# IMSA

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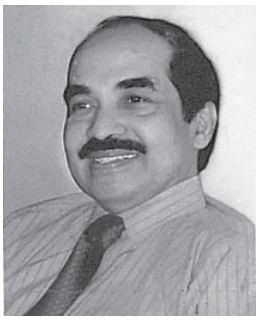
## PRESIDENT WRITES



Dear Fellows and Members,

It is indeed a great pleasure to write this page for the first issue of JIMSA for the year 2008. The theme of the issue is ***"Diagnostic Challenges in Neurology".*** The spread of articles included in this issue is vast, from cutting edge technology - loaded topics to every day clinical issues. I am definite that all of us will find the information rewarding.

IMSACON 2008 is to meet at Dubai on 12th and 13th October 2008. Dr. Shaheena, who very impressively held the IMSACON 2006 at Lahore, Pakistan, is guiding the organization of this first event at Dubai. I am certain that many of us will find it possible to meet at the IMSACON 2008 and make it a memorable event.

*Wishing all fellows & members of the Academy*
*a happy and fruitfull year 2008.*

K. Jagadeesan

**Dr. K. Jagadeesan**
President, IMSA

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**IMSA/ JIMSA WEBSITE**

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All fellows and members of IMSA can have **access** to the site and get information about its objectives, benefits to the fellows/members, chapters and their activities including seminars, refresher courses, rural CME;s etc. and also IMSACON - a regular annual event of international standard; *application form for enrollment as fellow/member can also be downloaded. Fellows - members and even not fellows - members can have access to full text in the quarterly journal - jimsa from July - Sept. 2003 onwards by putting their E-mail address under* ***'user name'*** *and using the* ***password 'UserJimsa'.***

## *Dr. Pinnamaneni Narasimha Rao International Award*

**Dr. P. Narasimha Rao**
*Ex. President, IMSA World H.Q.*

**Dr. R.R.Thukral**
*Vice President IMSA World H.Q.*

### *Appeal by Vice-President IMSA*

***Dear Fellows and Members***

***You are aware late Dr. P. Narasimha Rao, an international figure both in academic and teaching had been the President of this prestigious organization for more than a decade from 1990 to 2002. He was President of Medical Council of India and Vice Chancellor of various Universities. He had to his credit several outstanding contributions to the medical fraternity till his death . He had been in close association with IMSA since its very inception in 1981. The Academy has flourished tremendously during his tenure as President . Keeping in view his status, services rendered to the mankind and on the insistence of senior Fellows, the Academy has established an International Award in his honour named 'Dr. Pinnamaneni Narasimha Rao International Award', on the lines of Dr. B.C. Roy National Award. Substantial funds are needed for this pestigious award. Initially, the family of Dr. P. Narasimha Rao has contributed a fair amount of money and has also assured to contribute more.***

***I appeal to all our Fellows and Members to contribute generously for this noble cause in the memory of this dedicated acadamecian - Dr. P. Narasimha Rao. A separate account has been opened for this Award.***

***Wishing you all a happy and prosperous year 2008***

### *IMSA Fellows/Members Directory 2007*

*Dear Fellows and Members*

*International Medical Sciences Academy has published* ***Directory of IMSA Fellows and Members*** *containing information about their mailing addresses, telephone Nos. email addresses, wherever available. The Directory was released at the inaugural function of* ***IMSACON 2007*** *held at Manipal, Karnataka in November, 2007 . I shall request you to send a demand draft of Rs. 250 soon to enable us to send to you a copy of the Directory by post. You can also collect in person from IMSA office if you so wish.*

***H.K. Chopra***
***Secretary General IMSA***

### *IMSA Chapter Activities*

***CME Delhi Chapter***

19.1.2008 : ***Dr. Manoj Kumar :*** *"Knee Joint Replacement – Where are We Today"*
***Dr. Arun Goel :*** *"Alternative Surgical Management of Knee Arthritis"*
***Dr. Shiv Kumar :*** *"Rehabilitation after Knee Joint Replacement Surgery"*
23.2.2008 : ***Dr. Howard W. Fisher (Canada):*** *"Electro Magnetic Radiation & Mobile Phone New Dimensions – "Where are we today".*
5.3. 2008 : ***Dr. I.P. Kochhar:*** *"Pediatric Endocrinology."*
***CME in Neurology in April 08***
9.3.2008 : ***Dr. Murry Urowitz :*** *"Advanced Rheumatology Meeting"*
***Prof. Michelle Petri :*** *"Advanced Rheumatology Meeting"*

***CME Tamil Nadu Chapter***

13.1.2008 : ***Dr. Thirumalai Ganesan:*** *"Recent Advances in the Management of Benign Prostatic Hypertrophy"*
10.2.2008 : ***Dr. Nirmala Vijayakumar :*** *"Update on Contraception."*
10.2.2008 : ***Dr. C.D. Natarajan:*** *"Management of Chronic Diarrea in Children"*
9.3.2008 : ***Dr. M.C. Deepak :*** *"Ideal Oral Anti diabetic Therapy in Patients with Congestive Cardiac Failure"*

***RCME Tamil Nadu Chapter***

25.1.2008 : ***Dr. C.D. Natarajan :*** *"Management of Chronic Diarrea in Children"*
25.1.2008 : ***Dr. A. Govindan :*** *"Imaging of Pleural Effusion"*

***CME Andhra Pradesh Chapter***

29.1.2007 : ***Dr. Madhu Prasad :*** *The Role of Ablative Technologies in Treatment of Liver Tumors"*
12.3.2007: ***Prof. S. Mohan :*** *Time is Brain*
12.6.2007 : ***Dr. MBV Prasad :*** *Gallstones*
27.8.2007 : ***Dr. Vijay Y. :*** *Impact of HIV on India*
29.9.2007 : ***Dr. P. Raghu Ram :*** *Empowering Woman…..Impacting life"*
22.10.2007: ***Dr. M. Jwala Srikala :*** *Screening of Breast Cancer*
1.11.2007: ***Dr. P. Raghu Ram :*** *Screening of Breast of 30 Ladies*
20.12.2007: ***Dr. P. Raghu Ram :*** *Screening of Breast of 30 Ladies*
20.12.2007: ***Dr. M. Jwala Srikala:*** *Screening of Breast of 30 Ladies*

***CME Bihar Chapter***

4.11.2007 : ***Dr. Salil Sharma, :*** *Management update of Rhinosinusitis*
4.11.2007 : ***Dr. Gopal Prasad Sinha,:*** *Medical Genetics & Genetic Counseling*
2.12.2007: ***Dr. Pramila Modi :*** *Medical Genetics & Genetic Counseling*
2.12.2007: ***Dr. Gopal Prasad Sinha:*** *Medical Genetics & Genetic Counseling*
2.12.2007 : ***Dr. Amar Kumar Verma: :*** *Medical Genetics & Genetic Counseling*

### *Felicitation*

*Dr. N. Kulasekaran, Senior Professor of Radiology from Madras Medical College Chennai has taken over as National President of Indian Radiology and Imaging Association (IRIA) on 17th January 2008 during the 61st Annual Congress on Radiology held at Bangalore .*

***Congratulations to Dr. N. Kulasekaran from all Fellows and Members of IMSA .***

### *IMSACON 2008, Dubai, UAE - Registration Fee*

*Registration should be remitted to Dr. Nashi Khan the organizing Secretary on the following address. Registration fee & hotel booking advance for self and accompanying person should be paid in US $ much in advance and book hotel now as during October there is lot of activity in Dubai. and send to* ***Dr. Nashi Khan,*** *Organizing Secretary, IMSACON 2008,* Chartered Clinical Psychologist, PO Box 3222, Gulberg, Lahore, Pakistan, Mobile: +92 300 8441608
E-mail: nashi.khan@gmail.com

*(Details on page 4)*

### *Obituary*

***Dr. J.R. Danial,*** *former Director of Bernard Institute of Radiology and Professor of Radiology Madras Medical College* and lately working as Professor & HOD of Radiology, Pondycherry Institute of Medical Sciences, Pondycherry left for heavenly abode on 28.1.08 . He was an interventional Radiologist and an excellent teacher. We condole his sudden demise.

***Fellows and Members of IMSA***

# JIMSA

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January - March 2008
VOL. 21 No. 1





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## FROM EDITOR'S DESK

21st Century is witnessing an Information explosion in all fields; Neurology is no exception. The technological advances have progressively increased the survival in critically ill neurological conditions and have led to the prevention of morbidity through early diagnosis and timely therapeutic intervention. The medical fraternity should keep abreast about these advances and put them into use in day to day practice.

The present special issue **'Diagnostic Challenges in Neurology'** is the result of a commendable effort put in by **Dr. Pushpendra N. Renjen**, a senior consultant in Neurology at the prestigious Indraprastha Apollo Hospital at New Delhi, India. It is heartening to note that key topics relating to the crucial areas of diagnostic Neurology have been brilliantly covered with special emphasis on diagnostic usefulness of basic clinical examination in Neurology; as also rational use of the advanced diagnostic tools. No doubt a Herculean task has been achieved admirably by Dr. Renjen and his colleagues. Dr. Renjen deserves all appreciation for an excellent planning, selecting practical topics, identifying eminent authors and also devoting time to editing the various manuscripts so as to bring out this important document which will ever remain useful to the practicing and teaching Physicians and Neurologists; and also the postgraduate students of Neurology. I am personally grateful to Dr. Renjen for agreeing to be the guest editor at a rather short notice and completing the assignment well in time.

I take this opportunity to thank the members of the Editorial and Advisory Boards for their help and guidance in compiling this issue and also to the several advertisers without whose help, this publication would not have been possible.

***I wish to extend my greetings, to all readers of JIMSA for a very happy, prosperous and healthy year 2008***

**P. D. Gulati**

### *JIMSA BEST PUBLISHED ARTICLE AWARDS*

Journal of International Medical Sciences Academy has instituted award for **three (3)** best original articles published during the previous 3 years; **guidelines** are as below:

(1) **Original articles** belonging to any discipline of medicine published in JIMSA during the previous three years.
(2) Age Limit for the principal author/main researcher should be 45 years and below.
(3) Number of awards: Three (3) annually, carrying a gold plated medal, citation and cash prize (1st Rs. 3000/-, 2nd Rs. 2000/-, 3rd Rs. 1000/-)
(4) Awardee should preferably be a fellow/member of IMSA; non-fellows/ non members can also be considered for the award if the original work is outstanding; and if selected for the award will be required to apply for fellowship/membership of IMSA.
(5) Awardees should preferably plan to receive the award at the annual IMSA conference - IMSACON.


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## *IMSACON 2008, Dubai, UAE*

Annual Conference of International Medical Sciences Academy **IMSACON 2008** will be held on 12-13 October, 2008 at Dubai, UAE.
Dr. Nashi Khan is the organizing Secretary and Dr. Shaheena Asif is the Organizing Chairperson.

**Theme** : "New Horizons & Controversies in Medical Sciences"

**Venue** : Dhow Palace, Dubai, UAE

**Host** : Surgimed Hospital, Lahore, Pakistan.

**Visa**: Visa is required for Dubai and must be obtained before Travel. Please allow at least 3 months before conference date for application to be processed.

**First information brochure** can be seen on the IMSA website "**www.imsaonline.com**". The brochure contains all details about registration fee, registration form, details of Hotel stay etc.

Non fellows accompanying the Fellows of IMSA are welcome to participate. You are requested to register yourself early and participate with your spouse and enjoy hospitality of the hosts.

| **Registration Fee** | **Before 31st July 08** | **After 1st Aug 08 onwards** | **After 15th Sept. 08** |
|---|---|---|---|
| **Conference Delegates** | $ 200 | $ 250 | $ 300 |
| **Accompanying Person** | $ 150 | $ 200 | $ 250 |
| **Trade Delegates** | $ 300 | $ 350 | $ 400 |
| **PG Students** | $ 80 | $ 100 | $ 120 |

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| **Admiral Hotel** | $ 114 + tax | 129+ tax |

Tariff rates are approximate and are subject to revision. The Hotel reserves the right to revise the tariffs and taxes and the secretariat would not be in a position to intervene. The delegates are requested to send requisition for booking their choice of hotel with advance room rent for one day.

**Cancellation:** Request for cancellation of accommodation must reach the Conference Secretariat latest by 31st July 2008. Cancellation request received after 31st July 2008 will not be entertained.

In case participants intend to present paper in the Scientific Programme of the conference, they may send "Abstract" of the paper to the Chairman Scientific Committee the abstract must be in approximately 300 words in English. Only empirical work based on clinical data may be submitted. The paper must clearly state the objective, methods, results and conclusions. The presentation must have a title, names of all authors and the institution where the work was done. Please mention the name of the author who will present the paper and complete address, email and phone numbers.

Last date for submission of abstract: 30th June 2008. Kindly send the abstract on soft copy through email to Scientific Committee Chair, Prof. Dr. Rukhsana Kausar. Email: rukhsana.saddul@gmail.com

If any one has difficulty in sending registration fee to Pakistan bank from India; they can send registration fee to the following:-

**Us Dollars 200 (registration fee only)**, To **Shaheena Asif Choudhary Acc no 3513409044 ABN AMRO Bank Dubai UAE (BIC. ABNAAEAD)s Swift BIC ABNAAEADCCC(swift field 57 A)**. Those who intend to present paper at IMSACON-2008 should send their abstract ***to the Scientific Chair Dr. Rukhsana Kausar or Organizing Secretary, Dr. Nashi Khan by e-mail. Their e-mail addresses are given below:-***

1. ***rukhsana.saddul@gmail.com.***
2. ***nashi.khan@gmail.com***

Only those papers will be included in the programme whose registration fee is paid on time.

