **Apraxia:** According to Darley (1969), apraxia is an articulatory disorder resulting from impairment, as a result of brain damage of the capacity to program the positioning of speech musculature and the sequencing of muscle movement for the volitional production of phonemes. No significant weakness, slowness, or incoordination in reflex and automatic acts is seen (as cited in Freed, 2000). Treatment of apraxia of speech involves phonemic drills, giving proprioceptive and kinesthetic cues to the patients. MIT (melodic intonation therapy) is another technique used (as cited in Freed, 2000).

Darley (1975) stated that the goal of treating apraxia of speech is to help patients relearn the motor sequences needed to produce phonemes accurately.

iv) **Dysphagia:** Dysphagia means disordered swallowing. Swallowing disorders occur in all age groups from newborns to the elderly, and can occur as a result of CVA, presence of tumors and/ or progressive neurologic conditions. Swallowing consists of 4 stages namely oral preparatory, oral, pharyngeal and esophageal stage. Depending upon the stage affected, a swallowing therapist needs to make a judgement on the treatment modality.

A swallowing therapist aims to work on:

a) strengthening the oral and pharyngeal structures for swallowing.
b) modify the bolus in order to facilitate adequate swallowing.
c) recommend postures and maneuvers like chin tuck/ chin down postures according to the nature of disorder. During swallowing therapy, the therapist should ensure airway safety and rule out any silent aspiration. Children with autism, cerebral palsy, hearing impairment or mental

retardation present with either absence of speech or deficient speech and language skills as compared to their age. The main aim of the speech therapist is to bridge the gap between the chronological age and the language age of the child. The speech and language pathologist tries to explore the areas which the child would respond in and facilitate communication within child's impairment. Most widely used techniques for language learning are repetitions, modeling utterances, expanding a topic and role play. However, children with higher grade of severity may have to rely on alternative and augmented communication (AAC) in order to reduce the communicative burden on the caregivers.

48. Recent Advances in Neurosurgery

Modern Neurosurgical facilities have made the cures for serious Brain and Spine problems safer and more definitive. We now have better results with fewer complications, total cures, lower risks, lesser discomfort and shorter and lesser treatments. The modern neurosurgical advances include better and more specific pre-operative investigations more precise surgery in the form of micro-neuro surgery, minimally invasive surgery, and advanced technological assistance. The post-operative care has been improved by sophisticated intensive care monitoring and treatments. For conditions, where neurological deficits persists despite all medical and surgical interventions there is now the availability of stem cell therapy and aggressive neuro-rehabilitation. Together all of these, have resulted in significantly better outcomes in the present as compared to what the results were several years ago.

The recent advances in neurosurgery may be divided into following :

1) Micro neurosurgery
2) Minimally invasive neurosurgery

a) Stereotactic and functional neurosurgery

b) Neuroendoscopy

c) Interventional Neuroendovascular treatment

d) Radiosurgery

3) Neuromodulation and Neurostimulation

4) Advanced Spinal Surgery

Microneurosurgery

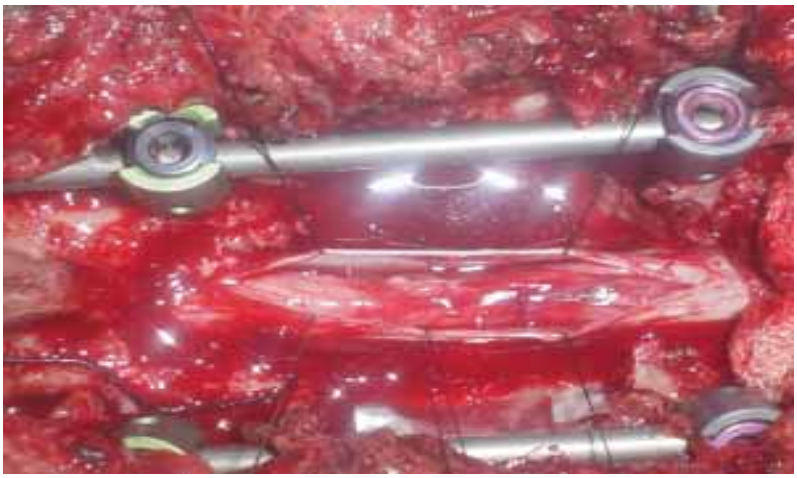
The availability of sophisticated operating microscope which have high magnification, have resulted in more accurate, refined and safer neurosurgery since the visualization of vital brain structures as well as normal areas is significantly enhanced. There is less blood loss as well as less damage to normal structures. The following procedures are now regularly done with the operating microscope. Large as well as difficult to access tumours are now much more easily resected through microneurosurgery. These include malignant as well as benign tumours.

A few examples of micro neurosurgery are shown below in pictures :

Brain Tumour surgery

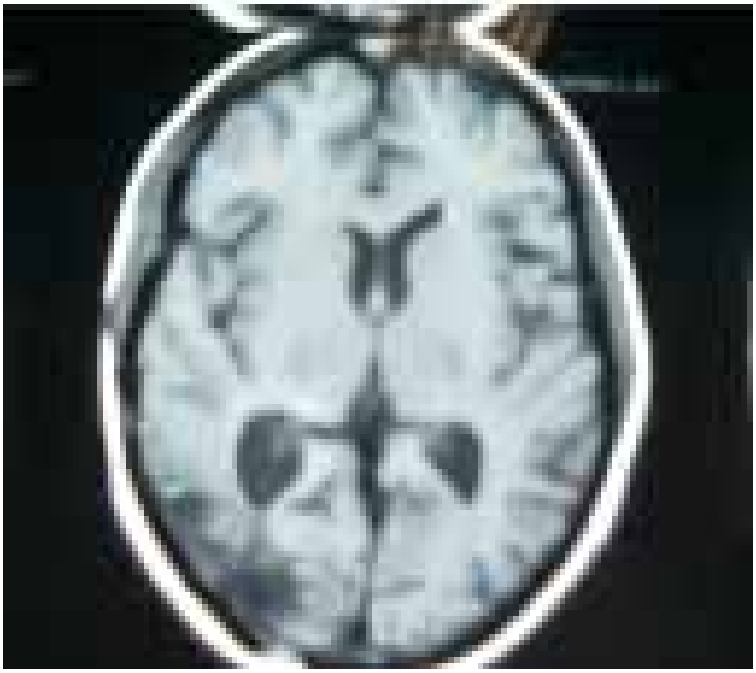
Brain tumors may be malignant or benign and when they are large need to be removed without causing damage to the surrounding normal brain. Microneurosurgery has made this possible now with good overall results. People can lead normal lives after major brain tumor surgery.

(i) This is a highly malignant brain tumour which has been totally excised.



A highly brain tumour (glioma)

Tumour removal being done with the microscope and CUSA (Cavitron Ultrasonic Suction Aspirator)



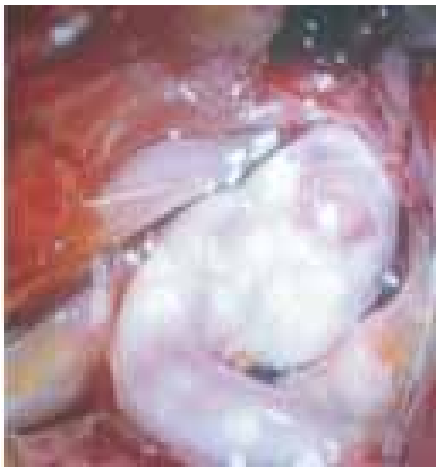
Total tumour removal done.

Vascular Surgery

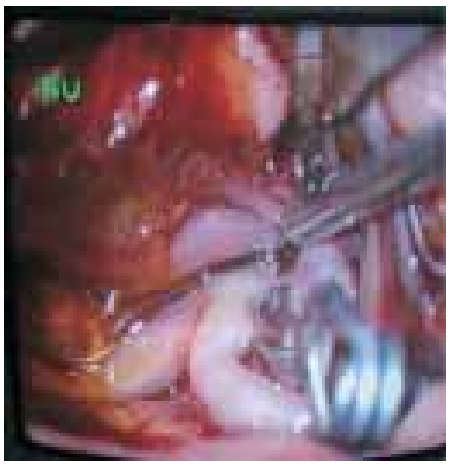
Aneurysms and Arteriovenous malformations can rupture and cause intra-cranial hemmorhage and therefore need to be treated. The 2 options are:

Microsurgical clipping for aneurysms/Excisions of AVMs or interventional coiling. This is a decision that the treating neurosurgeon makes in consultation with the family.

Clipping of Aneurysm

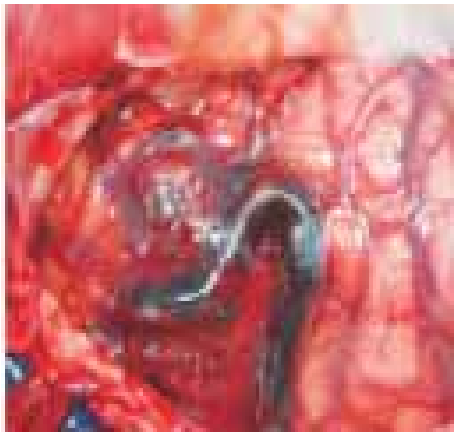


Intracranial aneurysm which had bled



Aneurysm successfully clipped with micro Neurosurgery

Excision of AVM

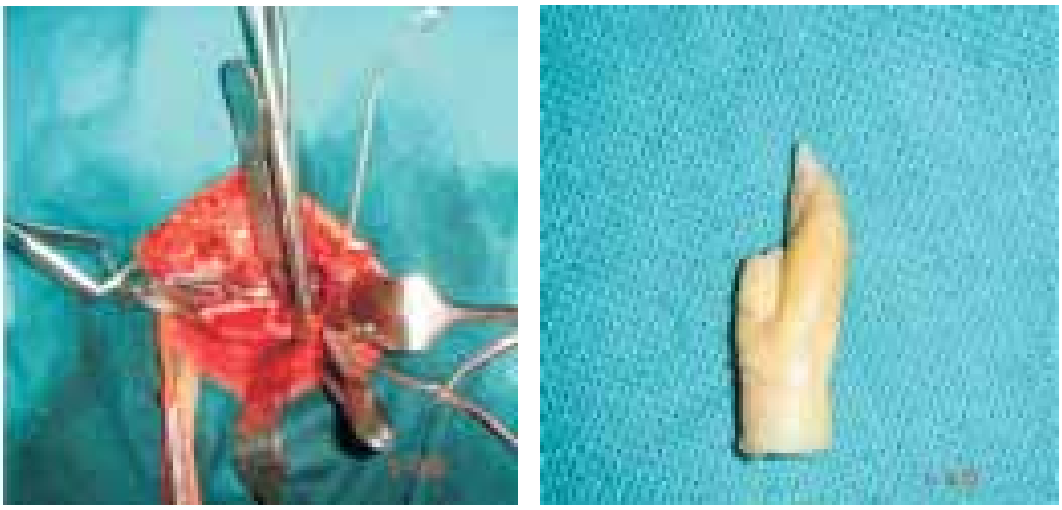


Intracranial AVM which had bled

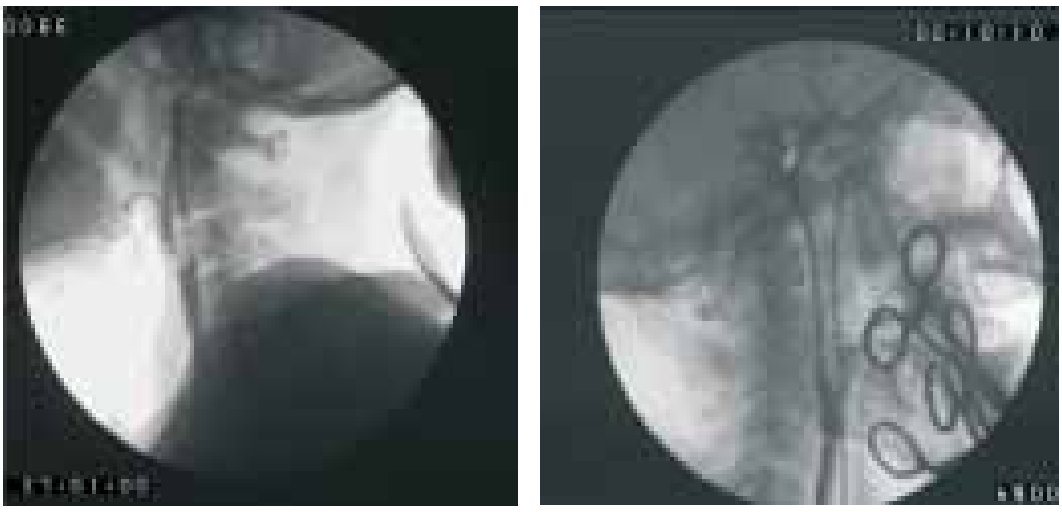
Successful micro-neurosurgical removal of AVM

Carotid Endartrectomy

Surgery for Carotid Artery Stenosis due to atherosclerotic plaque (Carotid Endareterectomy) effectively reduces the relative risk of stroke by 55% in patients with more than 70% carotid stenosis and by 35% in patients with stenosis between 50% and 69%. The surgery involves opening the carotid artery and removal of the plague. Interventional stenting is also an option if the stenosis is not very severe.