***For details contact:***

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***R.R. Thukral,***
***Vice President, IMSA WHQ***

## Our Guest Editor

**Dr. Pushpendra Nath Renjen** did his MBBS from Osmania University, Hyderabad (India) in 1975; DM (Neurology) from National Institute of Mental & Neurosciences (Deemed University), Bangalore (India) in 1982. He has to his credit several fellowships; those which deserve special mention include fellowship of American Academy of Neurology, European Federation of Neurological Societies, Indian Academy of Neurology and International Medical Sciences Academy. He was also awarded membership of the National Academy of Medical Sciences in 2005. Areas of his special interest in which he has made significant contribution include *stroke services* (*thrombolytic therapy*), *Botox therapy* and *neuro-rehabilitation.*

Dr . Renjen has published several papers in the National and International journals; his work on 'Stroke and thrombolysis' is well recognized . He has contributed chapters in several books and has edited a monogram on ***'Migraine Update'***. He is also on the editorial board of JIMSA and other reputed journals. He has regularly participated in the national and international conferences, he has been invited to deliver lectures and participate in programs organized by the Neurological Society of India, Association of Physicians of India, Indian Stroke Association and Indian Medical Association . He exhibited tremendous organizational ability as organizing secretary / chairman of various neurology forums at national, international and state levels.

In view of his achievements in the discipline of Neurology, Dr. Pushpendra N. Renjen has been the recipient of several awards and honours; notable amongst these are ***"Scroll of Honour"*** for contribution to cerebrovascular disease and brain stroke by Delhi Medical Association 2002; ***'Gem of India'*** by all India Achievers Conference 2002 ***'Man of the Year'*** by American Bibliography Society 1997; more recently, **Chikitsa Rattan Award** by International Study Circle in 2007. Dr. Renjen has delivered several prestigious orations on topics related to ***'Ischemic Stroke'***.

Dr. Pushpendra N. Renjen is presently a senior consultant in Neurosciences (stroke ) and academic coordinator, at Indraprastha Apollo Hospitals, New Delhi, India

## EDITORIAL

Neurology is one super-speciality where the diagnostics have totally changed its outlook. Advances in CT, MRI, EEG, Nuclear Medicine and Biochemistry, have given a *new dimension* to the speciality as a whole. In this issue of JIMSA, I have tried to highlight the various diagnostic and therapeutic modalities as to how these have evolved and helped in the diagnosis of some of the rarer conditions which would not have been possible otherwise. Infections like tuberculosis and cysticercosis of the nervous system have been rampant in our country; the authors have elaborately described unusual manifestations of rather common conditions; it is indeed a great revolution. However, I would like to impress upon the readers of this issue that clinical neurology still remains the backbone of diagnosis; a detailed clinical examination should always precede the investigative work-up. I hope the readers will be benefitted by the scientific contents of the articles; suggestion and comments, if any, are welcome.

**Pushpendra N. Renjen**
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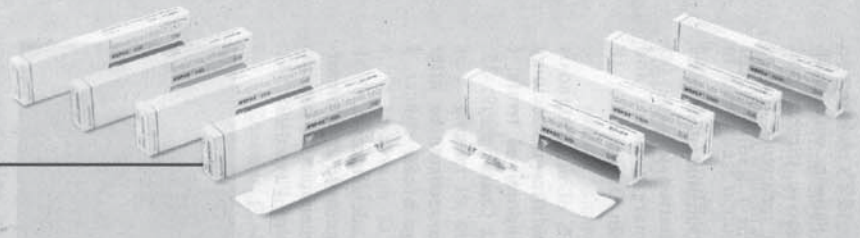


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# MRI CHARACTERISTICS OF ACUTE TRANSVERSE MYELITIS WITH CLINICOTHERAPEUTIC CORRELATION

**C.M.Sharma, Ravindra Singh, Narayan Pendsae, A.K.Sharma, A.K. Kankane, Shailesh Dixit**

*Department of Neurology, SMS Medical College, Jaipur (Rajasthan) India*

***Abstract :*** *Acute transverse myelitis is an acute or sub acute inflammation of spinal cord characterized by motor, sensory & autonomic dysfunction resulting from the involvement of both halves of spinal cord. 50 patients of noncompressive myelitis admitted in the department of neurology between January 2002 to June 2004 were included our study. 40 patients were diagnosed as transverse myelitis on the basis of criteria laid down by Jaffery & Madlee. All patents were subjected to routine biochemical investigations, CSF X-RAY of spine M R imaging spine and scan of brain if indicated. The presenting features were quadriparesis in 24 patients (60%) paraparesis in 16 patients (40%). Bladder & bowel involvement was seen in 35 patients (87%) sensory loss in 29 patients (72%). All the patients had acute onset of symptoms which peaked by 6.5 (range 1-15) days. High signal intensity on T2 weighted non contrast M R imaging was seen in 32 patients (80%), 5 patients showed only cord expansion while it was normal in 3. On contrast M R imaging, hyper-intense shadow was seen in 3 patients having normal M R imaging, 3 patients showed hypointensity on T1. Te lesion extended for a mean of 6 spinal segments (range 4-12 segments). Te high signal intensity occupied more than 2/3 of the cross sectional area of the cord in 34 patients (85%), 30 patients also had a small dot known as central dog sign. It was observed that the neurological deficit was severe and response to treatment was poor in patients having diffuse involvement of the cord (more than 8 spinal segments) and in the patients having necrosis of the cord. This study has shown a beneficial effect of methyleprednisolone.*

## INTRODUCTION

Spinal cord is the site of infectious and non infectious inflammatory process[1]. Acute transverse myelitis is an acute or subacute inflammation [1,2] of spinal cord, characterized by motor, sensory and autonomic dysfunction resulting from the involvement of both halves of spinal cord after secondary causes such as compressive lesions, tuberculosis, syphilis were arteriovenous malformation, trauma, malignant infiltration excluded. The essential features in acute transverse myelitis include oedema, necrosis and demyelination. White matter changes are more pronounced than thorin the grey matter. The brunt of disease falls on the thoracic or lumbar spinal cord although oedema and demyelination extend upwards to cervical cord or even higher[3]. Many reports of MR imaging in patients of acute transverse myelitis have revealed local enlargement of the cord and increased signal intensity on long repetition time/echo time (TR/TE) sequences[1,2.] However these findings cannot differentiate this condition from other lesions such as intramedullary tumours, multiple sclerosis, hematoma and vascular ischaemia.

There are very few reports on the prevalence and pattern of contrast enhancement in patients with transverse myelitis. This study was carried out to differentiate transverse myelitis from intramedullary abnormalities using contrast and to correlate these changes with neurological deficit at the onset and response to treatment.

## MATERIAL AND METHODS

Fifty (50) patients of noncompressive myelitis admitted in the Department of Neurology, between January 2002 to June 2004, were included in our study. 40 patients were diagnosed as transverse myelitis on the basis of criteria by Jeffery et al[4].

1. Acute or subacutely developing motor, sensory and sphincter disturbances.
2. Spinal segmental level of sensory disturbances with a well defined upper limit.
3. No clinical or laboratory evidence of spinal cord compression.
4. Absence of other known neurologic diseases such as syphills, previously diagnosed multiple sclerosis, malignant neoplasm, spinal cord arteriovenous malformation, saecoidosis and HIV infection.
5. Lack of clinical progression over 4 weeks.

Strict exclusion criteria included a history of spinal trauma, compressive myelopathy cardiac disease aortic aneurysm, a space occupying lesion in the spinal cord or spine, systemic malignancy, syringomyelia, multiple sclerosis (clinically and radiologically). Neurological examination was carried on all patients. Weakness was assessed by Medical Research Council (MRC) scale and spasticity by Ashworth scale[5].

Routine laboratory investigations included complete blood cell count, fluroscent antinuclear antibodies test, Rheumated factor, VDRL, test for vitamin $B_{12,}$ folate assay; cerebrospinal fluid examination that included white blood cells with differential count, protein, sugar, gram stain, acid fast bacillus, India ink preparation, enzyme-linked imunosorbent assay for parasites, electrophoresis, human T-cell leukemia/lymphotropic virus-1 and viral titre.

All patients underwent X-ray of spine depending on the level of neurologic deficit. Magnetic Resonance Imaging spine was obtained on 1.5 Tesla super conducting magnet. Both T1 and T2 weighted images were taken. Contrast study was done where ever required. Scanning of brain was done in 8 patients who had non specific symptoms like headache and dizziness in order to exclude possible intracranial lesion.

Te vertebral segmental length of the hypertense signal was estimated on the basis of findings on sagittal T2 weighted images cross sectional location; size and pattern of the high signal in the cord was determined by finding on the axial T2 weighted images. Cord expansion was evaluated with respect

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to adjacent normal cord on T1 weighted images. The central linear high signal intensity that was seen in some cases above and below the diffuse high intensity on T2 weighted images was not considered in determining the extent of abnormality. Location and extent of the intramedullary contrast enhancement were confirmed on saggital T1 weighted images 20 patients were treated with intravenous methylprednisolone at a dose of 1 gm/day for 5 days an the other 20 were not given methyl-prednisolone and the patients were followed for one year. The main outcome criteria were- (1.) proportion of patients able to walk independently at one month; (2.) proportion of patients with full recovery within one year; (3.) proportion of patients developing complications-namely corticosteroids side effects (persistent hyperglycemia, high blood pressure) bed sore and urinary tract infections.

## RESULTS

The study included 24 females and 16 males (F:M =1.5:1). Mean age was 40 years (range 15-50 years). The *antecedent event* was non specific infection of upper respiratory tract seen in 19 patients (47.5%) while it was *idiopathic* in rest of the cases.

The presenting *features* were quadriparesis in 24 patients (60%), paraparesis in 16(40%). Bladder and bowel

***Table-1:*** *Clinical presentation of Acute Transverse Myelitis*

| Clinical features | No. of patients |
|---|---|
| Paraparesis | 16(40%) |
| Quadriparesis | 24(60%) |
| Symmetrical | 32(80%) |
| Bowel and bladder | 35(87.5%) |
| Sensory level | 29(72.5%) |

involvement was seen in 35 patients (87.5%), sensory level in 29 patients (72.5%). The symptoms were symmetric in 32 (80%) while there was asymmetry in 8 patients (20%) as shown in table 1.

All the patients had acute onset of symptoms which peaked by 6.5 (range 1-15) days. 4 patients (10%) had suffered from similar attack some years back. In these patients screening of brain was also done to rule out any possibility of multiple sclerosis. *Cerebrospinal fluid* was abnormal in 36 patients (90%); it revealed mild to moderate lymphocytic pleocytosis with mean of 7 cells/$^3$ (range -10 cells/min) mild to moderate rise in proteins with a mean of 65 mg% (range 35-105 mg%). The CSF sugar was normal and there were no bacteria or fungi on smear or culture.

High signal intensity on T2 weighted non contrast Magnetic Resonance Imaging was seen in 32 patients (80%); 5 patients showed only cord expansion while it was normal in 3. On contrast M R Imaging, hyper-intense shadow as seen in the 5 patients having normal M R Imaging. 3 patients showed

**Table -2 :** *Spectrum of Magnetic Resonance Imaging changes*

| S.No | Magnetic Resonance Imaging findings | No. of Patients |
|---|---|---|
| 1. | High signal intensity on T2 weighted images | 32(80%) |
| 2. | Hypointensity on T1 | 5(2.5%) |
| 3. | Hyperintensity occupying more than 2/3$^{rd}$ of cross section | 34(85%) |
| 4. | Mean spinal segments involved by hyperintensity | 6 |

hypointensity on T1. The lesion extended for a mean of 6 spinal segments (range 4-12 segments). The high signal intensity on axial T2 weighted images was centrally located in all the patients and occupied more than 2/3$^{rd}$ of the cross sectional area of the cord in 34 patients (85%) as shown in table 2. Thirty (30) of the 32 patients having hyperintensity also had a small dot, isointense with the cord in the core of hyperintensity which is known as *central dot sign*. It was observed that the neurological deficit was severe and response to treatment was poor in the patients having diffuse involvement of the cord (more than 8 spinal segments) and in the patients having hypointensity on T1 weighted images signifying necrosis of the cord. Among 20 patients who were treated with methylprednisolone 14 patients (70%) walked independently after one year. Full recovery was seen in 10 patients (50%); the mean time of walking was 30 days. While in the non prednisolone group only eight patients (40%)walked independently after one year. Full recovery was seen in 7 patients (28%); the mean time of recovery was 45 days.

## DISCUSSION

Acute transverse myelitis, a fragment of disseminated vasculomyelinopathy[6,7], is pathologically identical with acute disseminated encephalomyelitis[8,9]. The hallmark lesion in *acute transverse myelitis* is perivenular inflammation and surrounding demyelination[10]. Middle aged adults are commonly affected and the most common site of involvement is the thoracic spinal cord. There are many etiological associations such as viral illness assignations, demyelinating processes such as multiple sclerosis, collagen vascular disease, vascular disorders and paraneoplastic syndromes but most cases are **idiopathic**[11]. M R imaging is the investigation of choice to delinate such lesions in the cord[12, 21].

In literature various studies have documented M R imaging changes in transverse myelitis but few studies have correlated the radiological changes with the severity of clinical presentation, response to methylprednesolone and prognosis[13]. Largest series of M R imaging changes in transverse myelitis was reported by Choi etal[14]. Earlier reports have documented local enlargement of the spinal cord and increased signal intensity on long repetition time/echo time sequences. In one series, high signal intensity over several spinal segments along with focal cord enlargement, has been observed.

The central isointensity or dot is believed to represent central gray matter, sequessed by the surrounding edematous cord. In our series and by the series reported by Choi et.al.[14] a significant number of patients had this centrally located high signal

intensity occupying more than 2/3rd of the cross sectional area of the cord. It is not a specific sign for transverse myelitis and has been reported in the cases of intramedullary tumors. When contrast was given in the patient there was a peripheral enhancement with maintenance of the cord contour, this contrast enhancement may be confused with intramedullary tumors but in those cases contrast enhancement is profound and occupies the entire cross sectional area of the cord on at least one T1 weighted axial image and it is heterogenous associated with central or marginal cavity. Similar observations were made by Choi et.al.[14], Barkos et.al.[15] & Aichner et.al.[16] Commonly 3-4 spinal segments are involved Barkos et al[15] & Bruna J[19]reported signal abnormality extending over at least six spinal segments. Misra and colleagues[13] have reported unusual cases of acute transverse myelitis with long segment involvement (cervical to conus). In our series the lesions extended for average 6 spinal segment. The length of spinal segments was directly related to the severity of neurological deficit and predicted prognosis as also reported earlier in the series earlier.

3 patients who showed hypointensity on T1 weighted images showed slow recovery suggesting that the hypointensity represent parenchymal or myelomalacic changes. Spinal multiple scelrosis is also associated with similar M R imaging findings but here the hypereintensity extends for not more than 2 segments, enhancement on contrast is central and the plaques are large, multiple, sharply demarcated and sometimes confluent *(kissing plaques).*

Our study showed a good response with high dose methylprednisolone; similar observation was made by Deference et al [17] and sabire et al[18] Chan K H, Tsang KL et al[20] but the results were unsatisfactory in few shades. However a multicentric study having a large sample size is needed to have final conclusion.

## CONCLUSION

The characteristic findings of transverse myelitis on M R imaging include normal size or segmental enlargement of the cord most commonly thoracic, central hyperintensity occupying more than 2/3rd of cross sectional area of the cord. It usually affects more than 3 spinal segments central; dot in the core of hyperintensity. There is peripheral contrast enhancement of lesion. Apart from this we can also appreciate necrosis of cord in form of hypointensity on T1 weighted images. These findings can differentiate transverse myelitis from multiple sclerosis, cord tumors or other intramedullary lesions. Prognosis is poor in the patients having long hyperintense signals and necrosis. This study has shown a beneficial effect of methylprednisolone. Our study is one of the few studies that has simultaneously analysed the clinicoradioloical correlation of transverse myelitis and response to high dose corticosteroids.

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## Renal Transplant Outcome in High Cardio Vascular Risk Recipients

*Jelka TK, et. al. Clin Transplant 2007:21: 609-614*

Cardiovascular (CV) disease is the foremost cause of morbidity in renal transplant recipients. The disease burden is likely to increase as older patients are accepted for transplantation. The outcome of these high-CV risk patients after renal transplantation, especially with known pre-transplant coronary artery diseases (CAD). All renal transplants performed between1998 and 2002 at our centre, followed up to 2005, were divided into high- and low-risk groups, based on the presences of one or more of the following: pre-transplant angina, myocardial infraction, and positive coronary angiogram. The two group were compared for post-transplant cardiac events and patient and graft survival. The factors predictive of post-transplant cardiac event were also determined by Cox-regression multivariate analysis.

Forty-five patients (10.5%), out of 429, had post transplant cardiac events; 31.3% in high risk, and 6.5% in the low-risk group (p= 0.001). Five yr patient survival was lower in the high risk group (82.8% vs. 93.1%, p= 0.004), while five-yr overall graft survival and death censored graft survival were statistically not different (74.8% vs. 84.1%, p=0.008 and 87.3% vs. 90%, p=0.25), 41% patients who were treated with angioplasty plus stenting or bypass graft prior to transplantation has post –transplant cardiac events, as compared with 28% of those without intervention in the high risk group and 6.5 % of patients in the low risk group (p=0.001). Age, pre-transplant cardiac disease, arrhythmias, and low – ejection fraction (≤ 40%) were significant independent predictors of post-transplant cardiac event.Post-transplant survival of high- CV risk patients (with Known CAD) is lower than that of low-risk recipients but remain acceptable. Cardiac interventions may reduce perioperative risk but do not reduce the probability of post transplant cardiac events of that of low-risk group.

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# POTENTIAL ROLE OF MR ANGIOGRAPHY IN SELECTING PATIENTS FOR THROMBOLYTIC THERAPY

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***Abstract :*** *Neuroimaging techniques are necessary for the evaluation of stroke which is, one of the leading causes of death and neurological impairment in developed countries. The multiplicity of techniques available has increased the complexity of decision making for physicians. Non-contrast computed tomography (CT) scan is an established imaging procedure for initial evaluation of stroke patients. However, the limited ability of CT for the detection of early ischemia may be disadvantageous as acute therapy must be rapidly initiated. Multimodal CT, incorporating CTA and CTP, may also be disadvantangeous in selected individuals due to concerns regarding contrast load. Magnetic resonance imaging (MRI) has a higher sensitivity than CT for the demonstration of infarcted or ischemic areas. Perfusion and diffusion MRI together with MR angiography (MRA) are very helpful for the acute evalaution of patients with ischemic stroke. For the non-invassive study of extracranial vessels, MRA is less portable and more expensive than ultrasonography but it has higher sensitivity and specificity for carotid stenosis. Current practice guidelines promote rapid evaulation of the stroke patient without mandating specific modalities or techniques. Neuroimaging of acute stroke with multimodal CT or MRI offers prompt diagnostic information that may be integrated into various aspects of patient management. Unlike the prethrombolytic era, clinicians now have several options for neuroimaging evaluation. The selection of a particular imaging modality should be tailored to the clinical scenerio.*

The emergence of very early treatment strategies for acute stroke, such as thrombolysis, raises a number of interesting questions regarding the approach to imaging in such patients. The traditional approach to imaging in acute stroke employs CT, mainly to exclude brain hemorrhage masquerading as infarction. Although more sensitive than CT for detecting brain infarction, the role of MR in the evaluation of patients with very acute stroke, and the impact of early MR imaging on the treatment decision process, has not been adequately studied. MR is attractive for the study of acute stroke because of its increased sensitivity to ischemia and, more recently, because of the introduction of new techniques including MR angiography (MRA) and, most recently, MR diffusion (MRD) and the perfusion (MRP) techniques. MRD requires special coil gradients which can be used to image very early tissue changes, possibly related to cytotoxic edema, occurring within 1 hour of stroke onset. MRP techniques permit analysis of cerebral blood flow and flow metabolism coupling. MRD and MRP are still in the developmental state and are not ready for routine clinical application. However, MRA has already reached the stage of clinical application and, when combined with conventional spin-echo MR, offers the potential for conjoint anatomic and vascular imaging in patients with acute stroke.

The principle of MRA has been extensively reviewed. A variety of phase contrast (PC) and time of flight (TOF) techniques are under investigation. PC is sensitive to very slow flow but is highly subject to complex flow and motion artifacts. PC also requires prolonged acquisition and processing time. For large vessel occlusive disease, 3-dimentional TOF techniques seem to hold the most promise for quick, accurate detection of stenosis or occlusion. 2D TOF may be superior for very low flow states, especially posterior circulation, either the extracranial carotid, circle of Willis, extracranial vertebrals, or basilar artery. Each vessel system analyzed with MRA adds only 8-10 minutes to the standard T2 MR study. Hence, the spin-echo MR combined with MRA of the suspected symptomatic vessel system should take 20-30 minutes in most patients.

Initial studies have shown a high degree of correlation in the degree of extracranial carotid artery stenosis when comparing 3-D-TOF-MRA image with intraarterial digital subtraction angiography (IADSA). More severe degrees of stenosis (>70%) tend to be slightly over-estimated by MRA. A number of potential problems, including motion artifact, have been described. Subacute (4-7 days) thrombus containing methemoglobin can give a false positive "flow" reading, and special sequences are needed to identify dissections. The accuracy of 3D-TOF MRA for detecting intracranial vascular disease is unknown since there have been no correlative studies done with IADSA. Accumulated experience, however, suggests a similar high degree of accuracy of the middle cerebral artery (MCA) bifurcation. MRA also appears highly accurate for detecting vertebral and basilar artery occlusion disease, and occlusive of the posterior cerebral arteries. Technical limitations prohibit accurate imaging of MCA branch occlusive disease, and smaller basilar artery branches including PICA, AICA & SCA. Nonetheless, MRA appears to be highly accurate for detecting occlusion of vessels most often treated with thrombolytic therapy.

CT combined with ultrasound (Carotid duplex plus transcranial doppler (TCD) has been suggested as an alternative to MR/ MRA for the vascular/anatomic evaluation of patients with acute brain ischemia. The advantages and problems of MR versus CT for anatomic imaging of very early stroke have been alluded to above. Ultrasound techniques, while in some ways less cumbersome than MRA, are highly technician dependent and of uncertain accuracy in patients with intracranial occlusive disease, especially vertebral basilar lesion. MRA

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offers the advantage of direct visualization of the occlusive process and is probably more accurate than TCD for detecting vertebral basilar occlusive disease. In some situations ultrasound may compliment MRA. The central point is, however, that if MR becomes the anatomic imaging modality of choice in patients with early brain ischemia, the additional 8-10 minutes required for MRA will become a standard part of the MR evaluation of patients with acute stroke. Assuming, therefore, that anatomic imaging of patients with acute focal neurological deficits remains necessary to exclude brain hemorrhage, the central question to be decided is whether we should continue with our traditional CT approach or shift to MR as the imaging modality of choice in patients with acute stroke. If MR imaging is advantageous over CT, then whether to do MRA becomes a moot point since it adds less than 10 minutes to the data acquisition time.

A final question might be whether vascular imaging is necessary at all in patients with very early brain ischemia. Most, I think would agree that ideally the state of the offending vessel should be known before initiating a specific therapy such as thrombolysis. The concern has been, however, that angiography in the acute stroke patient is not only hazardous but time consuming and may delay treatment for up to two hours. While the BW-tPA acute stroke study did not find angiography in the acute stroke hazardous, it did delay initiation of treatment for 1.5 hours. On the other hand, 25% of patients in that study were excluded from thrombolytic therapy on the basis of angiographic criteria (i.e., eligible by clinical and CT criteria). These results suggest that it will be difficult to select the best candidates for very early intravenous thrombolytic therapy on the basis of the clinical examination only. The great appeal of MRA, therefore, is the ability to acquire not only anatomic data but also vascular imaging in a very brief period of time so that a specific treatment plan can be initiated. When combined with MRD, treatment might be selected on a more physiologic rather than clinical (time from onset, severity of deficit) or anatomic (presence or absence of occlusion) basis.

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## RENAL TRANSPLANTATION OUTCOMES: A COMPARATIVE ANALYSIS BETWEEN ELDERLY AND YOUNGER RECIPIENTS

*MendonçaH.M. et.al. Clin. Transp. 2007, 2:59-64*

Renal transplantation is presently the best treatment for end-stage renal disease, although considered contraindicated for elderly patients. However, more investigation is needed due to higher life expectancy rates of the general population and the increasing number of over 60-yr-old patients with chronic renal failure dependant upon dialysis. This study aims to determine graft and patient survival rates of renal transplant patients 60 yr and older compared to a younger group (50–59 yr old). Relevant pre- and post-transplant clinical data related to graft and patient survival in both groups were also investigated. Three-hundred and twenty consecutive renal transplant patients were enrolled in this study and grouped based on age at the time of the transplantation: one-hundred and ten patients at or over 60 yr old (elderly group) and 210 patients ranging from 50 to 59 yr old (younger group). There were no statistical differences in either group regarding clinical characteristics and immunological risk factors. The incidence of acute rejection was higher in the younger group (37.6%) than in the elderly (22.7%) (p = 0.01). Censored to death graft survivals at five yr were respectively 86.7% for patients e" 60 yr and 82.1% for patients 50–59 yr old (p = 0.49). Patient survival rates at five yr were respectively 76.2% for patients e" 60 yr and 81.6% for patients 50–59 yr old (p = 0.33). Our data show that renal transplantation for elderly patients has similar results to those found in younger individuals, this age, itself should not be a contraindication for transplantation.

# HYPERCOAGULABLE STATES : DIAGNOSTIC CHALLENGES

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***Abstract :*** *Patient with cerebral venous thrombosis or recurrent arterial strokes often have an underlying hypercoagulable state; this may be inherited or acquired. Knowledge of these diseases is required in order to guide treatment and prevent further thrombotic episodes. However, indiscriminate testing in all patients is warranted especially as some of these tests are expensive. Moreover, correct interpretation is also needed before labelling a patient as having a prothrombotic state. Our knowledge of these disorders is expanding but serval lacunae still remain. In this review, we discuss various diseases associated with hypercoagulability and how to investigate these disorders.*

Patients who develop deep venous thrombosis or pulmonary embolism are often labelled as having **hypercoagulable state**. It is important to realize that clots develop for many reasons; therefore, all that clots is not hypercoagulable. For someone to be labeled as having a hypercoagulable state, there are certain criteria that should be ascertained[2]. Hypercoagulable states are of acquired and inherited types[5].

## INHERITED HYPERCOAGULABLE CONDITIONS INCLUDE

- Factor V Leiden (the most common)
- Prothrombin gene mutation
- Elevated levels of fibrinogen
- Deficiencies of natural proteins that prevent clotting (called anticoagulant proteins - such as antithrombin, protein C and protein S)
- "Sticky" platelets
- Abnormal fibrinolytic system, including hypoplasminogenemia, dysplasminogenemia, and elevation in levels of PAI-1
- Elevated levels of factor VIII (still being investigated as an inherited condition)[6,11]

## ACQUIRED HYPERCOAGULABLE CONDITIONS INCLUDE

● Cancer ● Recent trauma or surgery ● Pregnancy and exogenous estrogen use (including use of oral contraceptive pills) ● Hormone replacement therapy ● Prolonged bed rest or immobility (heart attack, stroke and other illnesses that lead to decreased activity) ● Heparin-induced thrombocytopenia ● Air travel ● Antiphospholipid antibody syndrome ● Previous deep vein thrombosis or pulmonary embolism ● Myeloproliferative disorders such as polycythemia vera or essential thrombocytosis

## HOW IS A HYPERCOAGULABLE STATE DIAGNOSED?

### *Careful medical history*

Certain conditions increase a person's risk for developing blood clots, but do not necessarily indicate a genetic hypercoagulable state[1,3]. Therefore, a careful evaluation of the patient's personal and family medical history is needed. Patients who should be screened for hypercoagulable states[7] include those who have:

- A family history of abnormal blood clotting
- Abnormal blood clotting at a young age (less than 50 years old)
- Thrombosis in unusual locations or sites: such as the portal (liver), mesenteric (intestinal) and cerebral (brain) veins
- Blood clots that occur without a clear cause (idiopathic)
- Blood clots that recur
- A history of frequent miscarriages
- Stroke at a young age

### *Unusual Venous Thromboembolic (VTE) Presentations of Hypercoagulable Conditions include :*

Prothrombin G20210A, antithrombin deficiency, essential thrombocythemia, paroxysmal nocturnal hemoglobinuria, cerebral vein thrombosis in women using oral contraceptive pills, inferior vena cava, renal vein, mesenteric vein, portal and hepatic vein thrombosis, myeloproliferative syndromes, migratory superficial thrombophlebitis(Trousseau's syndrome), cancer (particularly adenocarcinoma of the gastrointestinal tract) recurrent superficial thrombophlebitis Factor V Leiden, polycythemia vera, deficiencies of natural anticoagulants, Protein C and protein S deficiencies, neonatal purpura fulminans unexplained fetal loss (three or more first-trimester miscarriages or one second- or third-trimester unexplained death of a morphologically normal fetus) Antiphospholipid antibodies

### *Laboratory testing*

Laboratory tests (blood tests) should be performed only after clinical evaluation. These tests should be reserved for people who have one of the conditions listed previously. The tests should be performed in a specialized coagulation laboratory and interpreted by a pathologist or clinician with expertise in coagulation, vascular medicine or hematology. Testing is best performed when the patient is not having an acute clotting event[8].