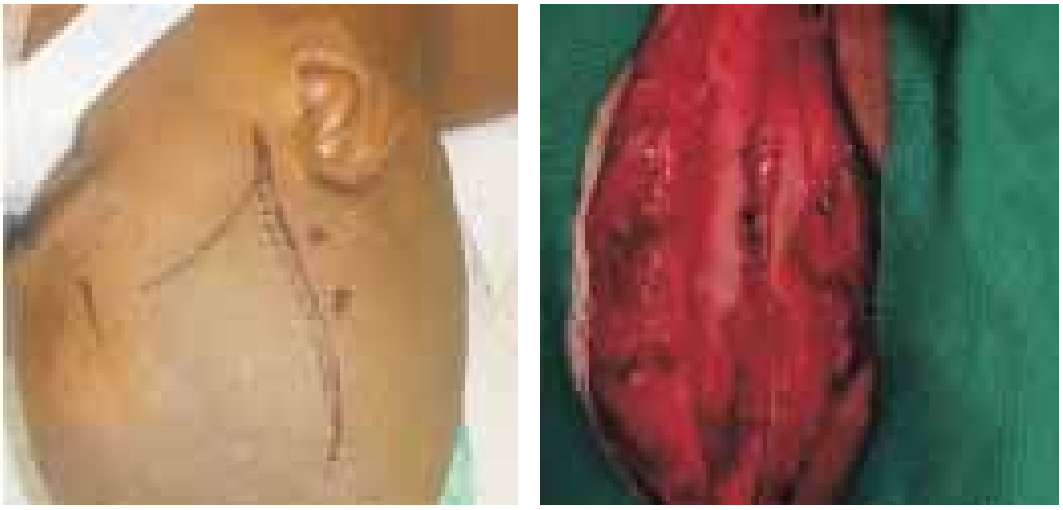
Athero matus plaque in the carotid artery removed microsurgically



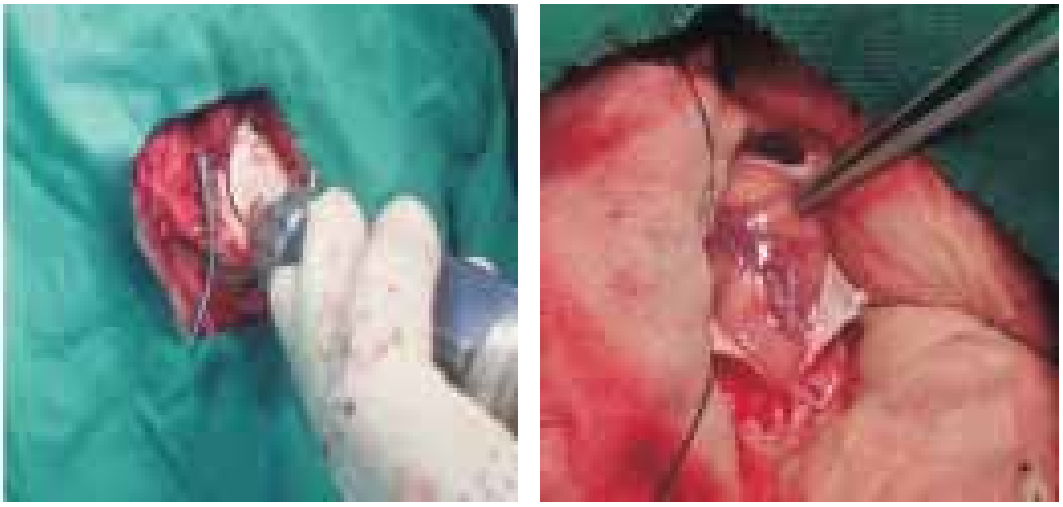
Pre-operative DSA showing the plaque obstructing the carotid and post operative DSA shows restoration of the blood supply

STA - MCA Bypass

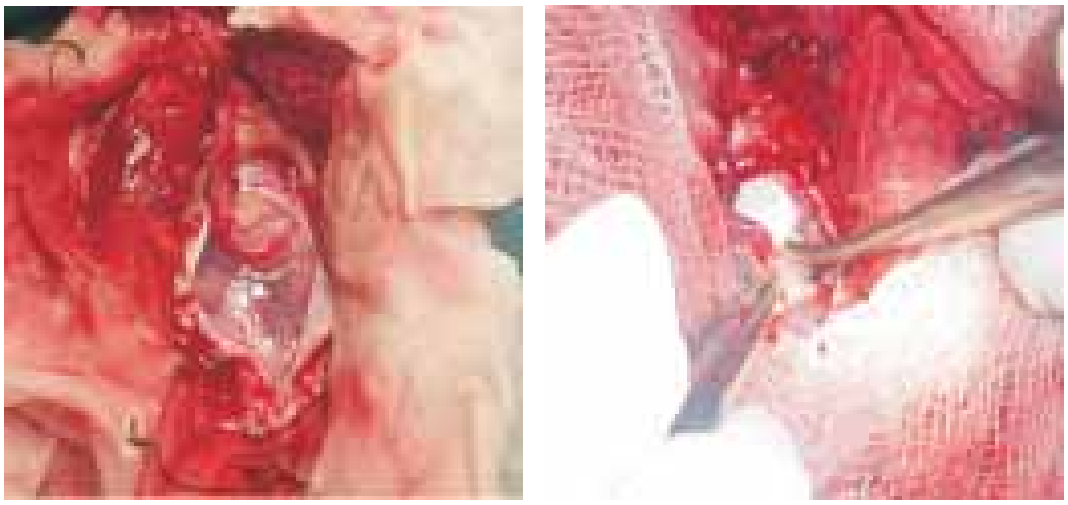
The superficial temporal artery to middle cerebral artery by pass surgery is indicated in some special cases. It helps revascularize the ischemic brain when the MCA blood supply is compromised.



Superficial artery dissected from below the scalp

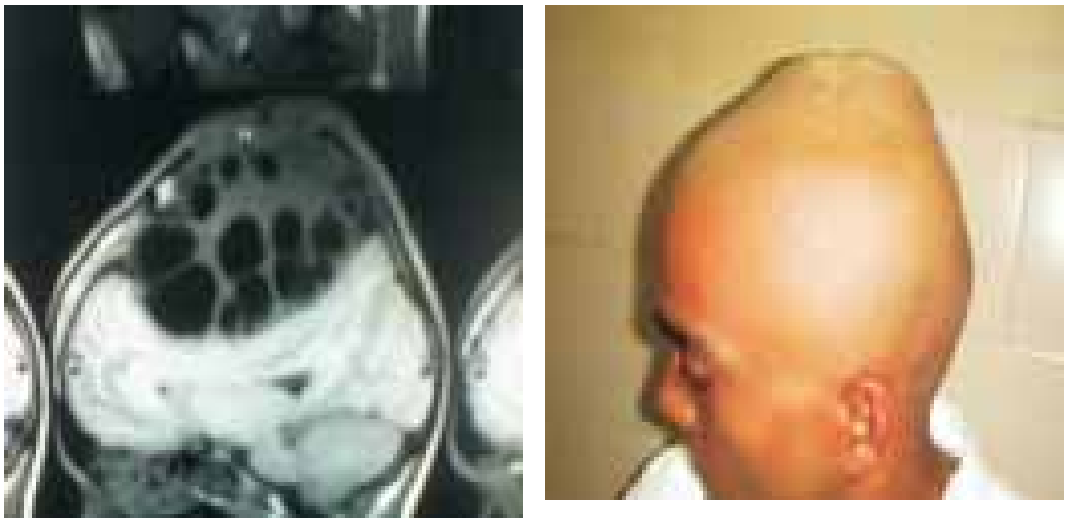


The skull opened and middle cerebral artery identified

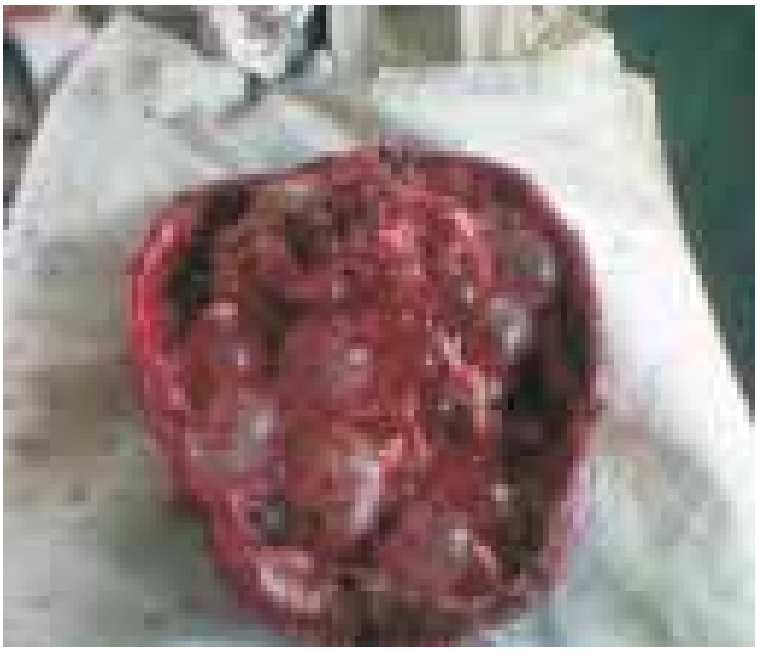


An anastamosis done of the superficial temporal artery to the middle cerebral artery bypassing the block in the middle cerebral artery and restoring blood circulation to the ischemic brain

Excision of Hydatid Worm Cysts in the Brain



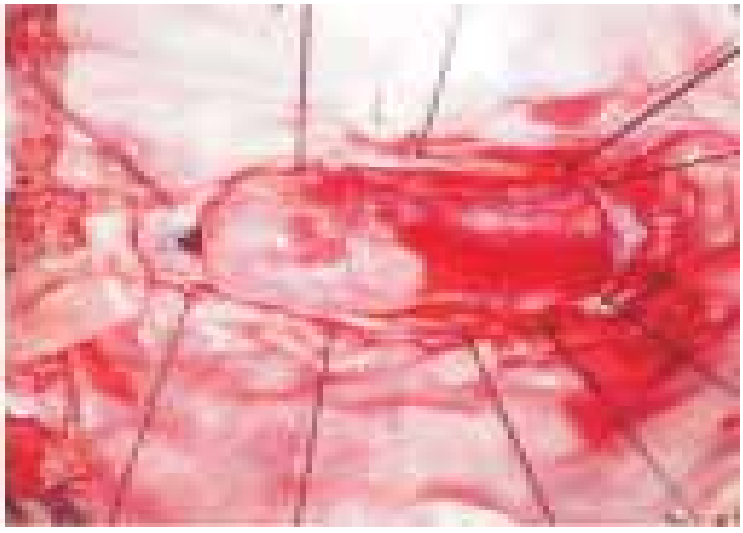
Large intracranial collection of hydatid cyst



Total microsurgical removal of the intracranial worm cyst

Removal of spinal tumour

Spinal tumprs by causing compression on the spinal cord can cause paraplegia or quadriplegia and so need to be surgically excised. The removal of these tumors microsurgically gives very good results.



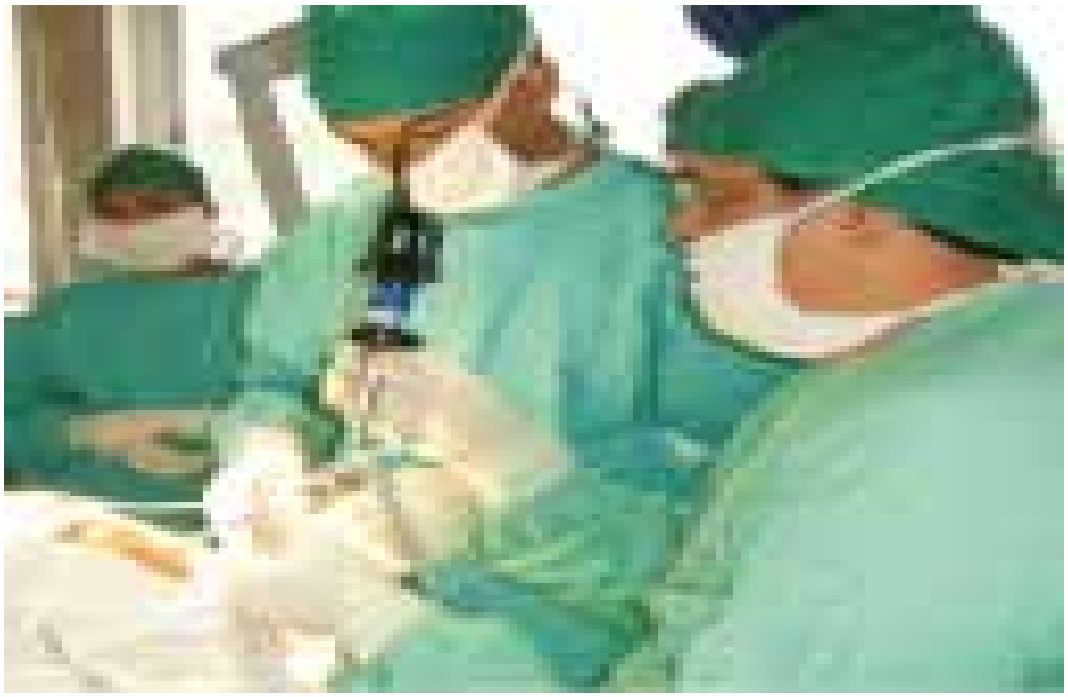
Intradural Spinal Tumours are safely removed through micro-neural surgery