***More common lab tests[12] include:***

- **PT-INR:** Prothrombin time (PT or protime) test is used to calculate International Normalized Ratio (INR). The INR will help to determine how fast the blood is clotting and whether the medication dose needs to be changed. This

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test is used to monitor the condition if the patient is taking Coumadin.

- **Activated partial thromboplastin time (aPTT):** measures the time it takes blood to clot; certain chemicals are added to the test. This test is used to monitor the condition if the patient is taking heparin.
- **Fibrinogen level**
- **Thrombin time:** measures the time it takes the blood to clot

Some of the tests listed previously help to detect the *antiphospholipid antibody syndrome* or *dysfibrinogenemias*, conditions which can be associated with hypercoagulable states.

***Tests used to help diagnose inherited hypercoagulable states :***

- Genetic tests include factor V Leiden (Activated protein C resistance) and Prothrombin gene mutation (G20210A)*
- Antithrombin activity
- Protein C activity
- Protein S activity**
- Fasting plasma homocysteine levels

**Factor V Leiden and prothrombin gene mutation (G20210A) are the more commonly identified genetic defects that increase a person's risk for blood clotting. Because of the very low prevalence of these disorders in Asian and African-American populations, it may be most appropriate to limit testing to Caucasian patients.*

***Additional lab tests, such as measurement of free (active) and total protein S antigen levels, may be required in order to validate protein S activity assay results.*

***Other tests used to help diagnose acquired hypercoagulable states include :***

- Anticardiolipin antibodies (ACA), part of the antiphospholipid antibody syndrome(APA)
- Lupus anticoagulant (LA), part of the antiphospholipid antibody syndrome
- Hyperhomocysteinemia
- Heparin antibodies

The presence of anticardiolipin antibodies (ACA) and a lupus anticoagulant (LA) is important when evaluating someone who has had recurrent miscarriages or arterial thrombosis.

Testing helps identify whether the patient is at risk for further clotting and helps determine an appropriate course and length of treatment to prevent future clots. Testing also may help to identify relatives who don't currently have symptoms but may be at risk.

There are no specific signs or symptoms associated with hypercoagulable states. The finding of *livedo reticularis* upon examination of the skin has been frequently associated with the presence of APA, but a true causality has not been established. The most common clinical manifestation of an underlying hypercoagulable state is lower-extremity deep venous thrombosis[10] with or without pulmonary embolism. Because the clinical signs and symptoms associated with deep venous thrombosis and pulmonary embolism are insensitive and nonspecific; objective diagnostic confirmation by the use of an imaging method, such as contrast venography and duplex ultrasound, is mandatory

## *Why Should a Patient Be Tested?*

Testing should be performed[8] if the results will affect management by guiding:

- Duration of anticoagulation therapy
- Choice of anticoagulant agent
- Intensity of anticoagulation therapy
- Therapeutic monitoring strategies
- Family screening
- Family planning
- Choice of concomitant medications

***When Should theTests Be Performed?***

Ideally, testing should be performed in the outpatient setting at least 4 to 6 weeks after any acute thrombotic event. This is because acute illness states, including VTEs, can cause elevations of a number of acute-phase reactants, including factor VIII, C4b-binding protein, fibrinogen, and IgM anticardiolipin antibodies, all of which may interfere with testing and often lead to false-positive diagnoses. Heparins (unfractionated and low-molecular-weight) can interfere with antithrombin activity and with lupus anticoagulant assays, and warfarin predictably lowers protein C and S activity levels. Low activity levels of natural anticoagulants also occur as a result of liver disease, because protein C, protein S, and antithrombin are all synthesized in the liver. Antithrombin activity level may be reduced in nephrotic syndrome and active colitis, and protein S activity may also be reduced in the setting of HIV infection[8].

***Pitfalls and cautions in investigation of prothombotic disorders***

- Assays performed during acute illness or while patient is anticoagulated may be unreliable, leading to misdiagnosis. For example, anticoagulant therapy with warfarin may influence the levels of protein C and S and antithrombin, tests for lupus anticoagulants, and some tests for APC resistance, while heparin may influence the measurement of antithrombin. Recent thrombosis, inflammatory disease and pregnancy may also affect some of these tests. Normal levels in children may differ from those in adults.
- With the exception of oral contraceptives, hyperhomocysteinemia, and antiphospholipid antibodies, risk factors that predispose to VTE probably do not normally predispose to arterial thromboembolism. Other thrombophilic disorders should not be routinely tested for in this setting, although stroke in some young people may be an exception.
- Abnormal results for inherited prothrombotic disorders

should in general be confirmed by a second measurement obtained under ideal circumstances.

- Confirmation of the presence of a familial abnormality in first degree relatives of patients with functional test abnormalities is desirable.
- Comprehensive testing is recommended. Subjects with VTE often have more than one abnormality.
- The significance of anticardiolipin antibodies in subjects with VTE is currently controversial

The issue of screening for thrombophilic defects is controversial[9]. The laboratory evaluation is expensive, and the short-term treatment of venous thromboembolism is the same in all patients, regardless of cause; therefore, it is unclear which patients warrant screening. In addition, there is little evidence to show that testing would influence the intensity or duration of long-term anticoagulation, except in the antiphospholipid syndrome

Although certain tests can be performed at the time of the initial event, heparin interferes with clotting-based assays for APC resistance, the lupus anticoagulant, and factor VIII levels. Protein C, protein S, and antithrombin functional and antigenic tests should be performed only in strongly thrombophilic patients: those with a venous thromboembolism prior to age 50, with recurrent venous thromboembolism, or with an extensive family history of thrombus. In addition, testing for protein C, protein S, and antithrombin cannot be reliably performed during an acute event or while the patient is taking anticoagulants, because the levels fluctuate during active thrombosis and are suppressed by warfarin therapy. If indicated, testing for antithrombin, protein C, and protein S can be performed 3 weeks after anticoagulant therapy has been discontinued. In contrast, there are many compelling arguments to test *appropriate* patients for inherited thrombophilia. Testing advances the knowledge base of the pathophysiology of venous thromboembolism, although data on specific recommendations for length and intensity of anticoagulant therapy are lacking. More importantly, identifying patients at risk for thrombosis carries significant implications in *family counselling* and high-risk situations. The affected family members of individuals with an identified hypercoagulable defect are also at increased risk of thrombosis.

When venous thromboembolism occurs in a woman taking *oral contraceptives*, testing may be warranted in order to provide adequate counseling about continued oral contraceptive use and the risks of thromboembolism in pregnancy. Similarly, testing for factor V Leiden may be warranted when venous thromboembolism occurs in breast cancer patients taking tamoxifen (Nolvadex), because of an increased risk of thrombosis in this group.

*Venous thromboembolism* is a common disease that causes significant morbidity and mortality[4]. In recent years, the ability to diagnose inherited genetic defects and common acquired conditions predisposing to thrombosis has greatly increased. Venous thromboembolism is now understood to be a complex interaction of genetic and environmental factors leading to thrombosis. Integrating the various factors to individually assess thrombotic risk still poses a challenging clinical problem that will likely become easier as more data accumulate. As the ability to accurately assess risk increases, the data can then be translated into tailored treatment regimens. Until then, only general guidelines regarding evaluation and management are available. In the future, it is likely that other prothrombotic conditions will be elucidated, adding to the pool of data

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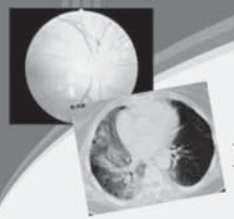

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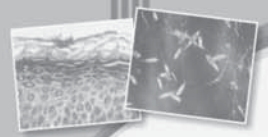

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# FUNCTIONAL BRAIN IMAGING

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***Abstract :*** *Neuronuclear imaging with SPECT and PET enables non-invasive evaluation and quantification of local tissue functions like regional cerebral blood flow, metabolism, receptor binding status and neurotransmission processes. SPECT and PET imaging therefore, is rapidly finding a place in routine diagnostic work up and management of a host of neurological and psychiatric disorders like epilepsy, neurodegenerative disorders, cereberovascular disease , movement disorders, malignant brain tumors, obsessive–compulsive disorder, schizophrenia, depression, panic disorder, and drug abuse. Potential of PET in radiotherapy treatment planning, neuropharmacology, and drug development also holds a lot of promise.*
***Key words:*** *Brain SPECT, PET, epilepsy, neurodegenerative disorders, neuroreceptor imaging*

## INTRODUCTION

Neuroimaging provides a direct window in to the brain's structure and functioning. Structural imaging techniques, such as CT and routine MRI, are used primarily to evaluate anatomy, providing a highly detailed but structural imaging of brain structure. Functional brain imaging techniques such as single emission computed tomography (SPECT) and positron emission tomography (PET), provide dynamic picture of the brain functioning i.e. metabolism and blood flow, chemistry and neurotransmission processes. While structural imaging techniques are very helpful in identifying gross changes in brain structure, functional imaging technique allows us to appreciate the working physiology of the brain[1].

PET studies have confirmed that regional cerebral blood flow changes are generally coupled with changes in regional brain metabolism. Decreased metabolic activity results in hypoperfusion, whereas increased metabolic activity results in hyperperfusion. Although hypoperfusion may occur as a result of vascular changes, functional brain imaging is particularly valuable for neuropsychiatrician for its ability to detect changes in perfusion that are secondary to metabolic changes. In comparison to PET scanning, SPECT scanning is about 3-4 times less expensive, is more widely available, and with the more recent scanner is able to provide spatial resolution images of 6-9 mm –closely approaching the 4-6 mm resolution of PET studies.

SPECT scanners typically use a rotating gamma camera gantry with one to three detector heads. The imaging data are subsequently reconstructed and reoriented in three orthogonal (coronal, sagittal and transaxial) image planes.

## CLINICAL APPLICATIONS OF FUNCTIONAL BRAIN IMAGING

These methods have increasingly been employed in the diagnosis and management of many neurological conditions such as epilepsy, neurodegenerative disorders, cereberovascular disease, movement disorders, malignant brain tumors, obsessive–compulsive disorder, schizophrenia, depression, panic disorder, and drug abuse.

### *SEIZURE DISORDERS*

SPECT brain scans can study perfusion in epilepsy patients , particularly those with focal epilepsy emanating from the medial temporal lobes and producing complex partial seizures. Ictal, postictal and interictal studies allow identifying focuses of epileptic discharges that increase cerebral perfusion during seizure and reduce perfusion postictally and interictally. These studies are used as preoperative investigations and have become important adjunct to clinical and electrophysiological evaluation of patients with epilepsy who are surgical candidates.F-18 FDG PET can localizes epileptic foci as areas of hypometabolism interracially.[3]

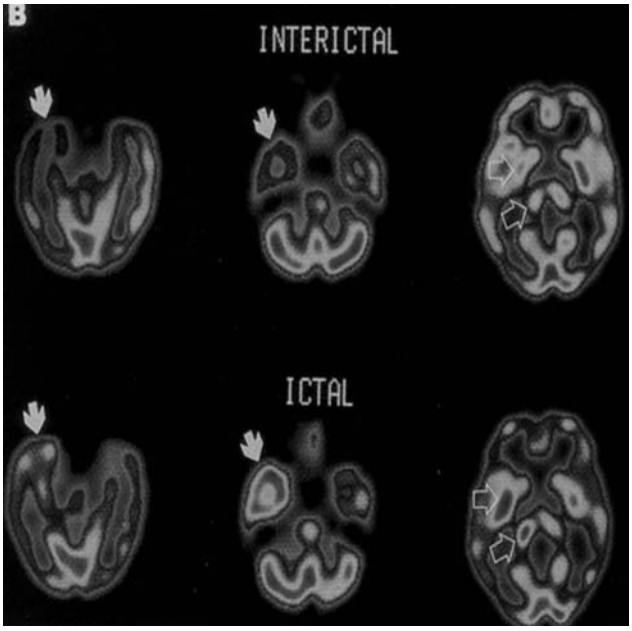


***Fig1:*** *Coronal view of ictal brain SPECT in a patient with complex partial seizures showing hyperperfusion in right temporal lobe..*

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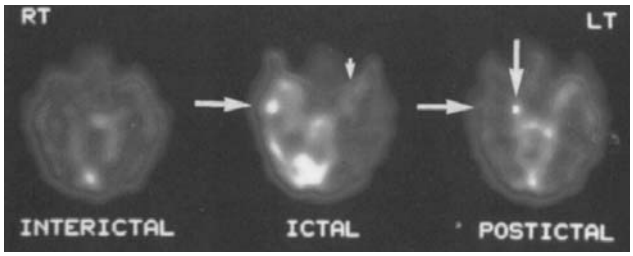



***Fig 2:*** *Coronal views depicting change in regional blood flow during ictal, inter ictal and post ictal phases.*

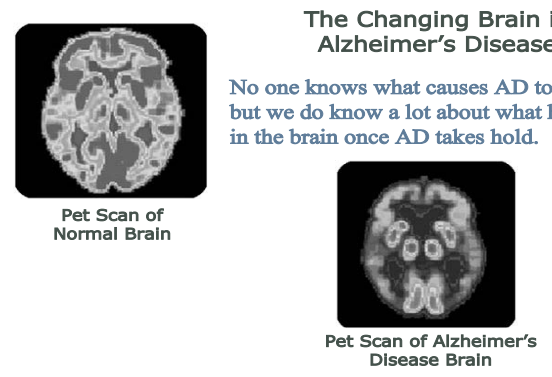
## *DEMENTIA*

SPECT and F-18 FDG PET imaging has shown clinical utility in the differential diagnosis and early detection before onset of clinical deterioration.