Minimally Invasive Neurosurgery

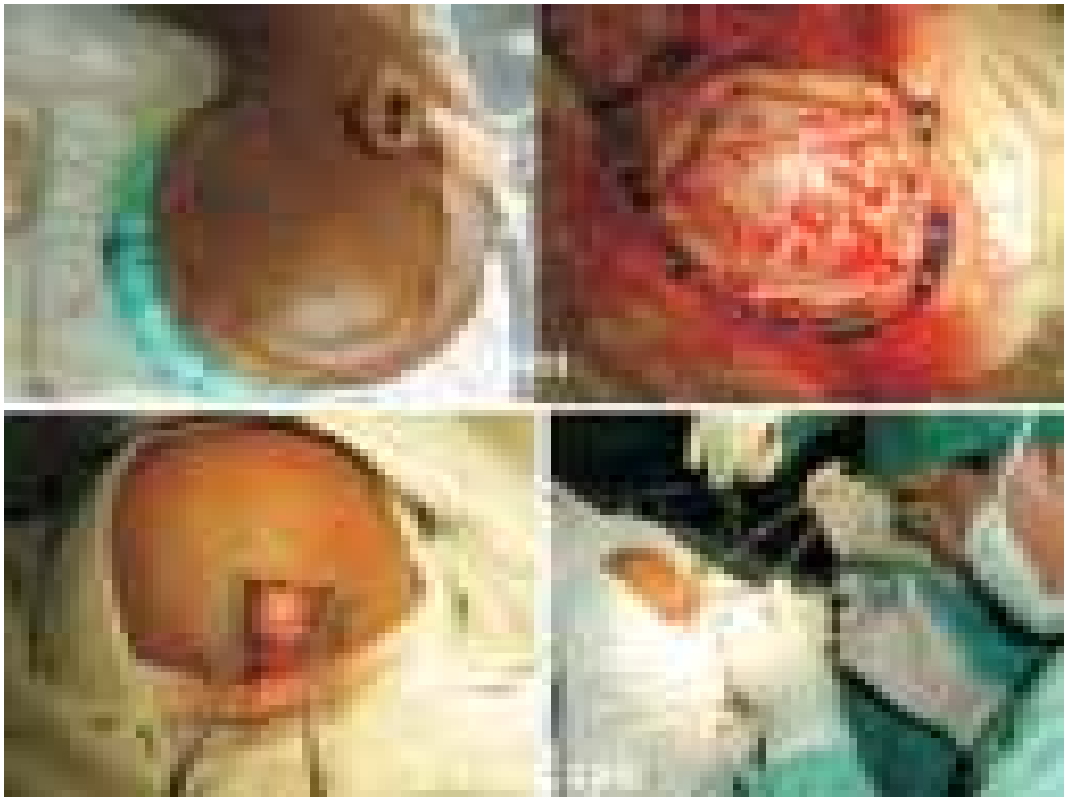
This includes neuroendoscopy, stereotactic surgery, interventional endovascular therapy and radiosurgery

Neuroendoscopy

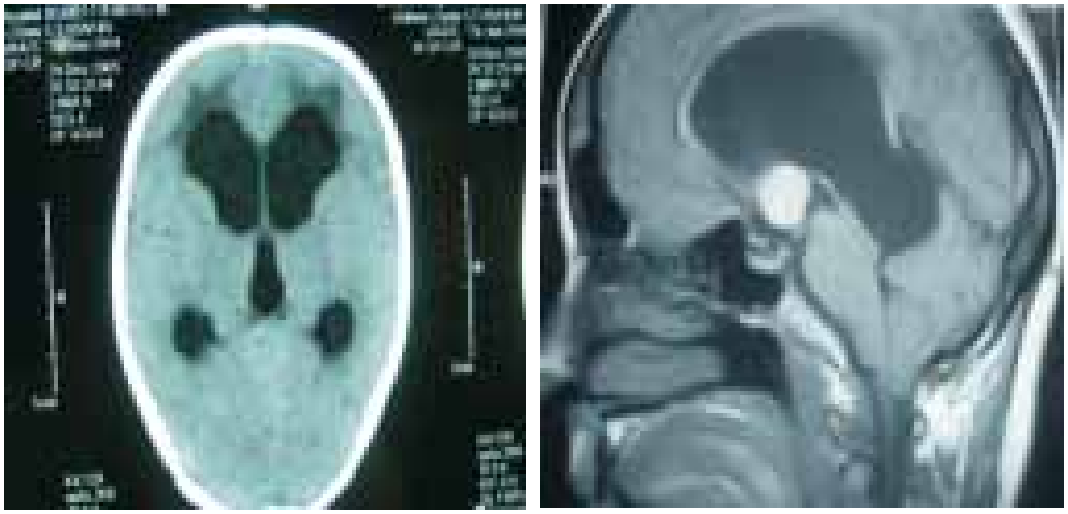
Neuroendoscopy involves the surgical treatment of disorders of the brain and the spine, using keyhole techniques and the use of specially designed endoscopes. There are three main areas where neuroendoscopy can be used. These are for intraventicular lesions and the treatment of hydrocephalus, surgical excision of pituitary tumors, spinal surgery in cases of prolapsed discs removal.Brain tumors and lesions within the ventricles can be removed with an endoscope through a small hole instead of opening the whole skull through a craniotomy. A major indication for intraventicular endoscopy is in the management of selected cases of hydrocephalus. The conventional treatment of the same involves the operation of the ventriculo-peritoneal shunt. This has many complications such as blockages and infections. Endoscopic cranial base Surgery for tumors on the base of the skull can be removed through the nose, via the endoscope in a stitch less surgery i.e. no external incisions are made. It is mainly useful for pituitary tumors and occasionally other tumors such as angiofibromas and clival chordomas. Complications are much less and patient can go home in 4 to 5 days.



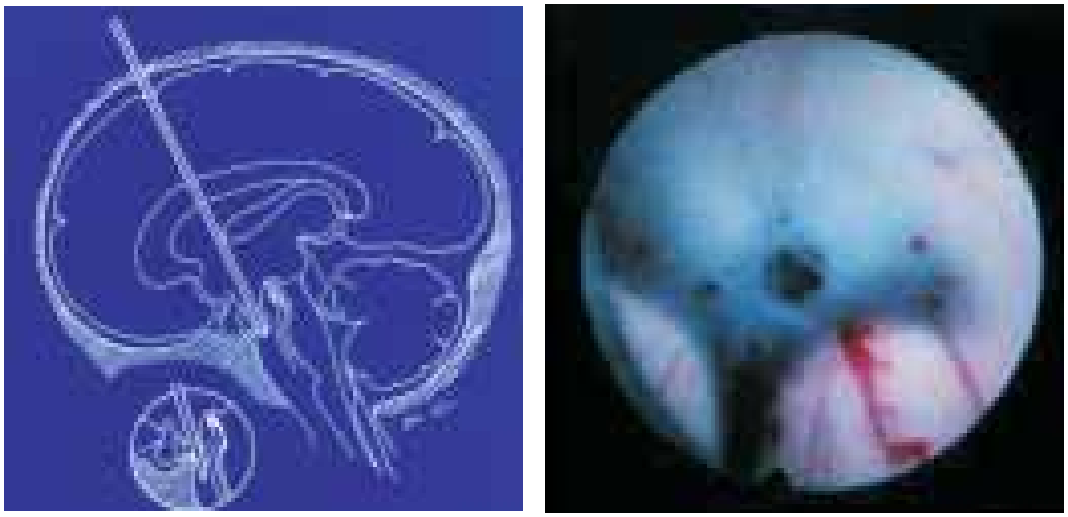
Operating with the help of a neuroendsocope, surgery can be done through a small opening in the skull instead of opening the entire skull.



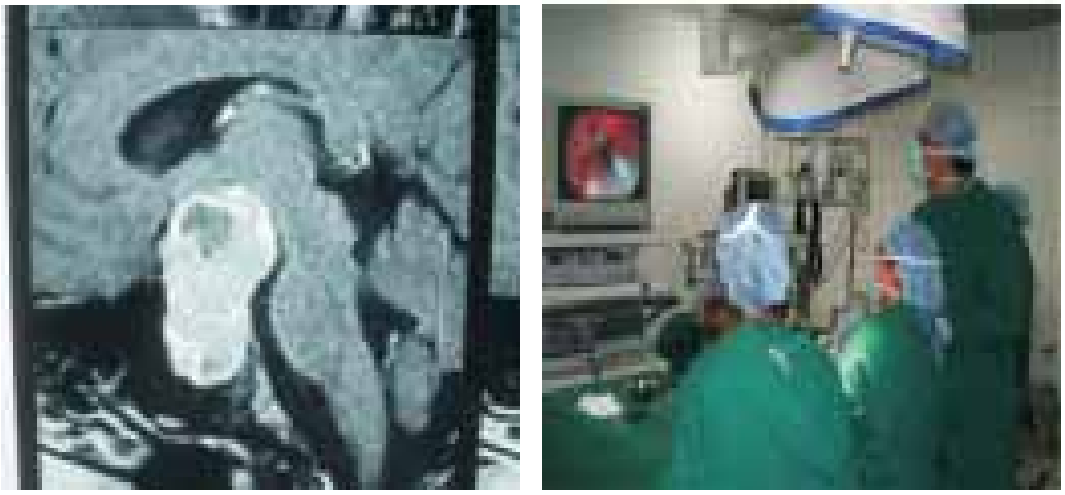
Difference between the skull opening made in open surgery versus endoscopic surgery



Conditions that can be treated with the endoscope include hydrocephalus and intraventricular cysts



The operation of endoscopic 3rd ventriculostomy is modern replacement operation for the conventional VP shunt surgery in selective cases.

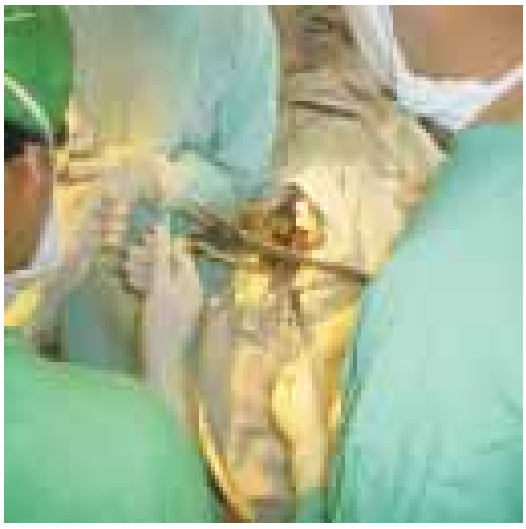


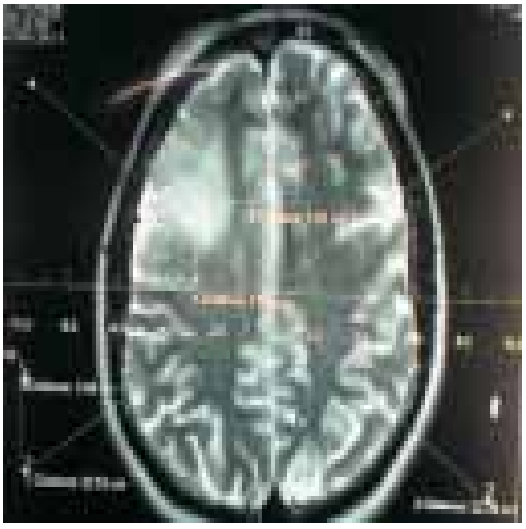
Large pituitary tumour successfully removed through the nose endoscopically

Stereotactic neurosurgery

With the use of the Leksell Stereotactic frame surgeries can be done from a small hole in the head instead of opening the whole skull. Stereotactic Surgery is useful for :-

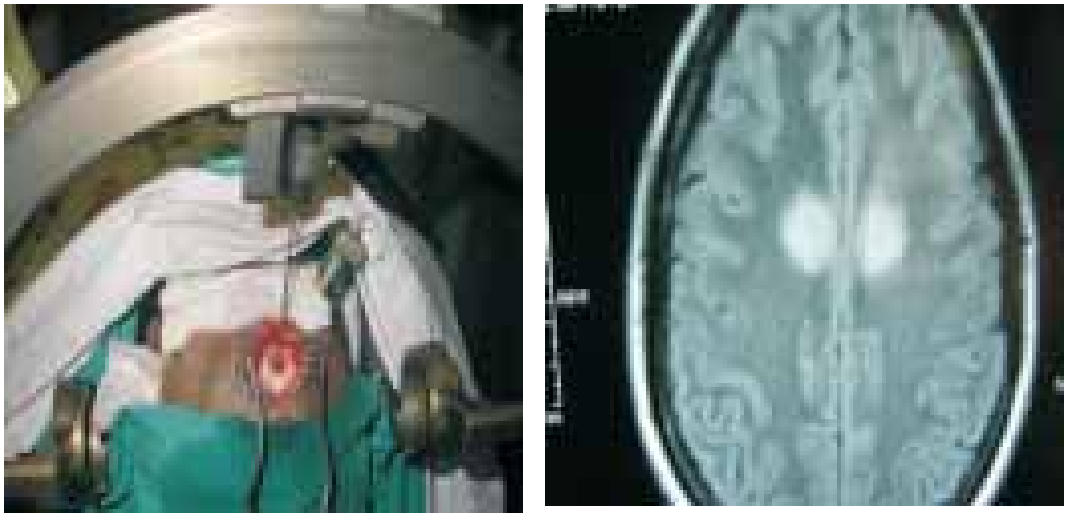
- Brain tumors
- Brain Hemorrhage
- Brain infections
- Brain cysts
- Parkinson's disease
- Psychiatric disorders
- Pain





Stereotactic biopsy can be done of malignant brain tumours

Intracranial Haematomas can be evacuated through minimally invasive method using Stereotactic frame.