Alzheimer's disease is now recognized as a common cause of dementia. AD has characteristic pathological findings. Abnormal tangles of nerve fibers and degenerative neurotic plaques are seen. The patient's degree of dysfunction is related to the number of these abnormal cortical structures.

The classical scintigraphic pattern for AD on SPECT perfusion imaging is bilateral posterior temporal and parietal hypoperfusion. The area of reduced perfusion is secondary to reduced brain metabolism in areas of neuronal depletion. With severe disease, frontal lobe hypoperfusion is seen as well[4].

Fronto-temporal dementia patients generally tend to show bilateral frontal and bilateral temporal lobes glucose hypometabolism.Vascular dementia tends to result in symmetric and focal areas of hypometabolism . In Picks disease most common PET findings is bilateral frontal and anterior temporal hypometabolism.[5]



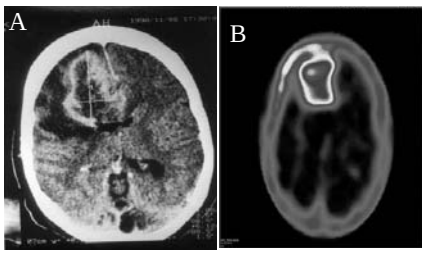




***Figure 3*** *A. Coronal section of frontal glioblastoma multiforme showing contrast enhancement in CT. B. Corresponding SPECT slice of the same patient showing avid $^{99m}$TC-GHA concentration*

## *BRAIN TUMORS*

Primary brain tumors constitute about 10% of all tumors. SPECT studies with Tl-201 and Tc-GHA are useful in determining tumor viability and differentiating recurrence/ residual tumour from post radiation fibrosis and tumour necrosis. Tumor cells of higher histological grades, because of their increased mitotic activity, exhibit increased metabolism in comparison with normal brain tissue. FDG-PET thus provides important prognostic information as higher uptake correlates with higher histological grade and shorter survival[6]. PET is also useful in monitoring and timely detection of transformation of low grade tumor into a high grade variety, which can significantly influence treatment planning in such cases. PET also provides objective evidence of response to therapy.

## *STROKE*

The role of SPECT with cerebral perfusion agents like HMPAO and ECD in the evaluation of cerebrovascular diseases is not significant in patients with obvious stroke. However, there are specific indications, where SPECT studies play a crucial role, such as determination of critical hemodynamically significant stenosis and carotid artery by-pass patients who are candidates for PTCA procedure.[7]

Cerebral perfusion SPECT is also widely used for estimation of degree for cerebral ischemia. Particularly, cerebral perfusion SPECT is valuable for decision if thrombolysis therapy should be done for embolic cerebral ischemia. When the ratio of ipsilateral to contra lateral perfusion is in the range of 0.4 to 0.7 on SPECT, thrombolysis therapy can be applied in patients without acute cerebral infarction.

## *NEUROPSYCHIATRIC DISORDERS*

The present status of brain SPECT in psychiatric disorders is still, investigational. In spite of considerable research interest in this area, specific perfusion patterns of the various diseases have not been conclusively identified.. However, perfusion and receptor imaging findings may be used as an additional diagnostic tool to guide clinicians searching for a definite diagnosis.

In conditions like Schizophrenia, which comprises a group of closely related disorders characterized by a particular type of disordered affect, behavior, and thinking . Brain SPECT aids in the diagnosis - most frequent pattern being hypofrontality, especially during a specific task; perfusional changes in the basal ganglia, possibly related to the use of neuroleptic drugs; and temporal lobe hypoperfusion, usually on the left side and frequently associated with ipsilateral frontal lobe hypoperfusion. In addition, Semi quantitative analysis of neurorecepter imaging may help predict treatment outcome: with therapy, the ratio of the basal ganglia to the frontal cortex decreased in good responders and increased in poor responders.[8]

In conditions like depression, The typical brain SPECT pattern is hypoperfusion of the the prefrontal area and temporal lobes,

cingulate gyrus, and left caudate nucleus in patients free of medication, the prefrontal, limbic, and paralimbic areas in both unipolar and bipolar depression; and the lateral frontal area in acute depression in the elderly. Hypofrontality is shown to be associated with severe negative symptoms. Functional imaging therefore is a potentially useful tool in initial evaluation and prognosis.[9]

The typical perfusion patterns in brain SPECT is also being used to study pathophysiology and diagnosis of other disorders like obsessive compulsive disorders, panic disorders, Gille's de la tourette syndrome etc.

### *EMERGING TRENDS FUNCTIONAL BRAIN IMAGING*

In the coming times, functional imaging with SPECT and PET is expected to play an important role in Neuropharmacology and drug development. PET and SPECT neuroreceptor ligand studies will allow use of in vivo techniques to study pharmacodynamics, biodistribution, receptor occupancy and also assess therapeutic efficacy of drugs.

PET and SPECT ligands for neurorecepter imaging, like F18 Flouro-L-dopa,11C-Nomifensine, I123-BCIT(10) etc are being evaluated for diagnosis of parkinsonism. Similarly, in vivo amyloidal plaque imaging with 18F-FDDNP holds a lot of promise in facilitating early diagnosis of Alzheimer's disease. The development of a host of ligands for benzodiazepine, serotogenic, opioid receptors would permit better understanding of the pathophysiology of various CNS disorders.

PET will also be crucial in radiation treatment planning, and will allow better delineation of biological target volumes as detection of microscopic extension, which is beyond the limits of conventional modalities, would be possible.

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# TRANSCRANIAL DOPPLER MONITORING

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***Abstract :*** *The evolution of Transcranial Doppler (TCD) as a diagnostic technique can only be surpassed by its growth and expansion as monitoring tool. The inherent characteristics of TCD, its simplicity, safety and reliability confer it the right dynamic qualities necessary for its use in the assessment of cerebral circulatory changes over period of time of variable length. The present paper is a summary of some of the basic concepts that govern the utilization of TCD for monitoring neurological patients. Examples of some of the most common clinical applications of this techniques, as well as suggestions regarding potential future roles that it will play in clinical practice are also included.*

## GENERAL CONCEPTS: TYPES OF MONITORING

Several types of TCD monitoring techniques are available, each with its own advantages and disadvantages.

## INTERMITTENT TCD MONITORING

This perhaps the one which is most commonly performed. Its principle is the repeated sampling of one or more cerebral blood vessels on multiple occasions over hours or days. Its main advantages are that it requires no specialized equipment, and that it can be performed in almost any environment, so long as the patient remains available. The obvious *disadvantage* are related to the diagnostic limitations of a short sampling period. In between sampling sessions, any changes occurring in the patient will go unnoticed. It is possible to monitor different types of patients using this technique. In fact, the earliest studies of the effects of cerebral vasospasm upon TCD measurements were conducted using this method; a technologist or a physician would record daily TCD measurements from selected brain arteries, especially the middle cerebral artery.

## CONTINUOUS DATA GENERATION

TCD monitoring, on the other hand, represents a more complex technique, requiring the utilization of specialized TCD monitoring transducers and transducer holders, in order to maintain the sampling probe in place for extended periods of time. Its basic advantage is the generation of continuous data over a single period of time, thereby reducing the risk of missing important information related to changes occurring in the patient during the sampling interval. Conversely, long-term monitoring is ideally performed in patients who are either immobile or those with limited mobility. When these conditions are not met, securing the TCD transducer in place becomes a major technical obstacle. It was this form of TCD monitoring was first utilized in the operating room to assess the effects of certain surgical procedures upon the brain circulation. Since then, it has been possible to apply it to a variety of clinical situations.

## INSTRUMENTATION

One of the characteristics of TCD that makes it such a desirable technique for monitoring is the compact and portable nature of TCD instruments. It is possible to carry the equipment almost into any environment, without occupying large amounts of space, and allowing the sonographer to operate without interfering with procedures being carried out concurrently. In general, ultrasound companies that manufacture TCD instrumentation have understood the importance of small, portable equipment. In addition, multi-channel instruments capable not only of trend analysis of the TCD data, but also of storing other types of monitoring information (e.g. blood pressure) are being introduced. Finally software that allows the detection of embolic material, as well as its characterization, is the latest link in the chain of technologic advantages that make TCD monitoring possible.

## TRANSDUCERS

As noted earlier, in order to carry out long-term continuous monitoring, the probe must be secured in place by means which preserve the spatial relationship between the Doppler sample gate and the blood vessel being monitored. Originally, elastic headbands secured with Velcro were utilized. Although capable of allowing monitoring of patients during intra-operative conditions, they were insufficient for holding the transducer in place in awake, sick, often highly mobile hospitalized patients. Several solutions were offered for this problem, including suturing the transducer holder to the skin intra-operatively. A few years ago, our group introduced a TCD transducer holder which could be “glued” to the skin with a variety of substances, including, collodion. The device could be secured and removed in a few minutes, and it allowed TCD monitoring of patients over periods of up to 72 hours. The main limitations were that electroconductive gel had to be reapplied at least every 4 hours, and that imaging procedures of the brain could not be properly carried out with the device was in place. In future, it is likely that even smaller transducers, shaped and sized like a 25 cents coin and attachable with the ease of electrocardiographic monitoring leads will be available.

## INTRA-OPERATIVE TCD MONITORING

The use of TCD monitoring during surgical procedures was first guided by the expectation of detecting hemodynamic changes that may compromise the cerebral circulation. Although this has certainly occurred, the detection of emboli is perhaps a more important finding related to the application of this technology, and one which could have an even greater impact upon the care of patients with cerebrovascular ischemic disorders. For practical purposes, the surgical procedures in which TCD monitoring has

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been most widely utilized are *carotid endarterectomy* and *cardiopulmonary* bypass grafting.

***Carotid Endarterectomy:*** The utilization of TCD monitoring during carotid artery surgery was fostered by the concern about hemodynamic complications of cross-clamping of the common carotid artery during surgical intervention. The possibility of cross-clamping resulting in cerebral ischemia (or infarction), and the need for defining parameters that would guide the surgeon about the requirement of shunting led to the use of TCD as a monitoring tool. Compared with other monitoring techniques such as electrophysiologic procedures (electroencephalography and evoked potentials), TCD provides quicker and more direct assessment of hemodynamic disturbances. In general it has been shown by multiple groups that a mean blood flow velocity (MBFV) drop of 33% or more in the middle cerebral artery during cross-clamping, is an indicator of the need for shunting. These results, in fact, are almost identical to the MBFV drop noted lobe associated with alteration of consciousness during global cerebral ischemia. Even more surprisingly, however, has been the finding of repeated embolization into the middle cerebral artery territory during carotid artery surgery.

***Cardiopulmonary Bypass Grafting:*** This is another area where TCD monitoring has allowed the identification of embolic phenomena as perhaps the most important finding during the surgical intervention. This is in contrast to the traditional idea that hemodynamic compromise results in the majority of the ischemic deficits following this type of surgical procedure. In the early years, however, TCD monitoring provided the first method for documenting the levels and effects of non pulsatile flow in the cerebral circulation, as the extra-corporeal oxygenator were being utilized.

## BEDSIDE TCD MONITORING

Perhaps the most attractive potential application of TCD monitoring has been ***performing it at the bedside***. Until TCD became available, it was practically impossible to assess on a moment-to-moment basis, the status of the cerebral circulation. In addition, issues about auto-regulation, the effects of therapeutic maneuvers or medications could now be explored fast and non-invasively. From a certain perspective, TCD monitoring could be considered the cerebral *Swan-Ganz* of the future. The application of **bedside TCD monitoring** continues to expand, to include clinical scenarios of a diverse nature. The following paragraphs will serve as a review of some of the most important.

***Ischemic Cerebrovascular Disorders :***

The moment-to-moment assessment of patients with cerebral infarction and transient ischemic attacks is perhaps one of the most exciting potential applications of TCD monitoring. The technique has allowed differentiation of hemodynamic changes which occur in eminently embolic infarction, and those secondary to lipohyalinotic occlusion of penetrating arterioles. The patterns found in the former, consistent with embolus recanalization and the evolving picture of "pseudostenosis" which often accompanies; underscores the presence of a dynamic process for which TCD appears to be a perfectly matched dynamic monitoring procedure. Furthermore, the ability of TCD to detect embolic phenomena has opened the door to the objective qualification of the effects of anti-coagulant medications upon the development of cerebral ischemic events.

***Hemorrhagic Cerebrovascular Disorders and Trauma :*** The majority of the TCD data has been collected from patients with subarachnoid hemorrhage. In this context, TCD has allowed the non-invasive assessment of patients at risk, and a better planning of interventional diagnostic or therapeutic procedures. Daily TCD monitoring of patients with ruptured intracranial aneurysms has invariably shown that MBFV in the basal cerebral arteries progressively increases during the first two weeks, reaching a peak at approximately the $8^{th}$-$10^{th}$ days following the original hemorrhage. This elevation of MBFV results from the narrowing of diameter of the arterial segments being monitored. At least for the middle cerebral artery, it is possible to classify the severity of vasospasm by the degree of increment observed in the MBFV. Perhaps, more important than the detection of vasospasm, once it is present, is the ability of TCD monitoring to predict its impending occurrence, early enough to allow the clinicians to intervene before it becomes clinically symptomatic. In fact, it has been reported that an increase of over 50% in MBFV over a 24 hours period is highly indicative of the risk for symptomatic vasospasm. Furthermore, the recent introduction of cerebral balloon angioplasty as a potential tool for treating vasospasm places TCD monitoring at the top of the list of ancillary procedure that could be used to monitor the hemodynamic effectiveness of the procedure.(Table)

**Table:** *Doppler criteria for the diagnosis of spasm of the middle cerebral artery*

| MBFV (cm/sec) | MCA /ICA MBFV | Interpretation |
|---|---|---|
| <120 | <3 | Normal, non-specific elevation or distal spasm |
| >120 | 3-6 | Proximal Vasospasm |
| >200 | >6 | Severe Proximal Vasospasm |

*(Reproduced from Seiler R and Newell DW. Transcranial Doppler)*

Vasospasm is not only observed in patients who have suffered rupture of intracranial aneurysms. In fact, the most common cause of subarachnoid hemorrhage is head trauma. The incidence of vasospasm in patients with head injury has been reported to be somewhere between 5-50%, this wide range directly results from the variety of definitions utilized in the diagnosis of vasospasm, as well as the requirement of cerebral angiography in the earlier studies. Several groups of investigators have shown that it is possible to document the presence of vasospasm in the majority of individuals who have suffered closed head injuries, and that its occurrence does not necessarily correlate with the presence or absence of hemorrhage in the admission computed tomography (CT) studies. Renewed interest in the subject of post-traumatic vasospasm has promoted the inclusion of TCD monitoring among the techniques utilized in neurologic and neurosurgical critical care units. An area of particular interest is the differentiation between vasospasm and vasoparalysis, as well as the effect of certain therapeutic maneuvers upon the TCD changes observed. Finally, it is important to note that cerebral vasospasm may also occur in the context of other clinical conditions including migraine.

***Cerebral Circulatory Arrest:*** The cerebral blood flow, and therefore the cerebral blood flow velocities, depend upon cerebral perfusion pressure and cerebrovascular resistance. The latter is a result of both the vasomotor tone of the cerebral arterioles, and

also of the intracranial pressure (ICP). As the ICP rises, greater resistance to flow will be encountered by the cerebral arteries. With regard to TCD monitoring, this is going to be reflected in a decrease in velocities and an increase in pulsatility. As the ICP continues to increase, resistance to flow will become even greater, to a point, where a "reverberating" waveform pattern will be noted by TCD; this pattern is associated with net blood flow, and usually implies absence of effective cerebral circulation an event associated with brain death. It is therefore possible to use TCD monitoring to detect the progression of intracranial hypertension and to document the present of cerebral circulatory arrest.

***Global Cerebral Ischemia :*** Theoretically, it is also possible to utilize TCD to monitor the effect of systemic circulatory derangements upon the brain. An example of this is the documentation of a global decrease in end diastolic blood flow velocities (EDBFV) resulting from aortic insufficiency. Even simple bradycardia will have an effect upon the EDBFW that can be measured with TCD. Several groups have studied the TCD changes occurring during syncope, showing that a drop of approximately 50% is frequently observed as patients pass out. In any case it is important to note that when systemic hypotension occurs, complete loss of EDBFV is not tolerated by the brain and is always associated with the loss of consciousness. The use of TCD monitoring during *head up tilt tests* (HUT) has introduced a new dimension in the assessment of patients according to the principal mechanism for their event, into vasovagal, vasodepressor and "cerebral" syncope. The latter is a poorly understood condition in which, for reasons yet unknown, patients seem to develop cerebral vasoconstriction and loss of consciousness.

Some groups have been also interested in assessing the effect of cardiopulmonary resuscitation upon the cerebral circulation. The use of TCD monitoring of the internal carotid artery during CPR has shown that, in spite of all maneuvers, MBFV drop progressively and relentlessly over time. This drop seems to be the direct result of a progressive increase in resistance to flow, leading to the development of "reverberating" TCD patterns; further work in this area might disclose ways in which TCD could assist in improving the outcome of patients who suffer cardiac arrest.

## DETECTION OF CEREBRAL EMBOLI

In 1990, for the first time, Spencer et al. reported the detection of asymptomatic formed emboli to the cerebral blood vessels using TCD monitoring of patients undergoing carotid endarterectomy. This report was followed by great general interest in further investigating the capability of this technique, as well as its potential clinical applications. The theoretical basis for the detection of emboli using Doppler ultrasound is actually very simple. The Doppler effect generally relies upon the frequency shift caused upon the ultrasound beam by a moving reflector, in this case the red blood cells. The intensity of the returned ultrasound depends upon the proportion of the transmitted beam that is reflected. This, in turn, depends upon the tissue through which the ultrasound passes, and the reflection from the interface between two materials. The latter is proportional to the difference in acoustic impedance compared with circulation blood, the Doppler ultrasound beam reflects readily and intensely from them, generating characteristic sounds and changes within the Doppler waveform. It is possible to utilize TCD to detect gaseous or solid embolic material. There is preliminary information to suggest that the technique may even be used to differentiate among different types of pathologic embolic material, conferring TCD monitoring a very important place in the evaluation and follow up of patients during surgical procedures, or of patients at risk of recurrent cerebral embolisation for a variety of other reasons (e.g. prosthetic heart valves, patent foramen ovale). The task of applying TCD monitoring the detection of emboli is likely to be facilitated by the development of instrumentation capable of automatically recognizing the Doppler characteristics of emboli, differentiating it from ultrasonic artifacts.

## CONCLUSION

The technique of TCD monitoring is a safe and reliable method for longitudinal assessment of the status of the cerebral circulation over time. Its applications are as diverse as the imaginative efforts of the user. In general, TCD monitoring appears to have a great future, becoming more entrenched into the daily care of patients with neurological disorders. The future is yet to see even further improvements in the instrumentation and transducer utilized for TCD monitoring, perhaps adding more potential applications of this technique.

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**IMSA orations to be delivered in IMSACON-2008**

Following orations have to be delivered in IMSACON- 2008 to be held on 12-13 October, 2008 in Dubai.

1. Dr. Pinnamaneni Narasimha Rao, International Award;
2. Dr. T.M.A. Pai oration ;
3. Mrs. Sushila and Dr. K.N. Rao Memorial oration ;
4. Dr. B.C. Bansal and Mrs. Uma Bansal oration;

BOT & CEC members and Fellows and Members of IMSA are requested to recommend names of national and international fame for delivering the above orations. The recommending persons should send biodata and achievements of the recommended persons for consideration by the Award Committee. The recommendations should reach IMSA headquarter at New Delhi by 10th May 2008.

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# HOW TO INVESTIGATE INTRACEREBRAL HAEMORRHAGES? DO WE KNOW, WHOM, HOW & WHEN TO INVESTIGATE?

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***Abstract :*** *Intra cerebral Haemorrhage (ICH) is much less common than ischaemic stroke (15% vs 85% in most western studies), but is associated with a significantly worse prognosis.*

*ICH is more common in Asian population, probably reflecting higher rates of small vessel disease, hypertension and genetic factors. Over all ,ICH mortality rates approach 50% and there has been little effective treatment to date, except for the overall benefits from stroke unit care. Hypertension, trauma and cerebral amyloid angiopathy cause the majority of these hemorrhages. Advanced age and heavy alcohol consumption increase the risk and, cocaine use is one of the most important causes in the young.*

## CAUSES OF INTRACRANIAL HEMORRHAGE

### *HYPERTENSIVE HEMORRHAGE:*

Hypertensive Intracerebal hemorrhage, one of the most common causes, usually results from spontaneous rupture of small penetrating artery deep in the brain. The most common sites are the basal ganglia (putamen, thalamus and adjacent deep white matter), deep cerebellum and pons. The hemorrhage may be small or a large clot may form and compress adjacent tissues, causing herniation and death. Blood may dissect in to the ventricular space, which substantially increases mortality and may cause hydrocephalous.

Clinically they present with abrupt onset of focal neurological deficit, occasionally seizures diminishing level of consciousness and signs of increased ICH, such as headache and vomiting.

### *Common Sites & Presentations:*

**a) Putamen:** Most common site for hypertensive hemorrhages, contra lateral hemi-paresis along with slurring of speech, gradual weakness of arm and leg, and the eye deviate away from the site of the hemiparesis. When hemorrhages are large, drowsiness gives way to stupor as signs of upper brain stem compression appear. Coma ensues accompanied by deep, irregular or intermittent respiration, a dilated and fixed ipsilateral pupil, and decerebrate rigidity.

**b) Thalamus:** Thalamic hemorrhages also produce a contralateral hemiplegia or hemiparesis from pressure on adjacent internal capsule. A prominent sensory deficit & aphasia may be seen in dominant thalamic involvement or mutism in non dominant hemorrhages. They also produce a lot of ocular disturbances like nystagmus, ocular palsies, Horner's syndrome etc.

**c) Pons**: In Pontine hemorrhages deep Coma with quadriplegia usually occurs over a few minutes with prominent decerebrate rigidity and pin point pupils that react to light and impaired ocular movements. Hyper apnea, severe hypertension and hyper hidrosis are common.

**d) Cerebellum:** Cerebellar hemorrhages develop over several hours and are characterized by occipital headache, repeated vomiting and ataxia of gait. In mild cases there may be no other neurological signs other than ataxia. Dizziness and vertigo may be prominent. There is often paresis of conjugate lateral gaze towards the side of the hemorrhage, forced deviation of the eye towards the opposite side, or an ipsilateral sixth nerve palsy. Dysarthria and dysphagia may occur. As hours pass the patient may become stupor and then comatose from brain stem compression or obstructive hydrocephalous; immediate surgical evacuation before brain stem compression occurs, may be life saving.

Hydrocephalous from fourth ventricle compression can be relieved by external ventricular drainage, but definite haematoma evacuation is essential for survival.

### *LOBAR HEMORRHAGES*

Most lobar hemorrhages are small and cause a restricted clinical syndrome caused by embolus to an artery supplying one lobe. For example in occipital hemorrhages characterized by hemianopia, Left temoral hemorrhages:aphasia and delirium, parietal hemorrhages hemi sensory loss, frontal hemorrhages;arm weakness. Large hemorrhages may be associated with stupor or coma if they compress the thalamus or mid brain. Most patient with lobar hemorrhages have focal headaches, and more than half vomit or are drowsy. Stiff neck and seizures are uncommon.

### *CEREBRAL AMYLOID ANGIOPATHY*

Disease of the elderly in which arteriolar degeneration occurs and amyloid is deposited in the walls of the cerebral arteries. It causes both single and recurrent lobar hemorrhages and is probably the most common cause of lobar hemorrhage in the elderly. It also includes some intracranial hemorrhages associated with intravenous thrombolysis given for MI. This disorder can be suspected in patients who present with multiple hemorrhages (and infarcts) over several months or years or in

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patients with "micro bleeds" seen on brain MRI sequences sensitive for haemosiderin and is definitely diagnosed by demonstration of congo red staining of amyloid in cerebral vessels. There is no specific therapy.

### *COCAINE INCLUDED HEMORRHAGE*

This is frequent cause of stroke in young age (>45 years) patients. Intra cerebral hemorrhages, ischemic stroke and SAH are all associated with cocaine use.

### *HEAD INJURY*

This often causes intracranial bleeding. The common sites are intracerebral (esp. temporal and inferior frontal lobes) and in to the subarachnoid, subdural and epidural spaces. Trauma must be considered in any patient with an unexplained acute neurologic deficit (hemiparesis, stupor or confusion), particularly if the deficit occurred in the context of a fall.

### *ANTICOAGULANT THERAPHY*

Intracranial hemorrhages associated with anticoagulant therapy can occur at any location; they are often lobar or subdural. Anticoagulant related intracerebral hemorrhages may evolve slowly, over 24 to 48 hrs. Coagulopathy should be reversed with FFP or factor replacement, vitamin K and platelet transfusion in case of & decreased platelets, to limit the volume of hemorrahages.. Intra cerebral haemorrhages associated with hematologic disorders (leukemia, aplastic anemia, Thrombocytopenic pururas) can occur at any site and may present as multiple intracerebral haemorrhages.

### *BRAIN TUMORS*

Haemorrhages in the brain may be the first manifestation of neoplasm; cholangio carcinoma, malignant melanomas, renal cell carcinomas and bronchogenic carcinomas are among the most common metastatic tumors associated with intracerebral haemorrhage. Glioblastoma multiforme in adults and meduloblastoma in children may also have areas of intracerebral haemorrhage.

### *HYPERTENSIVE ENCEPHALOPATHY*

This condition is a complication of malignant hypertension, characterized by severe hypertension associated with headache, nausea, vomiting, convulsions, confusion, stupor and coma. There is retinal haemorrhages, exudates, papillodema (hypertensive retinopathy ) and evidence of renal and cardiac disease.

## INVESTIGATIVE APPROACH

**CT Scan:** This is the most important tool and confirms the diagnosis in most ICH cases. It defines the size, site and surrounding oedema and midline shift. It can also identify hydrocephalous, tumour bleed and occasionally AV malformations.

**MRI Scan:** MRI brain is not routinely used but in situations like tumour bleed, AV malformation and other bleeds gives better view of tumours, malformations and aneurysms.

**CT Angio or MRI Angio & Conventional Angiography** of intracranial vessels are needed in cases of atypical ICH or suspected AV malformation, particularly if the patient is young or not hypertensive and the hematoma is not in one of the four usual sites for hypertensive haemorrhage; for example, haemorrhage in to the temporal lobe suggests rupture of a MCA saccular aneurysm.

**A detailed history and examination** along with routine laboratory investigations esp. liver function tests (LFT's) and Coagulation profiles are essential to identify and treat the underlying basic systemic illness.

## CONCLUSION

Hypertension, trauma and cerebral amyloid angiopathy cause the majority to these haemorhages. Advanced age and heavy alcohol consumption increases the risk, and cocaine use if one of the most important causes in the young.

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**ETHICAL GUIDELINES FOR BIOMEDICAL RESEARCH**

The need for uniform ethical guidelines for research on human subjects is universally recognised. It has acquired a new sense of urgency as the critical issues in the area of biogenetic research involving human subjects have become acute. Apart from the mandatory *clinical trails* on new drugs, a number of *diagnostic procedures, therapeutic interventions and prevention measures* including the use of vaccines, are being introduced which involve human subjects. Further the advent of *new medical devices* and *radio-active materials* and therapeutic benefits of *recombinant DNA products* have added a new dimension to the ethical issues that need to be considered before evaluating these for their efficacy, utility and safety.

Any research using the human beings as subjects shall bear in mind the following **principles** of : i) **essentiallity**, (ii) **voluntariness, informed consent**, (iii) **non exploitation**, (iv) **privacy** and **confidentially**, (v) **precaution** and **risk minimisation**, (vi) **professional competence**, (vii) **accountability & transparency**, (viii) **maximisation of public interest** and **distributive justice** (ix) **institutional arrangements** (x) **public domain** (xi) totality of **responsibility** and (xii) **compliance**.

Recent advances in the field of **Assisted Reproductive technologies, organ transplantation, Human genome analysis**,and **gene therapy** promise unquestionable benefits to mankind. At the same time, they raise many questions of law and ethics, stimulating public interest and concern.