Electrodes can be inserted into the brain to make lesions as part of functional Stereotactic Surgery such as Bilateral Anterior Cingulotomy for Obsessive Compulsive neurosis.(OCD)

Differences between Stereotactic Surgery v/s Open surgery are as follows :-

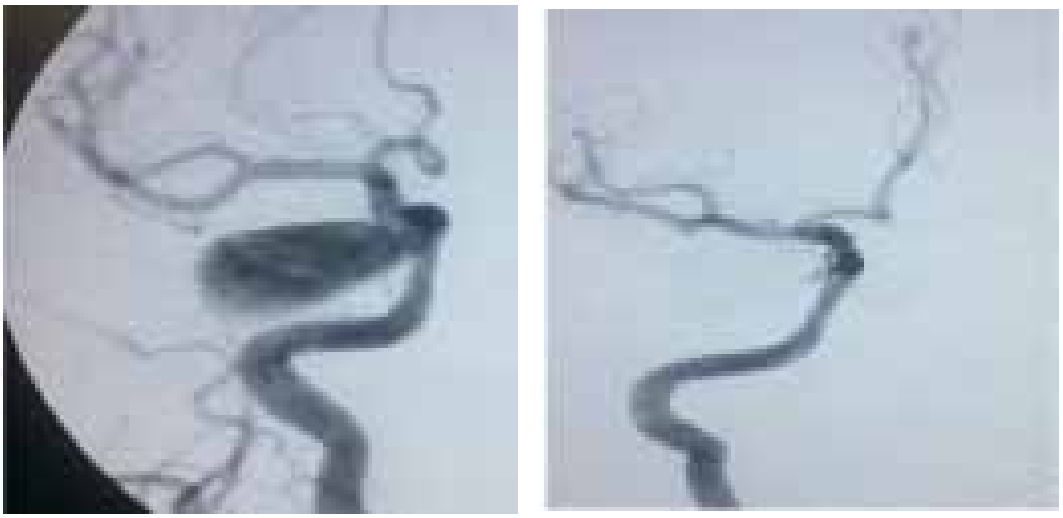
Stereotactic Surgery	**Open surgery**
• Opening: Small hole	• Opening: Whole skull
• Time 30 minutes	• Time: 5-6 hours
• Local Anesthesia	• General Anesthesia
• Stay in hosp - 3 days	• Stay in hosp - 10 days
• Less complications	• More complications
• Less expensive	• More expensive

Interventional endovascular therapy

Interventional therapy is done by passing a catheter from a puncture in the thigh and sending it through the blood vessels all the way into the brain vessels. Similar to the way angioplasty & similar procedures are done in cardiac patients. The Advantages of Interventional therapy are that they are very significantly less complications as compared to open surgery. Many cases that are untreatable by open surgery can be treated with Interventional. Sometimes supplements open surgery and the hospital stay is shorter.

The indications for Interventional therapy are :-

- Aneurysms of the brain
- AVM's in the brain
- Carotid artery stenosis / block
- Blockage of Intracranial blood vessels
- Vascular brain tumours



Interventional endovascular treatment of intracranial using coils

Radio Surgery

Radio Surgery is a treatment technique that use external radiation to treat certain type of brain tumours and vascular malformations. There are 3 types of radio surgery available :

[a] Gama knife

[b] X knife

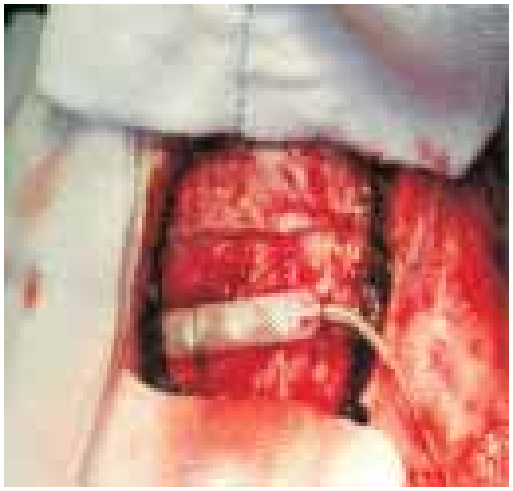
[c] Cyber knife

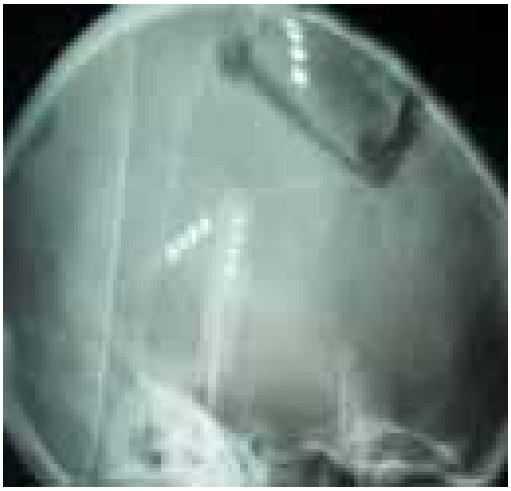
All these have comparable results but for specific indications one may be better than the other. Since this is an external treatment , it is completely non-invasive and therefore, totally safe. However its limitations are not all brain tumours can be treated with radio surgery. Availability as well as high cost are also the limitations.

Neuromodulation & Neurostimulation

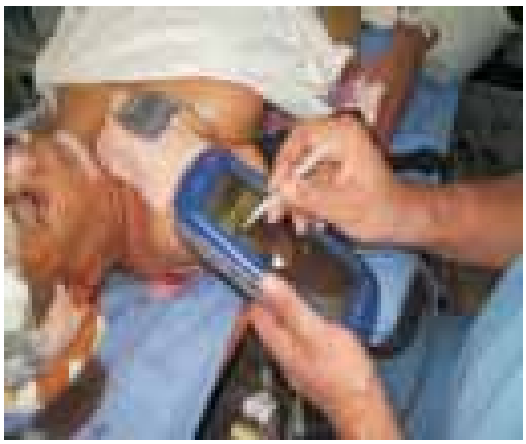
Neurostimulation is the implantation of electrodes into the brain or spinal cord along with an internal pacemaker and an external handheld programmable device. Neuromodulation and neurostimulation can be used for many conditions such as intractable pain, Parkinsons disease, movement disorders, coma, spasticity, psychiatric disorders, etc

Motor cortex stimulation being done for intractable pain

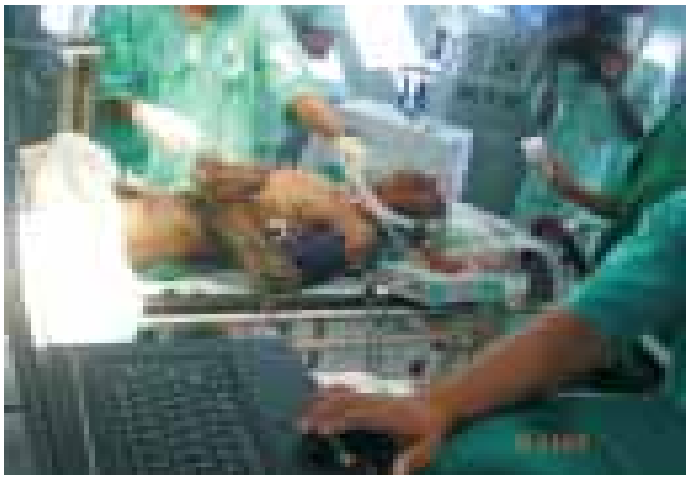




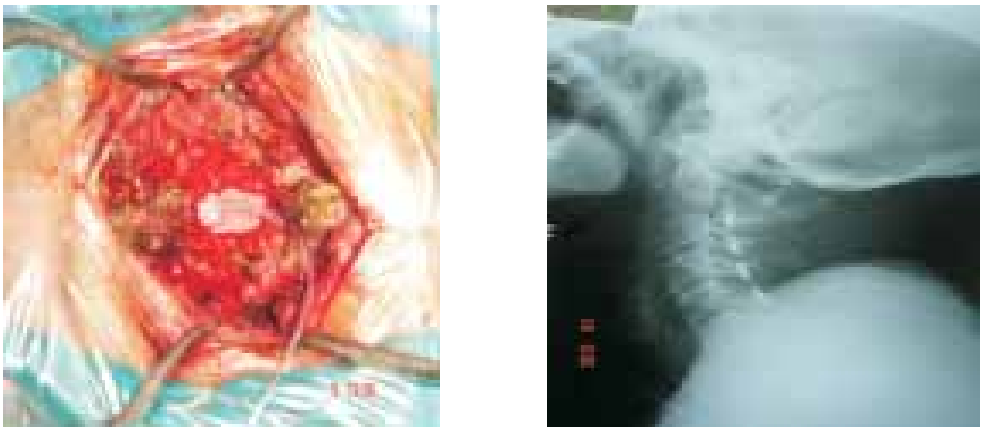
Electrodes within the brain



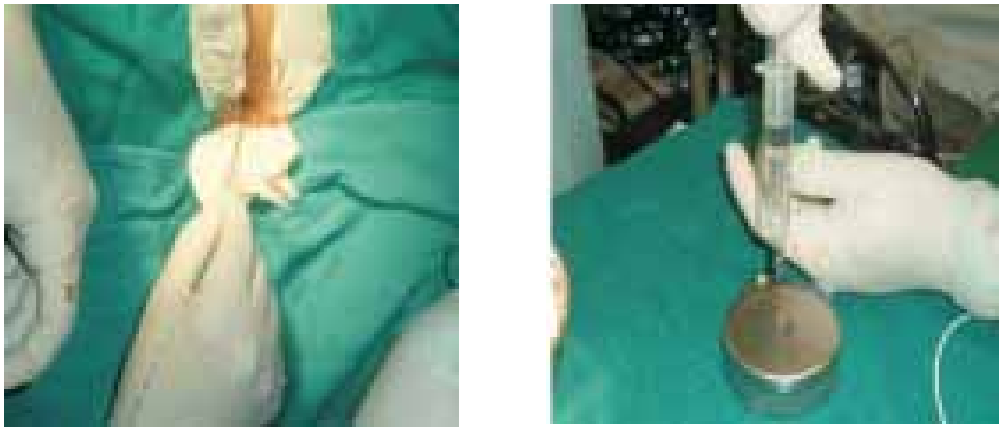
External programmer being used to program the stimulation



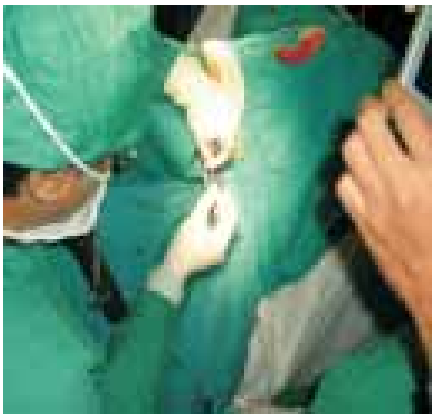
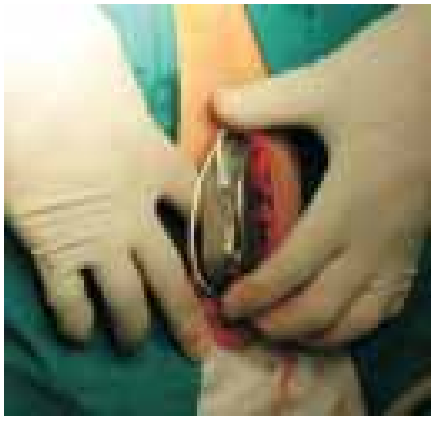
Dorsal column spinal stimulation being done for persistent vegetative state (coma)

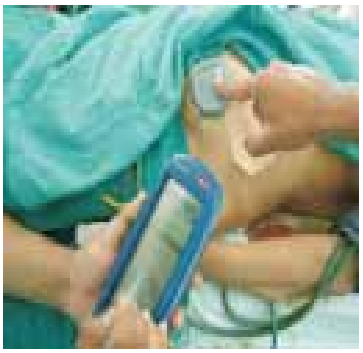


Electrodes placed on the spine



Implantation of intrathecal baclofen pump through which continuous drugs (baclofen for spasticity or morphine for pain) can be infused directly into the CSF surrounding the spinal cord and the brain.