*(Source : ICMR Publication 2000)*

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# ELECTROENCEHALOGRAPHY IN NEUROLOGY

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***Abstract :*** *Electroencephalography (EEG) is the technique of recording from the scalp spontaneous electrical activity of the brain and correlating it to the underlying brain function. However with recent advances in neuroimaging, its role has become restricted and more focused. It remains an extremely valuable test in patients with suspected epilepsy and in patients with altered mental status and coma. EEG pattern helps to clarify the seizure type and are indispensable for the diagnosis of non-convulsive status epilepticus and for separating epileptic from non-epileptic episodes. There are EEG patterns predictive of the cause of encephalopathy or the location of the lesion. An EEG is most helpful in diagnosing severity and hence the prognosis of cerebral dysfunction. Lastly EEG is very helpful in assessing normal or abnormal functioning in a newborn because of the serious limitation in performing an adequate neurological examination on the newborn. Under such circumstances the EEG may be the only available tool to detect an encephalopathic process or the occurrence of epileptic seizures.*

## EEG IN NORMAL SUBJECTS

The EEG in a normal awake child and adult shows an *alpha rhythm*[1]. However there may be normal variants which are often mistaken as abnormal patterns. In general the alpha rhythm is higher in amplitude in the right hemisphere. If the amplitude on the right side is more than 1½ times that on the left or is over 25% higher on the left than on the right side, it is considered significant[2]. The EEG during non-rapid eye movement (NREM) sleep in children shows very prominent spike –like vertex sharp waves which are often mistaken for epileptiform activity. Similarly 'positive occipital sharp transients (POSTs)' in children may also be mistaken as abnormal spikes . In a small proportion of normal adults, alpha rhythm may be entirely absent and the background may consist of a low amplitude rhythm of 5-30 cps frequency. This EEG is reactive to stimuli like sleep and drugs and hyperventilation may bring out an alpha rhythm. Moreover, during sleep normal activites like vertex sharp transients and sleep spindles are generated[3]. The alpha frequency decreases with normal aging to a minimum of 8cps.

## EEG IN EPILEPSY

The value of an EEG lies in the fact that it not only shows specific ictal discharges during a clinical seizure but also characteristic epileptiform abnormalities in many epileptic patients even in the interictal period. Specific patterns may help to classify the seizure type and guide the choice of antiepileptic medication. An EEG may be the only test demonstrating focal abnormalities responsible for the patient's epilepsy. It is indispensable for the diagnosis of nonconvulsive status epilepticus presenting as a 'twilight' state or a prolonged episode of abnormal behaviour. It may be the only way to establish whether the abnormal behavior is due to an epileptic seizure or a nonepileptic event. It is also required to localize the epileptogenic focus when resective surgery is undertaken in a patient with medically refractory focal epilepsy.

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Morphologically, interictal epileptiform abnormalities consist of spikes, polyspikes, sharp waves and spike slow wave complexes. Generalized discharges that are bilaterally synchronous and symmetrical are associated with generalized epilepsies, whereas focal discharges are seen in partial epilepsies. The topographic distribution of these interictal discharges is more important in the classification of epilepsies since most patients do not have a clinical seizure during an EEG. However, although the interictal epileptiform abnormalities have a high correlation with the occurrence of clinical seizures they do not necessarily mean that the patient has epilepsy. Different studies have found an incidence of less than 2% of epileptiform abnormalities in the EEG of nonepileptic subjects[4]. The irrefutable evidence of an epileptic seizure is a clinical seizure associated simultaneously with ictal discharges in the EEG, although this evidence may only be obtained on prolonged video EEG monitoring. Ictal seizure pattern is characterised by epetitive EEG discharges with relatively abrupt onset and termination, and characteristic pattern of evolution lasting several seconds. It is generally rhythmic and displays increasing amplitude, frequency and spatial spread during the seizure.

There are many EEG transients that resemble epileptiform discharges but need to be distinguished from epileptiform abnormalities to avoid over diagnosis. These include artifacts (e.g. electrode problem, muscle potentials, eye movements, ECG etc.), normal background activity (e.g. vertex sharp transients of sleep, POSTs etc and other epileptiform variants of dubious clinical significance. Useful criteria have been formulated to properly identify epileptiform discharges[5]-

1. Epileptiform discharges should be discrete and clearly separable from ongoing background activity by higher amplitude and with their morphology and duration.
2. Most epileptiform discharges have a bi-or triphasic waveform.
3. The epileptiform events show asymmetric rising and falling phases.
4. Most spikes and sharp waves are followed by a slow wave
5. Epileptiform discharges should involve more than one electrode which helps to distinguish them from electrode related artifacts or muscle potentials.

6. Epilepsy manifested by loss of consciousness is accompanied by demonstrable changes in the scalp EEG. The absence of such changes during an episode of 'unconsciousness' or seizure like motor activity can be particularly important in diagnosing pseudo seizures.

The yield of epileptiform abnormalities in an interictal EEG study can be increased by various methods. Serial EEG studies increase the yield from 50% in the first record to 84% by the third EEG and 92% by the fourth EEG. Thus four or five EEGs spread over a few years provide diagnostic abnormalities in over 90% patients with epilepsy[6]. Serial negative EEGs in a patient with continuing paroxysmal events raise a suspicion of nonepileptic episodes. Obtaining an EEG immediately after a clinical seizure will also increase the chances of capturing interictal epileptiform discharges. Hyperventilation[9] for at least 5 minutes at the beginning and the end of the study and photic stimulation are potent activators of generalized discharges associated with primary generalized epilepsies. Photoparoxysmal response (PPR) has a high correlation with clinical epilepsy and is characterized by generalized bilaterally synchronous spike wave discharges occurring with photic stimulation. The incidence of epilepsy[7] is particularly high if the PPR is prolonged (93%) rather than self –limited (52%). About 10% of patients with primary generalized epilepsy show PPR with the highest incidence in juvenile myoclonic epilepsy[8]. PPR in noneileptic subjects has a prevalence of 1-4% and is usually brief[1]. Other EEG responses induced by photic stimulation, like the photomyoclonic response have no significant correlation with epilepsy. Sleep tends to bring out focal epileptiform abnormalities in patients with focal epileptic seizures. All patients with suspected epilepsy should have a sleep recording unless there is an unequivocal abnormality seen during wakefulness. To ensure a sleep EEG one can instruct the patient to come for the EEG after remaining awake for the entire or at least a major part of the previous night. Sleep deprivation has a further activating effect that is additive to natural sleep, particularly in patients with complex partial seizures and juvenile myoclonic epilepsy. The use of special electrodes improves the chances of recording epileptiform abnormalities. They are particularly helpful in detecting abnormalities arising from the mesial temporal lobes which have high epileptogenicity but are not fully explored by conventional placement. Nasopharyngeal electrodes were used in the past but anterior temporal electrodes have now been found to be better in patients with temporal lobe epilepsy[9]. Sphenoidal electrodes have the best yield but are invasive and are used only as a part of the presurgical evaluation of patients with medically intratable temporal lobe seigures. However, seizures that remain very localized, including epilepsia partial's continua, may not have changes in the EEG because the diagnostic discharge may be deep-seated or involve only a small pool of neuronal tissue. In rare patients with reflex epilepsy, the specific trigger may be carried out during the EEG recording to promote a clinical seizure. Examples of these are playing specific music in music epilepsy, asking a patient to read from a book in reading epilepsy, bathing the patient in bathing epilepsy, asking a patient to eat his meals in eating epilepsy etc.

*Generalized epilepsies* may be primary (idiopathic) or secondary (due to diffuse cerebral hemispheric insult). The EEG hallmark of *primary generalized epilepsy* (PGE) is rhythmic, anterior-dominant generalized bisynchronous 3 Hz spike wave discharges superimposed on a normal background. More common however are generalized paroxysms of spike wave complexes occurring at 3-5 Hz. Transient asymmetry and isolated focal spikes may also be seen. Although there are no interictal abnormalities which are specific for individual syndromes included under PGE, polyspike waves are more common with myoclonic epilepsies, paroxysmal occipital-dominant rhythmic delta activity is seen in absence epilepsy and PPR is most common with juvenile myoclonic epilepsy. In *secondary generalized epilepsy*, the background activity is disorganized,there are variable degrees of slowing and other patterns may be seen like hypsarrhythmia (high amplitude, asynchronous, slow waves associated clinically with infantile spasms) and generalized paroxysmal fast activity(bisynchronous 12-25 Hz discharges seen mainly during sleep and usually not associated with any clinical change).

*Focal epilepsies* may be primary (idiopathic) or secondary (due to acquired focal cortical processes). The intertictal EEG hallmark of focal epilepsy is a focus of epileptiform activity. The frequency of epileptiform discharges do not correlate with the frequency of clinical seizures. However the interictal epileptiform discharges do become more frequent immediately after a clinical focal seizure [10]. Postictally, there may be a period of generalized followed by transient (from seconds to days) focal delta activity which is a reliable sign of a focal origin of the previous epileptic seizure. When the focal epileptiform activity occurs along with a focal abnormality of the background activity the possibility of a structural lesion is more likely and the epilepsy is more likely to be symptomatic. The most common primary focal epilepsy is ***benign Rolandic epilepsy*** in which epileptiform discharges are seen over the centrotemporal regions especially during sleep.

## EEG IN STATUS EPILEPTICUS

A common reason for ordering an emergency EEG is for the diagnosis and management of status epilepticus (SE). SE may be generalized convulsive status, epilepsia partial's continua or nonconvulsive status (including absence status and complex partial status). Patients with nonconvulsive status present with confusion and rarely coma. Some patients may continue to be obtunded and show epileptform discharges in their EEG even after treatment of generalized convulsive status and are also grouped under subtle or nonconvulsive status.

Nonconvulsive status associated with focal epilepsy is easy to diagnose when there are frequent electrographic focal seizures. However, the ictal EEG pattern in complex partial status may be generalized as in absence epilepsy. Some helpful ***criteria are proposed by Young et al[11]***. In patients who show continuous generalized epileptiform discharges in their EEGs, a rate faster than 3 per second likely represent an ictal pattern. Such discharges at a frequency less than 3 per second are likely to be ictal if significant clinical and/or EEG improvement is seen following small doses of IV lorazepam or diazepam. This type of improvement is most commonly seen in typical absence status. Rhythmic sinusoidal waves of any frequency may represent an ictal pattern if there is an evolving pattern at the onset (increasing amplitude and/or frequency) or a decremental pattern at the termination (decremental amplitude or frequency) or if there is post discharge slowing or attenttation. Reviewing the previous EEG and obtaining follow up EEGs also help to

distinguish between ictal and interictal discharges. A period of repetitive generalized spike wave discharges associated with worsening of sensorium is more likely an absence status, particularly if the previous EEGs or follow-up EEGs display fewer epileptiform abnormalities.

The EEG of patients with subtle SE often shows repetitive discharges including unilateral or bilateral periodic discharges (PLEDs or BiPLEDs) or generalized periodic discharges (PEDs). Some epileptologists feel that this is an intermediary pattern before disappearance of all paroxysmal EEG activity and needs further aggressive treatment[12]. *Refractory SE* is usually treated by pentobarbital, propofol or midazolam infusions and requires continuous bedside EEG monitoring. The dose is regulated to control all clinical and electrographic seizures and to maintain a burst suppression pattern on the EEG.

## EEG IN FOCAL CEREBRAL LESIONS

The use of EEG in localizing focal cerebral lesions has become limited since the advent of computerized tomography and magnetic resonance imaging. However, it is still used to evaluate the epileptogenic potential of a focal lesion. There is slowing and decreased amplitude of the alpha rhythm on the side of the lesion, finally with replacement by slower frequency theta/delta activity[13]. Irregularity in the waveform, slower frequency of waves and persistence indicate a more severe and acute focal process. The process is best localized to the area showing the lowest amplitude. Such focal delta activity can appear transiently after a complex migraine attack or focal epileptic seizure. In such cases, a repeat recording in a few days is indicated to assess persistence of this focal abnormality. The amplitude of the background activity may be paradoxically higher on the side of the focal cerebral lesion [14] as in healed cerebral infarcts, in slowly progressive tumors and after craniotomy. Often this enhanced background activity is slower in frequency and less reactive to eye opening which alert the interpreter to the abnormality. Epileptiform activity such as focal spikes or sharp waves may occur in localized indolent hemispheric lesions. With acute hemispheric lesions, periodic lateralized epileptiform discharges (PLEDs) are seen which occur at one per second over a large area of the hemicranium during most of the EEG study.

## EEG IN PATIENTS WITH DIFFUSE ENCEPHALOPATHIES

The EEG in most encephalopathies shows a diffuse alteration of background activity and varying degrees of slowing. *Focal EEG findings* in a diffuse encephalopathy are seen in some conditions like hyperosmolar nonketotic coma, herpes simplex encephalitis (HSE ) and early Creutzfeldt-jakob disease(CJD). *Periodic patterns* are specifically seen in anoxic encephalopathy and some encephalitidis. *Triphasic waves* and *positive spikes* characteristically occur in metabolic encephalopathies. The EEG findings in most encephalopathies are nonspecific and the main contribution of the EEG[15] in providing an objective measure of severity of encephalopathy, the prognosis and effectiveness of therapy[15].

With increasing severity of encephalopathy there is progressive slowing of the posterior dominant rhythm to theta and then delta activity with decreasing amplitude of the waveform. Some tracings reveal burst suppression pattern with regular alternation of very low amplitude EEG with higher amplitude EEG segments. The most extreme abnormality is electrocerebral inactivity. The latter two patterns carry a grave prognosis unless they are due to drug intoxication in which case they are reversible. To determine the severity of encephalopathy, one must also look for spontaneous variability of the EEG over several seconds to minutes and the reaction to stimulation. An EEG lacking spontaneous variability (invariant EEG) and total lack of reactivity to intense and prolonged stimulation indicates a severe degree of encephalopathy.

Triphasic waves are highly suggestive of a metabolic encephalopathy and are high amplitude, bilaterally synchronous and symmetrical. They consist of a short negative sharp wave, followed by a positive sharp wave and then a long negative slow wave. They are not specific for any particular metabolic encephalopathy[16] and are rarely seen in patients below the age of 20 years. Patients with metabolic encephalopathies showing prominent triphasic waves in their EEG have an overall poor prognosis.