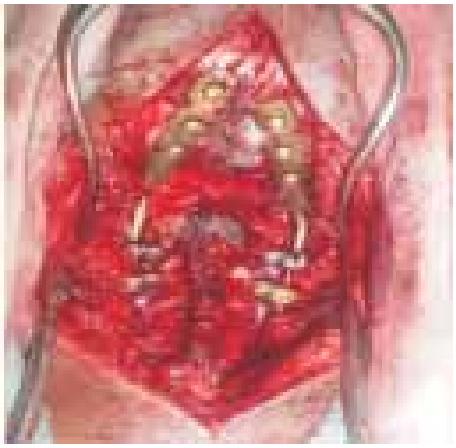
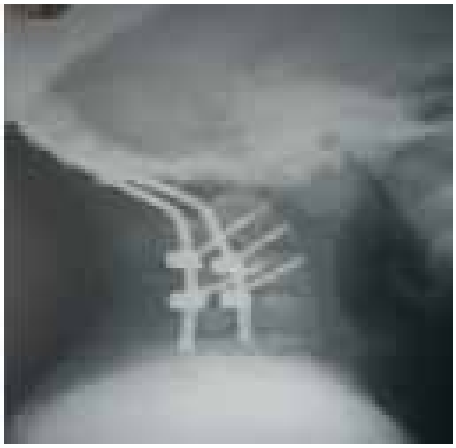



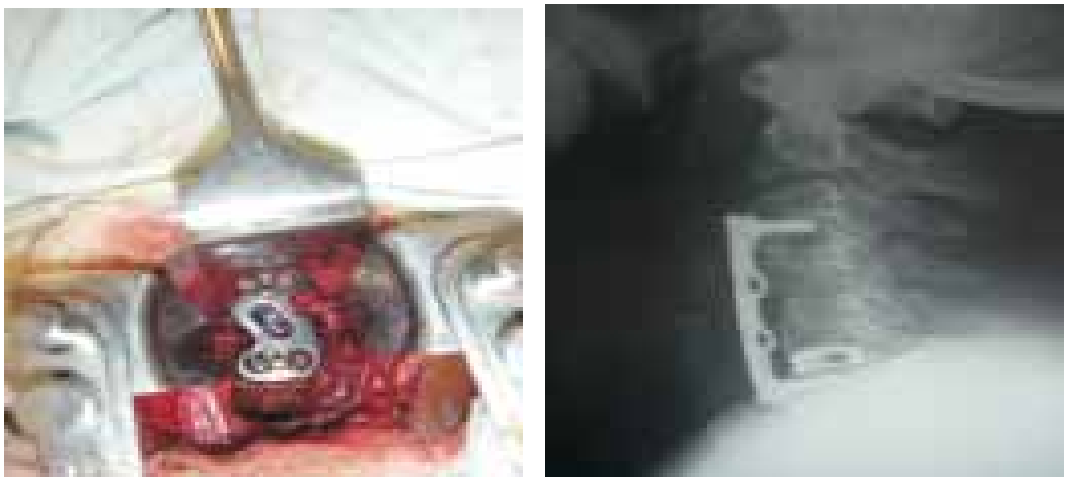
Spine Surgery

Spine Surgery for degenerative spinal conditions, trauma, infections, etc has become much safer and much effective due to two main reasons :-

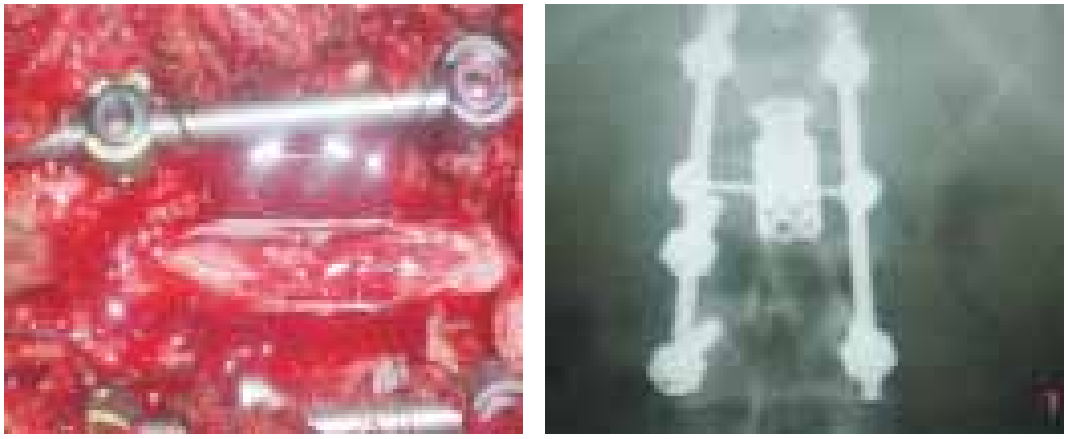
a) The availability of sophisticated instrumentation using titanium implants
b) The possibility of minimal invasive spinal surgery

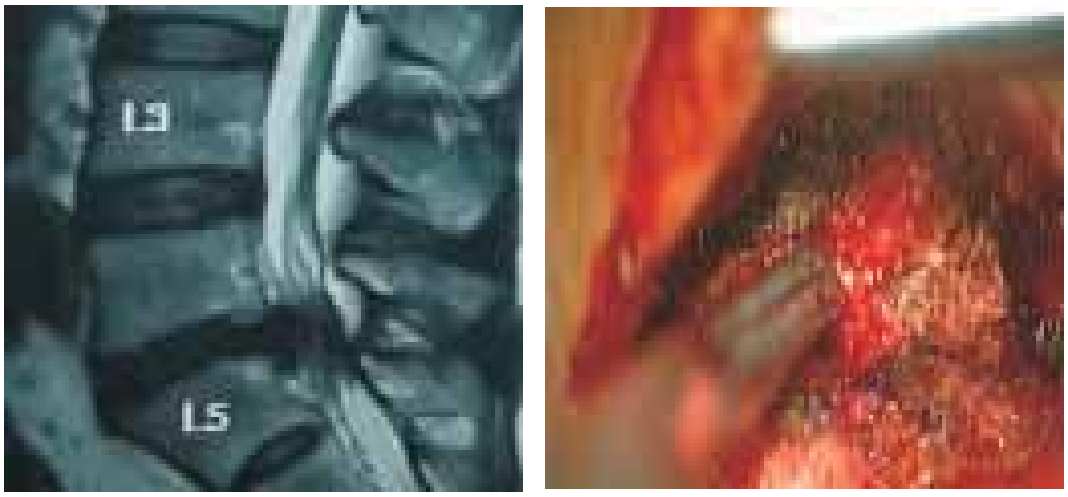
Decompression and Stabilization for the cranio vertebral junction



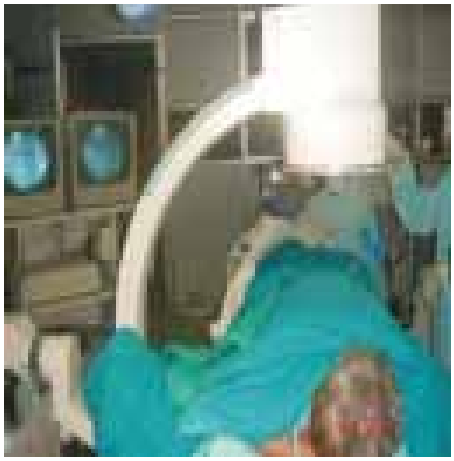
Anterior decompression and fusion surgery for the cervical spine

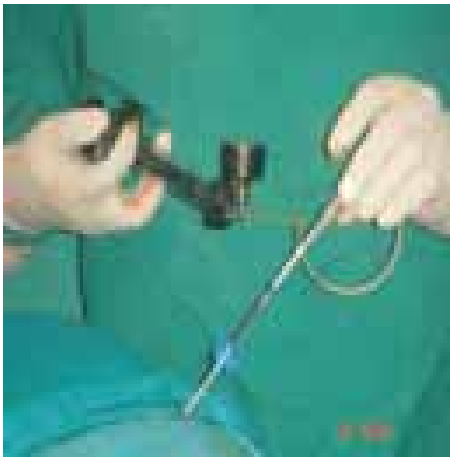


Stabilization Surgery for the dorsal spine injury



Microlumbar discectomy surgery for lumbar spine prolapse disc





Percutaneous spine surgery (kyphoplasty) for vertebral collapse in dorsal spine done under local anaethesia.

Conclusion

Advanced technology has made available to the neurosurgeon micro neurosurgery, minimally invasive surgery and sophisticated implants which have resulted in much safer and more effective neurosurgical treatments for various brain and spine disorders.

49. Stem Cell Therapy for Incurable Neurological Disorders

Stem cell therapy has brought in a revolution in the field of medicine. Diseases, which were thought to be incurable and untreatable, can now be treated, using stem cells and cellular therapy.

What are stem cells?

Stem cells are building blocks of our body. These are very special cells, which have special properties, which make them useful tools for healing or regenerating tissues which are lost.

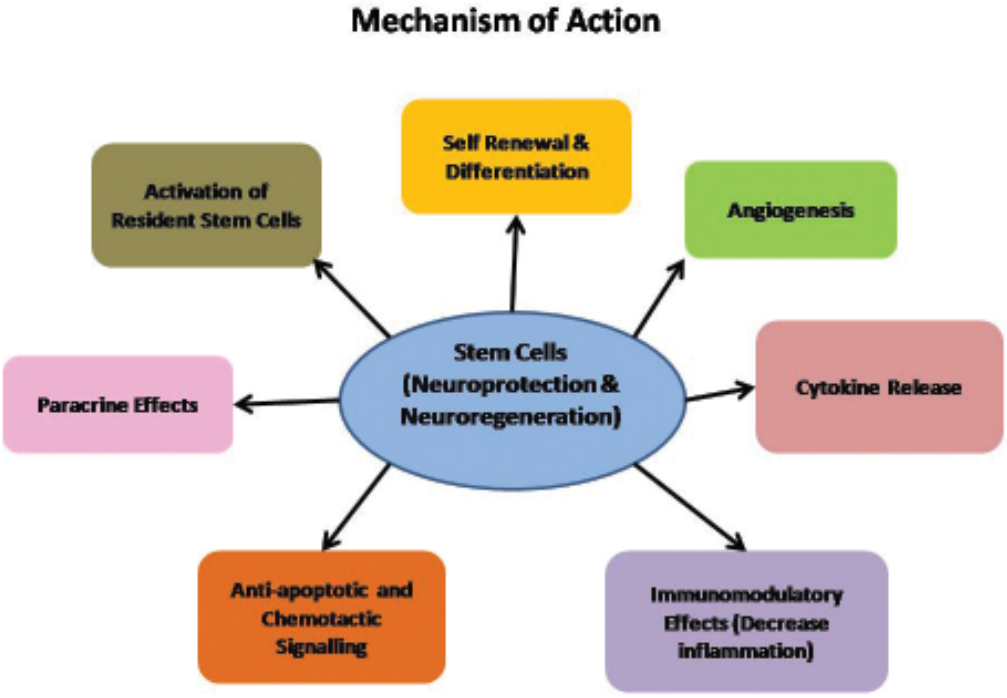


Fig. 46.1: Mechanism of action of stem cells

These properties are: ability to multiply manifold and also convert into specific cells types depending on environmental cues.

Stem cells are of different types and potencies, depending on where they are taken from.

Types of Stem Cells:

Embryonic stem cells are derived from IVF clinics, from 3-4 days old embryos. These are most potent,but have ethical issues surrounding there use.Side effects include potential teratoma formation. (We donot use embryonic stem cells at Neurogen BSI)

Umbilical cord blood derived stem cells and stem cells from placental tissue are also a rich source.

Adult stem cells derived from bone marrow, adipose tissue, dental pulp, etc, are the most used in clinical practice. They have no ethical issues or controversies, are safe for use (especially if used for the same patient) and efficient. (At Neurogen BSI, we only use autologous adult stem cells)

What disorders/diseases can stem cell treat?

NeuroGen Brain and Spine institute, now has an experience of treating over 2700 patients with incurable neurological disorders, such as cerebral palsy, autism, mental retardation, brain stroke/paralysis, head injury, cerebellar ataxia/atrophy, cerebral atrophy, dementia, spinal cord injury, muscular dystrophy, genetic neurological disorders, neuromuscular disorders, etc.

How is stem cell therapy done?

The protocol of stem cell transplantation followed at NeuroGen BSI is MINIMALLY INVASIVE, hence simple, safe and effective.About 100 ml of bone marrow is aspirated from the anterior superior iliac spine ,mononuclear cells are purified/separated and injected intrathecally .

In special cases, such as patients with muscular dystrophy, stem cells are also injected intramuscularly.This is followed by an extensive holistic neurorehabilitation.

Refer Fig. 46.2- 46.4

What are the results of stem cell therapy ?

Autism :

The improvements seen in 100 children with autism who underwent stem cell therapy. Out of these 91% showed clinical improvements. These were reduction in abnormal stereotypical behavior, reduction in self stimulatory behavior, improvement in eye contact, attention span, speech, communication skills and social interactions.

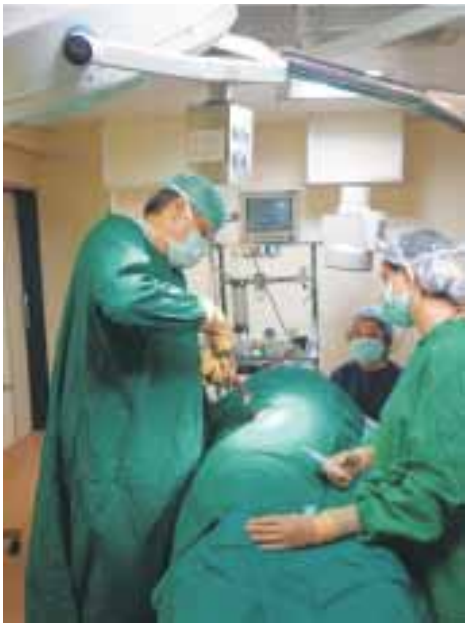


Fig. 46.2: Aspiration of cells from the bone marrow

Fig. 46.3: Separation and purification of stem cells

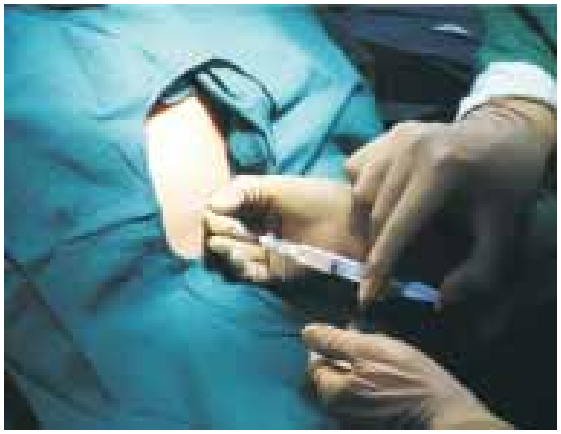


Fig. 46.4: Intrathecal administration of stem cells

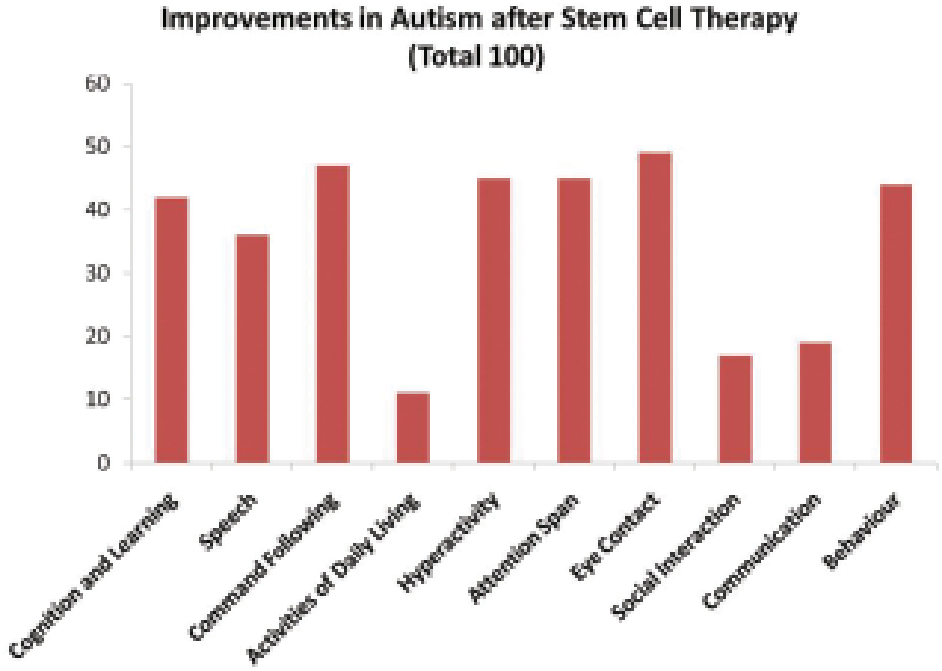


Fig. 46.5: Graph representing improvements in Autism after stem cell therapy

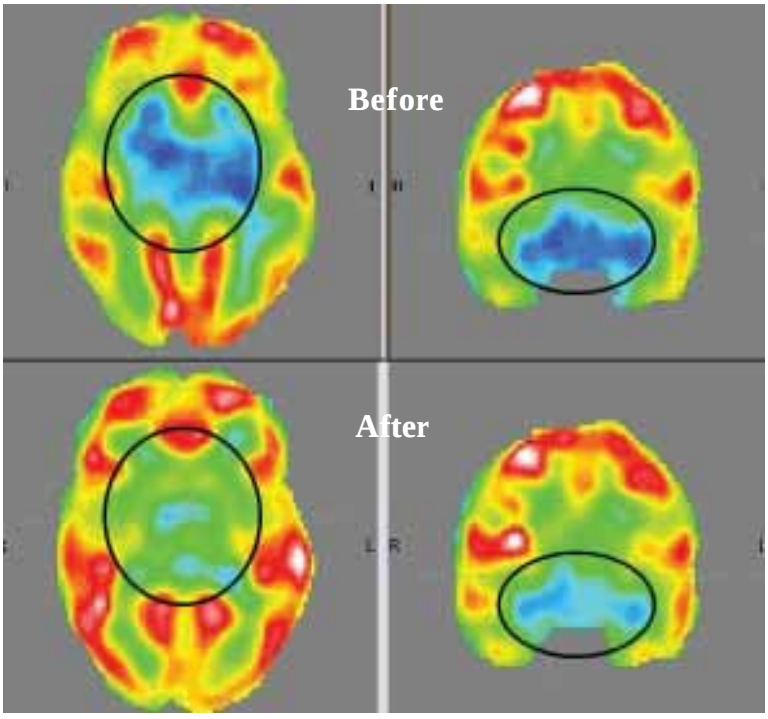


Fig 46.6: Pre and Post PET CT Scans showing improvements in Autism

Cerebral Palsy:

In an analysis of 108 patients with maximum follow up of 4 years, stem cell therapy was found to be safe and effective in 92.6% of the patients. Improvements were in seen in symptoms like oromotor/speech, balance, trunk activity, upper limb activity, lower limb activity, muscle tone, ambulation and activities of Daily Living .

Out of the 108 patients, 15.74% showed significant improvements, 48.14% of patients showed moderate improvements and 28.7 % showed mild improvements.

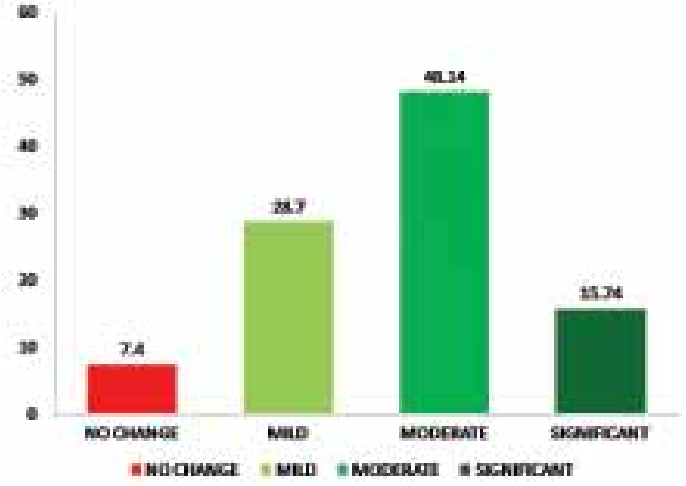


Fig 46.7: Graph representing improvements in Cerebral Palsy after stem cell therapy

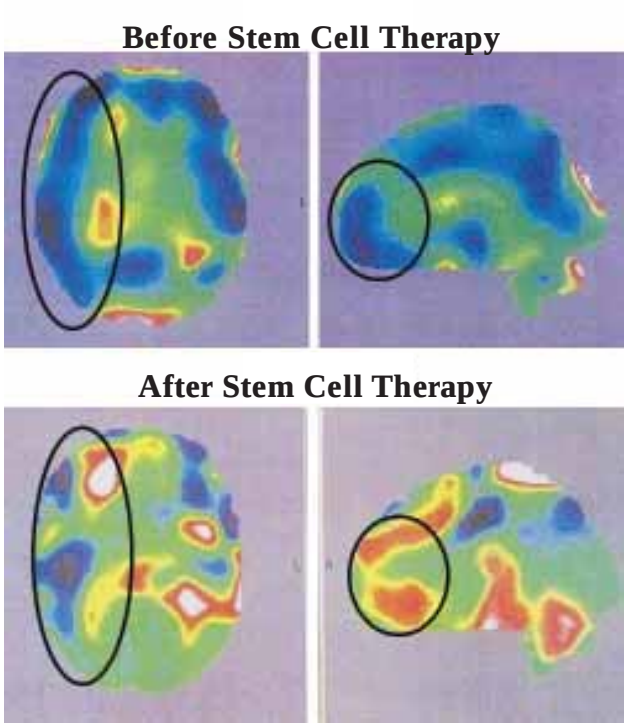


Fig 46.8: Pre and Post PET CT Scans showing improvements in Autism

Fig 46.9a: A child with cerebral palsy unable to sit before the treatment and able to walk with support after the treatment.

Fig 46.9b: Cerebral Palsy Patient showing functional improvement after stem cell therapy

Muscular Dystrophy

332 muscular dystrophy patients who underwent intrathecal autologous bone marrow derived mononuclear cell transplantation were followed up and reviewed. 93.98% showed improvements in symptoms such as hand function, balance, stamina, trunk activation, standing and ambulatory status. 42.77% showed significant improvement, 36.14% showed moderate improvement while 15.06% showed mild improvement.

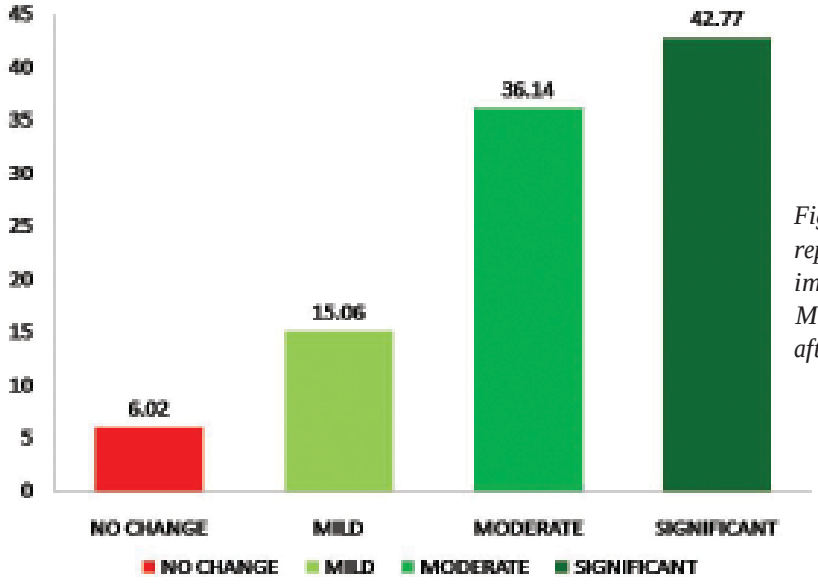


Fig 46.10: Graph representing improvements in Muscular Dystrophy after stem cell therapy

Fig 46.11a : Patient wheelchair bound before stem cell therapy

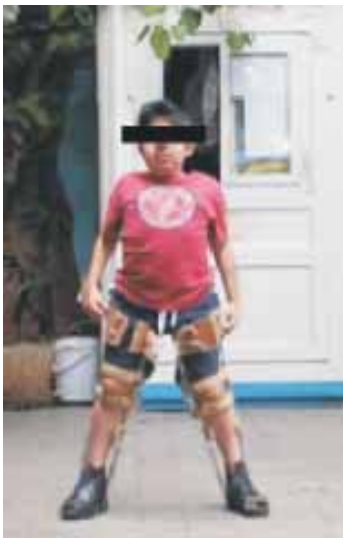


Fig 46.11b: Patient is now able to walk with calipers after stem cell therapy.

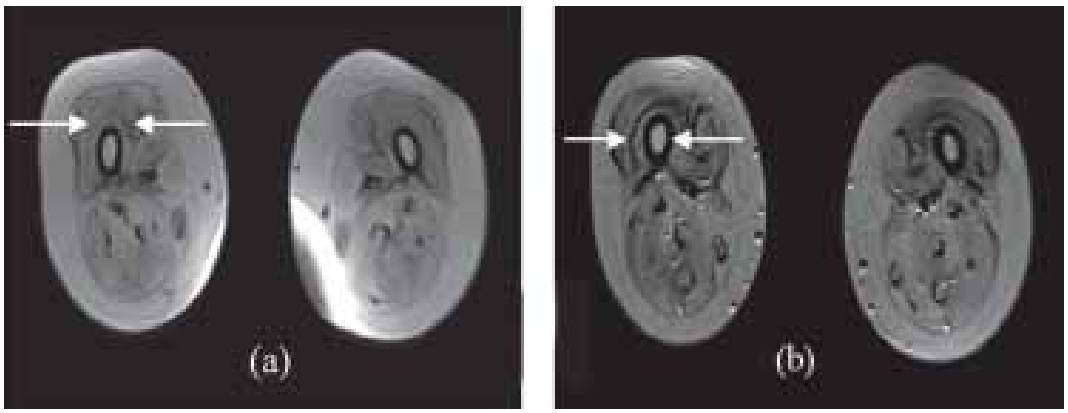


Fig 46.12: MRI of vastus medialis and vastus lateralis of a patient with MD. Fig (a) pre stem cell therapy. Fig (b) showing regeneration of muscle shown by white arrows

Spinal cord injury:

Paraplegia :

110 thoracolumbar SCI patients who underwent autologous bone marrow derived mononuclear cells, intrathecally were assessed. On a mean follow up of 2 years ± 1 month, overall improvement was seen in 91% of patients, including reduction in spasticity, partial sensory recovery, and improvement in trunk control, postural hypotension, bladder management, mobility, activities of daily living, and functional independence. A statistically significant association of these symptomatic

improvements with the cell therapy intervention was established. Some patients showed a shift on the ASIA scale and changes in electrophysiological studies or functional magnetic resonance imaging. No major side effects were noted.

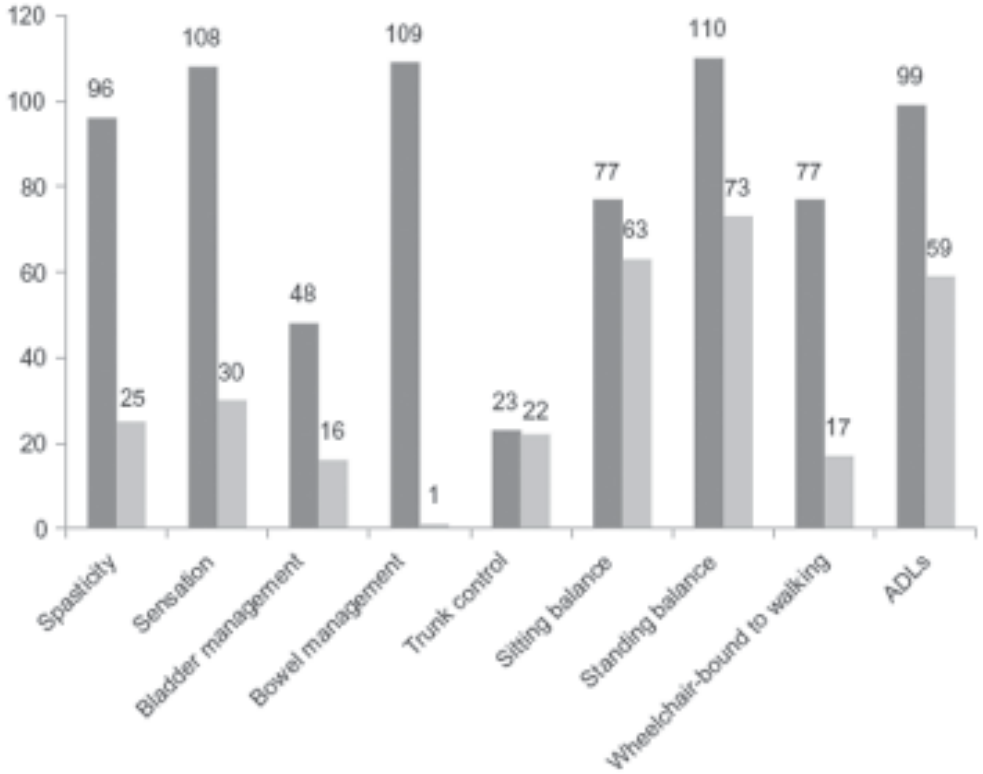


Fig 46.13: Graph representing improvements in thoracolumbar SCI after stem cell therapy. Published data: Sharma A.,et al, . Journal of Neurorestoratology. 2013;1:13-22

Quadriplegia:

A detailed analysis of 50 chronic cervical SCI patients who underwent intrathecal administration of autologous bone marrow mononuclear cells followed by neurorehabilitation,showed that on a mean follow up of 2 years ±1 month, 37 out of 50 (74%) showed improvements. Sensation recovery was observed in 26% cases, improved trunk control in 22.4%, spasticity reduction in 20% and bladder sensation recovery in 14.2%. All the 50 cases had improvement in postural hypotension. 12.24% wheelchair bound patients started walking with assistance. Functionally, 20.4% patients showed improved ADLs and 48% showed a positive. No major side effects were noted in the duration of 2 years in both the studies. A better outcome was observed in thoracolumbar injury as compared to the cervical injury suggesting that the level of SCI greatly influences the recovery of the patient. Both studies demonstrated statistically significant clinical and functional outcome.

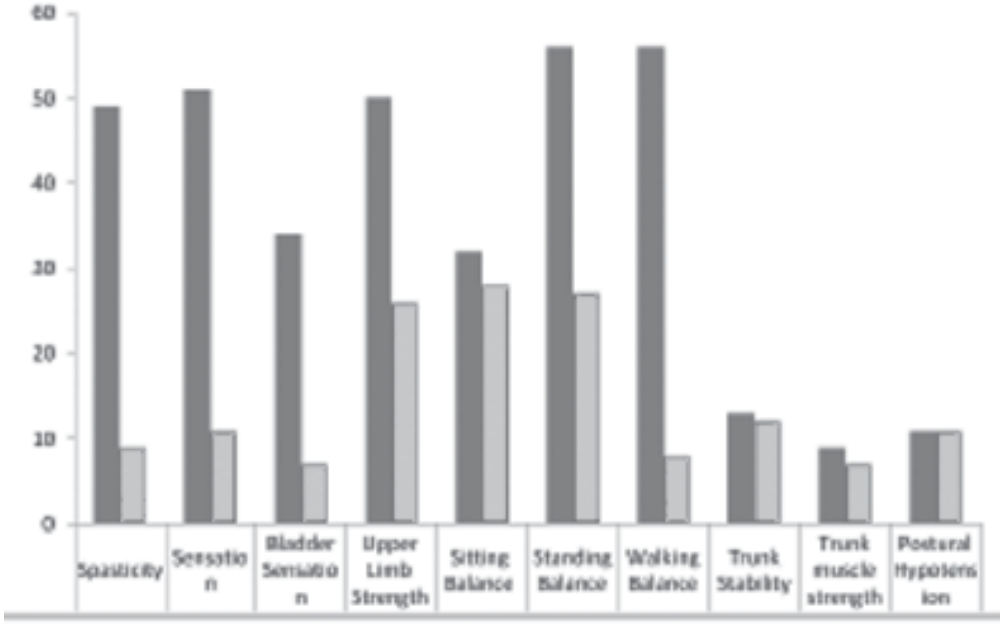


Fig 46.14: Graph representing improvements in cervical SCI after stem cell therapy. Published data : Sharma A.et al.,, J Neurol Disord 1: 138

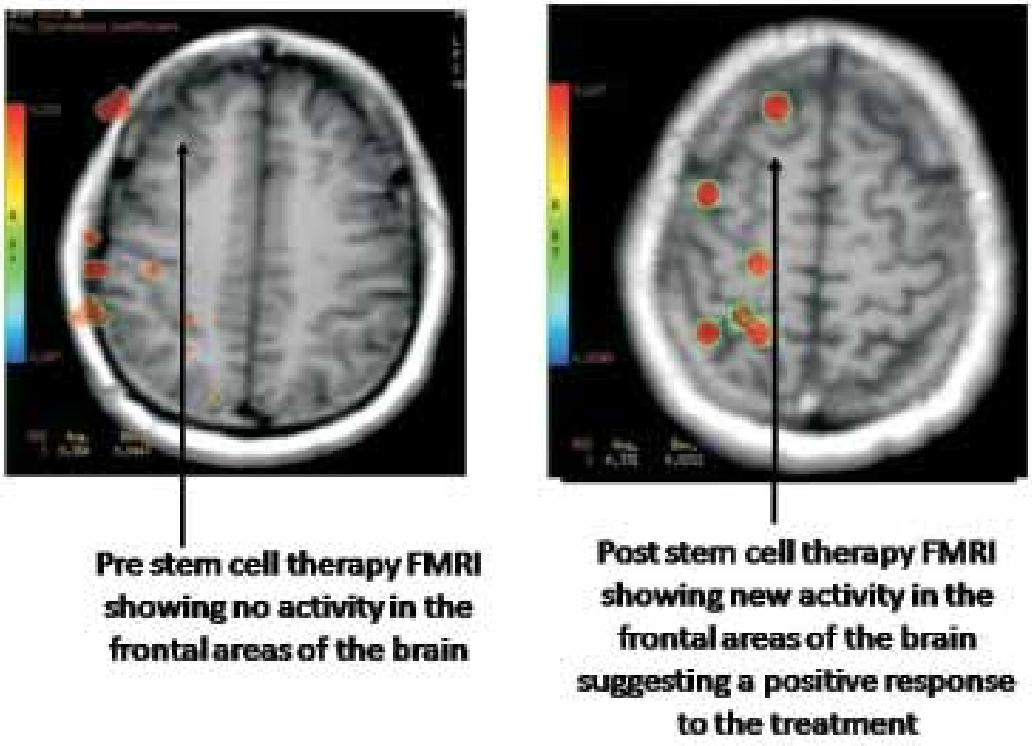


Fig 46.15: Pre and Post fMRI showing improvement after stem cell therapy.

Fig 46.16a : Totally wheelchair bound patient before treatment

Fig 46.16b :Patient able to stand up and walk with minimal support after the stem cell therapy

Mental Retardation:

18 patients with mental retardation were administered with stem cell therapy. On a mean follow up of 6 months, 70% cases showed improvement in toilet training, 64.29% in home living, 60% in communication, 57.14% in self-care, 50% in cognition and social skills amongst others. However, the improvements recorded were minimal as majority of the patients belonged to the older age group. Hence, the results might vary when children are treated at an early age.

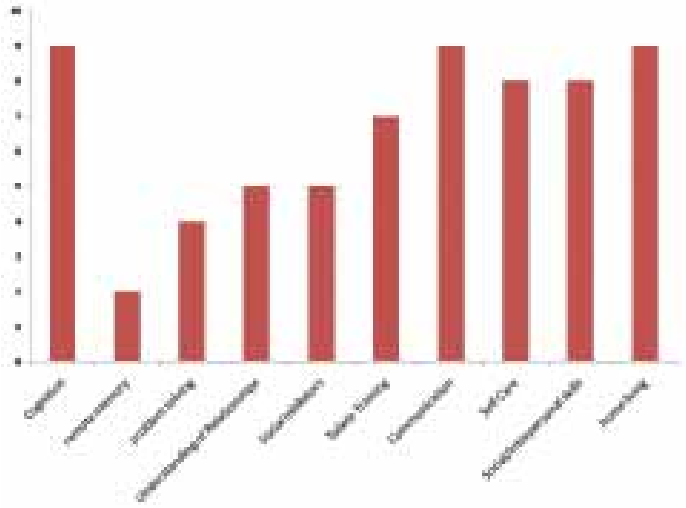


Fig 46.17: Graph representing improvements in intellectual disability after stem cell therapy

Traumatic Brain Injury (TBI)

A pilot study of 14 chronic TBI patients who underwent stem cell therapy was conducted. These patients were followed up at 1 week, 3 months and 6 months after the therapy. The outcome measures utilized were Functional Independence Measure (FIM) scale, SF-8 Health Survey Scoring and Disability rating scale. At the end of 6 months, these scales showed a positive shift in scores. Improvements were observed in various symptoms along with activities of daily living. Improvement in PET CT scan performed before and 6 months after the intervention in 3 patients corresponded to the clinical and functional improvements observed in these patients. The results of this study suggest that stem cell therapy may promote functional recovery leading to an improved quality of life in chronic TBI.

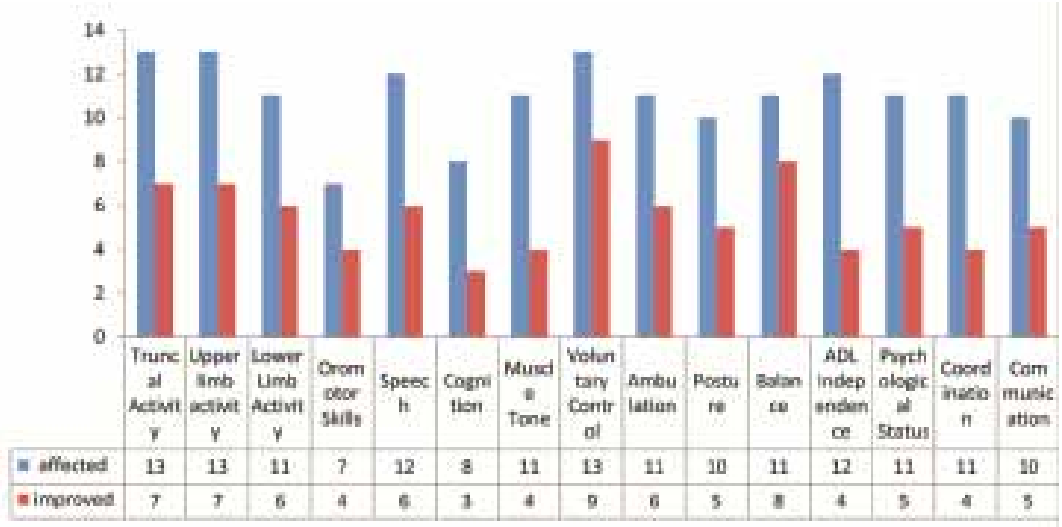


Fig 46.18: Graph representing symptomatic improvements in traumatic brain injury after cell therapy. PUBLISHED DATA: Sharma A,et.al., SpringerPlus Jan 2015.

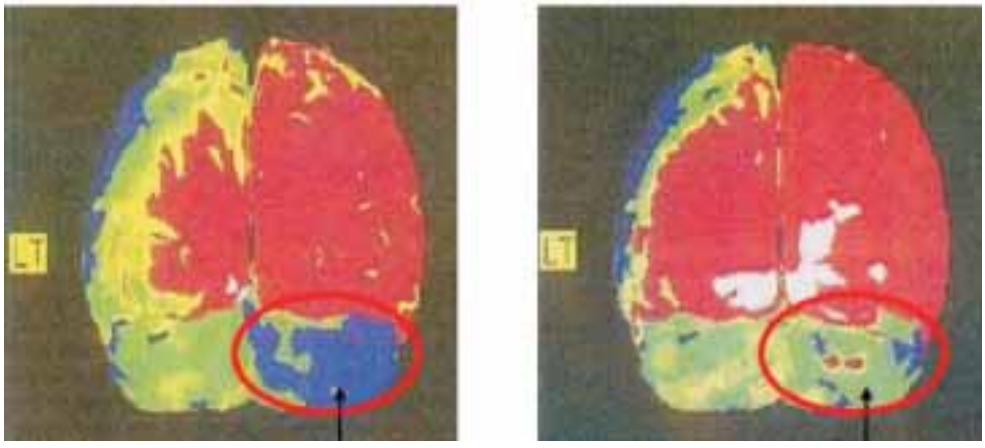


Fig 46.19: Pre and Post PET CT scans showing improvement after stem cell therapy in TBI

Stroke

24 patients diagnosed with chronic stroke were administered stem cell therapy, followed by multidisciplinary neurorehabilitation. They were assessed on Functional Independence Measure (FIM) objectively, along with assessment of standing and walking balance, ambulation and hand function. A higher percentage of improvement in all dimensions was observed in patients belonging to younger groups. Patients who underwent stem cell therapy less than 2 years after the stroke showed better changes. These results suggest that stem cell therapy may be a safe and effective treatment approach in improving the functional outcomes in the chronic stage of stroke.

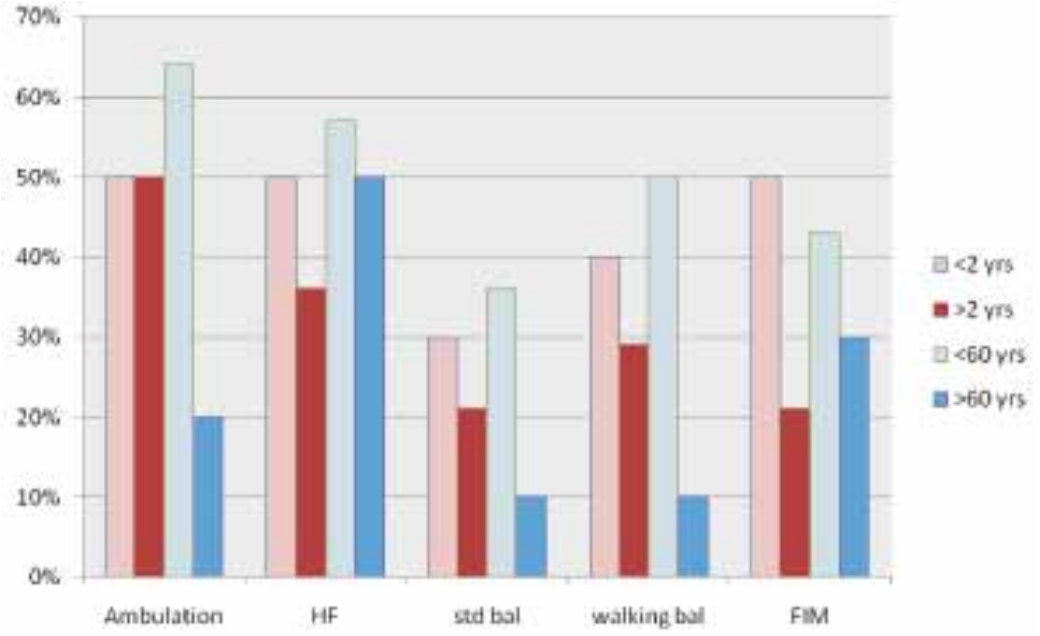


Fig 46.20: Graph representing improvements in stroke after stem cell therapy. Published data : Sharma A.et al.,Stroke Research and Treatment, Volume 2014, pages 1-9

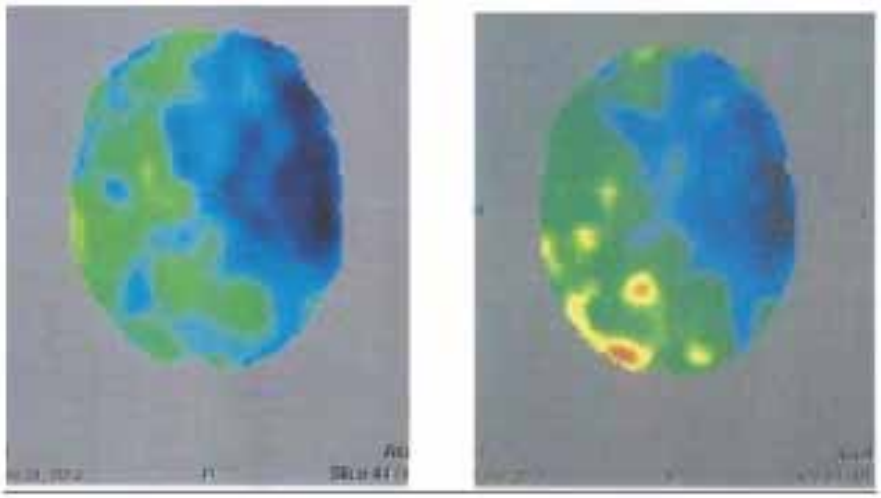


Fig 46.21: Pre and Post PET CT scans showing improvement after stem cell therapy in stroke

Fig 46.22a : Non functioning hand in a case of right hemiplegia before the treatment

Fig 46.22b : Improvement in hand function seen after stem cell therapy

Motor Neuron Disease (MND)

A total of 46 ALS patients underwent stem cell therapy. A detailed analysis was conducted to compare the survival duration of these patients with 20 patients that did not undergo stem cell therapy. Both patient groups shared similar baseline demographics. The comparison was carried out using Kaplan-Meier survival analysis and suggested that the mean survival duration of the patients treated with stem cell therapy (104.069 +/- 10.985 months) was longer than those who were not treated

(57.38 +/- 5.31 months) (Table 1). The difference between the two groups was statistically significant (p=0.43). We also noted that patients who were given Lithium and were young had better survival than the others. This could be attributed to better survival and growth of the transplanted cells. Hence, this study suggests that in addition to the standard treatment with Riluzole and neurorehabilitation, there is a possibility that early intervention with combination of stem cell therapy and Lithium may have a positive effect on the duration of survival in ALS.

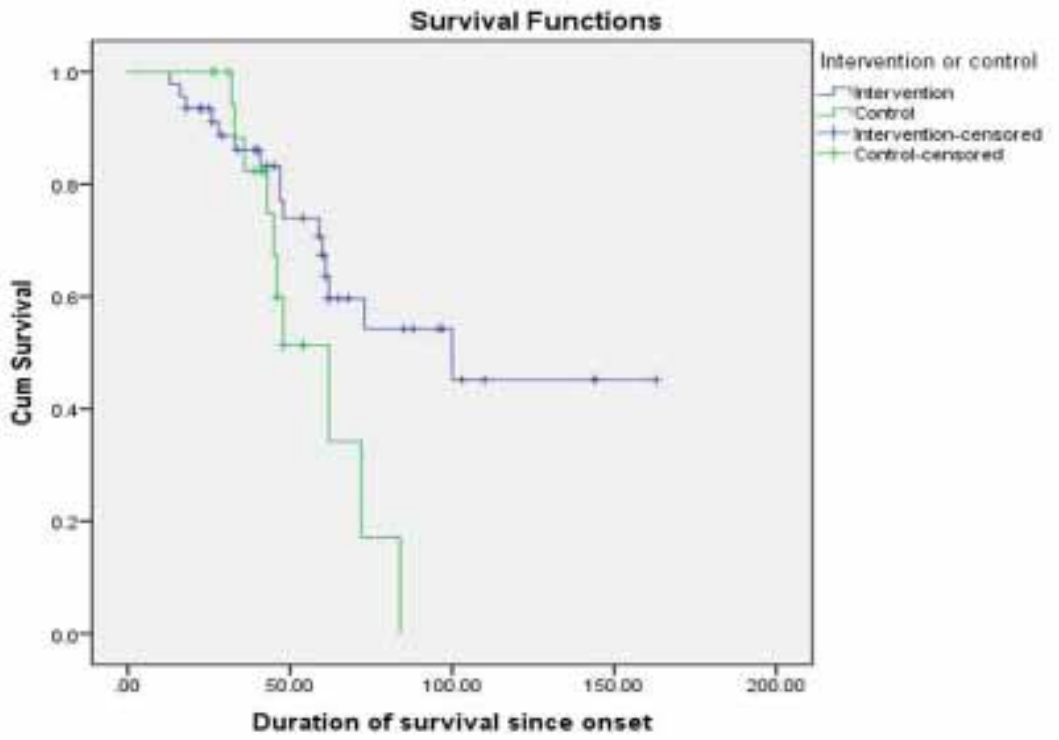


Fig 46-23: Graph showing Kaplan Meier survival analysis comparison between control and intervention group

Table 1: Survival analysis

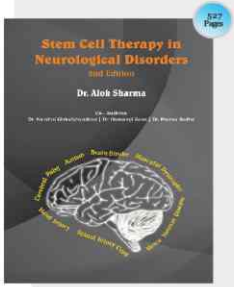
Survival analysis	Intervention group	Control group
Total mortality	35%	50.00%
Range of survival duration (months)	13 - 158	26-84
Mean survival duration (months)	104.069 (10.985)	57.38(5.31)

Conclusion

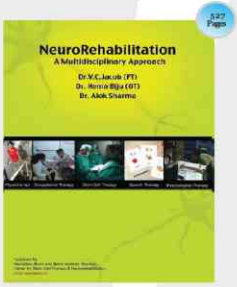
Stem cell therapy is the new hope for many incurable neurological disorders. The use of Autologous adult stem cells is completely safe and there are no serious side effects. The procedures are minimally invasive and so there is no risk factor. The patients show significant clinical and functional improvements and investigations such as PET CT Scans , MRis , EMG /NCV etc also show objective evidence of the improvements. Children with autism, cerebral palsy and muscular dystrophy show the best results. Adults with brain stroke, spinal cord injury, and head injury also show very good results. There are many scientific international and national papers in medical journals that have documented the safety and effectiveness of stem cell therapy in various neurological disorders. In can therefore be concluded that for those patients suffering from serious neurological disabilities, both physical and intellectual, this new therapy is definitely worth considering.

NeuroGen Publications

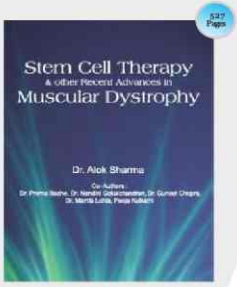
Stem Cell Therapy in Neurological Disorders 2nd Eddition



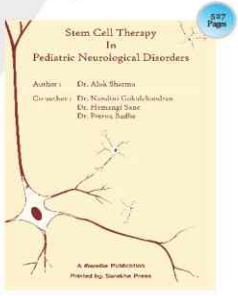
NeuroRehabilitation- A Multidisciplinary Approach



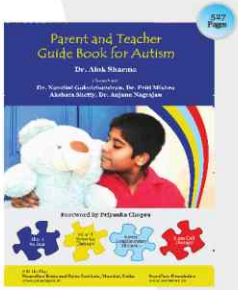
Stem Cell Therapy & Other Recent Advances in Muscular Dystrophy



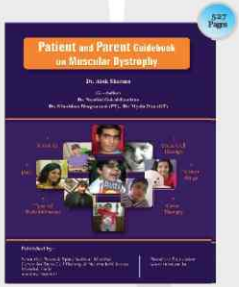
Stem Cell Therapy In Pedratric Neurological Disorders



Parent & Teacher Guide Book for Autism



Patient & Parent Guidebook on Muscular Dystrophy



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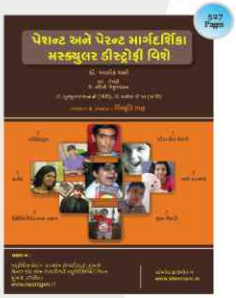

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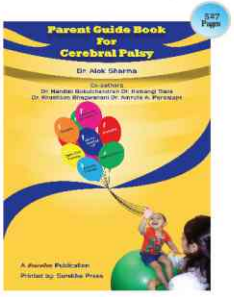

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