*Excessive beta* activity over the anterior head regions in the EEG is seen with overdose of hypnotic sedative drugs. With more severe intoxication, the fast activity assumes a slower frequency. An alpha coma pattern, burst suppression pattern or electrocerebral inactivity may also be seen but these do not carry as ominous a prognosis as in anoxic encephalopathy[1].

EEG is commonly used to assess the degree of cerebral insult and to judge the prognosis in patients with anoxic encephalopathy. An EEG should be obtained at least 5-6 hours after successful resuscitation since it takes an hour or more for the EEG to stabilize after the episode[17]. Normal or near normal EEGs after an anoxic episode indicate an excellent prognosis. Poor prognosis is indicated by bilateral PLEDs, alpha coma pattern (severe coma with alpha frequency activity and lack of reactivity to sensory stimulation)[18], burst suppression pattern and electrocerebral inactivity.

The EEG is being increasingly employed for *determination of brain death* particularly when organs have to be salvaged for transplantation. It has to be emphasized however, that electrocerebral inactivity is only one of the criteria and should always be considered along with other findings of brain death. The American EEG Society has laid down recommendations for EEG recordings in all cases of suspected brain death[19]. The EEG activity may be obscured by very low amplitude fast activity due to sustained contraction of scalp muscles which can be eliminated by giving a short acting muscle relaxant. A single EEG and at least 12 hours of clinical observation after an unequivocal acute cerebral insult are minimum requirements for diagnosing brain death in any individual older than 1 year. Brain death should not be determined until at least 7 days of age. From 7 days to 2 months, 2 examinations and 2 EEGs separated by at least 48 hours are required; from 2 months to 1 year, 2 examinations and 2 EEGs separated by at least 24 hours are required.

In *viral encephalitis*, the severity of the EEG abnormalities generally parallels the clinical picture[20]. The EEG changes are usually nonspecific with a few exceptions. In HSE, the EEG may show a focus of polymorphic delta activity over a temporal region. The most characteristic feature is the occurrence of PLEDs usually over the more recently involved lobe and between 2-15 days after the onset of the illness. These are pseudo-periodic, focal or unilateral, large amplitude, sharp wave complexes that repeat at regular intervals of 1-3 seconds.

They are not unique for HSE (occurring also with infarcts, abscesses or tumors) but are highly suggestive in the appropriate clinical setting. The EEG in subacute sclerosing panencephalitis (SSPE) is highly specific and shows high amplitude, bilateral synchronous, symmetrical period complexes. They repeat every 4 to 10 seconds and each complex is associated with a clinical myoclonic jerk. In the early stages of the disease, they may occur after long intervals and sleep may active them. A sleep recording is therefore recommended when the awake tracing is normal in a suspected case of SSPE . The characteristic EEG pattern in CJD consists of periodic, bilaterally synchronous bi- or triphasic sharp waves which repeat at a frequency of around one per second.In the early stages, focal periodic sharp waves (PLEDs) may be seen . As in SSPE, each periodic complex is associated with a clinical myoclonic jerk and this EEG pattern in the right clinical setting strongly supports the diagnosis.

## EEG IN NEONATES

In recent years,EEG has been used to evaluate full term or premature neonates due to limitations in performing an adequate neurological examination in newborns[21]. It is an important tool to assess an encephalopathic process or the occurrence of epileptic seizures and to predict neurological outcome. The EEG of a neonate shows distinctive patterns related to the conceptional age and the behavioral state (awake, active sleep and quiet sleep). Some of these neonatal EEG patterns resemble the burst suppression pattern that carries a poor prognosis. However the burst suppression pattern is invariant and not reactive to stimulation unlike the neonatal EEG. Severely abnormal neonatal EEG patterns consist of persistent low voltage tracing, invariant nonreactive burst suppression pattern and the presence of gross asymmetry over the two sides of the head. In neonates, seizures are often characterized clinically by subtle motor behavior and the EEG is indispensable in establishing epileptic activity by demonstrating an associated ictal pattern. This pattern often differs from that in older children and adults and is usually unifocal or multifocal. Interictal epleptiform abnormalities are rarely present to aid in the diagnosis.

Some technical points are important to optimize *neonatal* EEG recordings. The study should be long enough to include both active and quiet sleep. It may be necessary to record the EEG for 45-60 minutes instead of the usual 30 minutes. Non – EEG variables like respiration, extraocular movements, ECG and chin activity should be routinely recorded as they are critical in identifying different states (awake, active or quiet sleep) and in recognizing various artifacts.

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**LONG-TERM FOLLOW-UP ABO-INCOMPATIBLE ADULT LIVING DONOR LIVER TRANSPLANTATION IN CIRRHOTIC PATIENTS** *Matsuno N. et.al.Clin. Transp. 2007,1:229-233*

ABO-incompatible liver transplantation is usually contraindicated. The presence in the recipient of preformed anti-A/B antibodies located on endothelial cells raises the risk of antibody-mediated humoral rejection of the graft. We describe four successful cases of steroid withdrawal in adult patients who had living-donor liver transplantation from ABO-incompatible donors. Antirejection therapy included multiple perioperative plasmapheresis, splenectomy, and a triple immunosuppressive regimen with tacrolimus, methylprednisolone (MPSL), and cyclophosphamide or mycophenolate mofetil (MMF). The maintenance dose of immunosuppression did not differ from that of ABO-identical cases. After transplantation, intrahepatic arterial infusion therapy with prostaglandin E1 (PG E1) was used. As a result, all four patients were able to achieve long-term graft survival without steroid use. They all have good liver function and are leading normal lifestyles. Our experience with these four patients suggests the feasibility of controlling humoral rejection and other complications in adult ABO-incompatible living donor liver transplantations with intrahepatic arterial infusion of PGE1, splenectomy, and plasmapheresis with a regular base of immunosuppression protocol to prevent antibody-mediated humoral rejection.

# MR FEATURES IN A CLASSICAL CASE OF MULTICYSTIC ENCEPHALOMALACIA AND ITS DIFFERENTIAL DIAGNOSIS

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***Abstract :*** *Multicystic encephalomalacia is a pediatric entity and a rare disease in childhood where the brain tissue is substituted by cavities of variable sizes. The cause is the insult to the brain tissue. This disease has a very poor outcome, for this reason early diagnosis is very important. Therefore, we are presenting classical radiological features of multicystic encephalomalacia, its differential diagnosis is also discussed.*

## INTRODUCTION

Encephalomalacia represents the end stage injury to the brain tissue in the late fetal or early neonatal life. It is multifactorial in etiology. It is characterized by fluid filled cavities associated with gliosis. The cavities show internal septations. The multicystic variety is characterized by several such cavities and represents the diffuse insult to the brain tissue. This entity needs to be differentiated from the closely resembling porencephaly and hydranencephaly.

## CASE REPORT

A 6 month old infant presented to our hospital with the complaint that the child is not doing well for few months. Clinical examination of the child revealed delayed milestones, past history, antenatal and perinatal history were unremarkable. Laboratory tests did not reveal any significant abnormality.

The child was referred to the radiology department for evaluation of the brain. Cranial sonography revealed multiple fluid filled cavities with internal septations in both the cerebral hemispheres. Thalami, brainstem and cerebellum appeared normal. Lateral ventricles were dilated.

MR imaging of the brain also revealed multiple fluid filled cavities with internal septations in both the cerebral hemispheres involving primarily the frontal and parietal lobes. The cavities were hypointense on T1W1 and hyperintense on T2W1. Septations appeared isointense on T1W1 and hyointense on T2w1. The cavities did not reveal any significant internal heterogeneity. Thalami, brainstem and posterior fossa were normal. Lateral and third ventricles were dilated with bending of the lateral walls of the lateral ventricles (Figure 1a to 1c)

Based on the above findings, the radiological diagnosis of classical multicystic encephalomalacia was made.

## DISCUSSION

Multicystic encephalomalacia is an irregular cystic area in the brain parenchyma which is the final result of the diffuse brain insult in late gestation, during or after birth[1,2]. There is formation of multiple cystic cavities of variable sizes with multiple glial septatitons in the area of necrosis[2]. It is pathologically characterized by astrocytic proliferation and glial septations in the damaged areas of the brain.

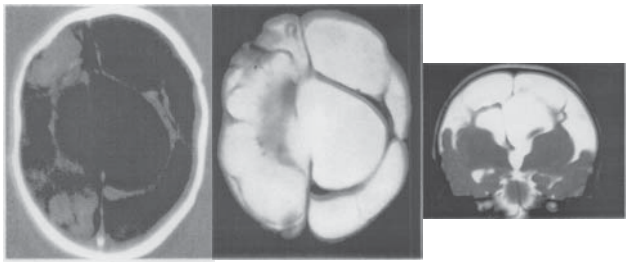

*Figure 1a-1c: Axial T1w1 and axial & coronal T2W MR images show classical features of multicystic encephalomalacia.*

The condition may be caused by infarction, infection or trauma. They may be focal or diffuse and their distribution will depend on the cause and severity of the injury and the post conceptual age of the patient. In cases of embolic or thrombotic insult, the lesions are distributed in the territory of the major cerebral artery. However, if the insult is due to mild to moderate hypotension, the watershed zones intervascular boundary of the cortex and white matter are affected In contrast, when the insult is due to severe hypotension, the entire cortex is affected with sparing of the deep periventricular white matter only. In cases of infection, only the involved region of the brain is necrosed.

Ultrasonography, within one week of the insult shows increased echogenicity in the affected areas with cystic degeneration appearing after 1-4 weeks in term infants[3]. Cranial ultrasonography is the most sensitive modality for detection of the glial septa but it lags behind MR in the overall brain evaluation. In their study, however, orejon de Luna G et al[4] concluded that cerebral ultrasonography is the imaging modality of choice in the evaluation of the multicystic encephalomalacia.

CT initially shows diffuse hypodensity in the affected area which eventually becomes cystic and CSF attenuating. Septations are common and calcification may be seen[1]. CT cannot reliably differentiate between porencephaly and encephalomalacia.

On MR, the affected areas (areas of reactive astrocytosis and the areas of tissue injury) appear hypointense on T1 and hyperintense on T2 paralleling fluid[3]. All patients have cortical thinning, white matter destruction, atrophy and gliosis. Basal

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ganglia or cerebellar involvement may be seen MR imaging. Microencephaly and spastic tetraplegia develops mostly in patients with diffuse involvement, whereas hemiplegia in patients with asymmetric involvement. The clinical outcome is worse in patients with cerebellar and brainstem involvement. Therefore, the symmetry of lesions and cerebellar or brainstem involvement might be used as a prognostic indicators[5].

The important differential diagnosis of multicystic encephalomalacia is porencephaly and hydranencephaly.

Porencephaly refers to focal cavities with smooth but shaggy walls and minimal surrounding glial reaction[1,2,7]. To differentiate it from schiencephaly (also known as agenetic porencephaly), it is often referred to as encephaloclastic porencephaly. The latter is the result of insult to the area of brain in late gestation, perinatal or postnantal period[1,8,9].

On imaging, encephaloclastic porencephaly appears as smooth walled cavities that the isointense to CSF on all sequences. The cavities are devoid of internal features as septae and the surrounding brain is of normal signal intensity (figure 2).

*Figure 2: Axial T2W MR images shows a large porencephalic cyst in the left cerebral hemisphere.*

Hydranencephaly is a condition in which most of the brain mantle has been damaged liquefied and resorbed[10] and can be considered as porencephaly of the nearly the entire brain. Thin walled sacs containing CSF lined by leptomeninges replace the cerebral hemispheres[1,2]. Multiple causes have been advocated including vascular and infectious (toxoplasmosis and CMV).

Clinically, the head may be normal small or large in size. The child is always mentally retarded.

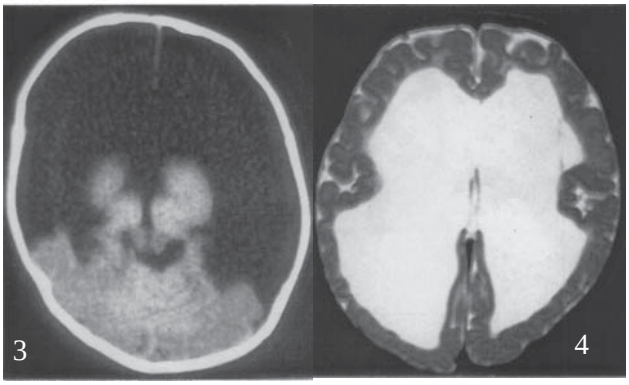


*Figure 3: Axial CT image shows a classical case of hydranencephaly with relative sparing of thalami and cerebellum.*

*Figure 4: axial T2W MR image shows dilated lateral ventricles surrounding by cortical mantle in a case of hydrocephalus.*

On imaging, the cerebral hemispheres are nearly completely replaced by CSF[1,6]. The thalami are usually preserved. The inferior and medal aspects of the frontal and temporal lobes may also be preserved. The brainstem is usually atrophic. The cerebellum is almost always normal (figure 3). Hydranencephaly, sometimes, has to be differentiated from severe hydrocephalus. There is a thin rim of cerebral tissue around the dilated ventricle than can usually be identified only on MR imaging (figure 4).

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***Next Issue Highlights***

***Editorial : Screening for Breast Cancer: Finding an Indian Solution !***

***Organ phosphorus Poisoning - An update***

***Current Therapy of HIV/HIDS***

***Symposium : Interventional Gastroenterology***

# UNUSUAL CLINICAL PRESENTATION OF NERUROCYSTICERCOSIS – A REPORT OF 3 CASES

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***Abstract :*** *Neurocysticercosis is one of the common parasitic diseases of central nervous system with variable clinical presentation. Brainstem is infrequently involved in patients with neyrocysticercosis. Usually it occurs in association with disseminated form of neurocysticercosis. We are reporting three cases who had large isolated cysticercus lesions in brainstem which presented as acute neurological syndrome. The diagnosis of neurocysticercosis was established by the presence of characteristic granulomatous intraxial lesions in the brainstem along with strongly positive ELISA for cysticercal antigen in cerebrospinal fluid as well as in serum. All the three patients responded well to corticosteroids and albendazole. Repeat CT scan showed significant alteration in size of the lesion.*

## INTRODUCTION

Neurocysticercosis is the most common parasitic disease of the central nervous system (CNS). It occurs when man becomes the intermediate host of Taenia solium and harbours the larval form, Cysticercus cellulosae. They have special predilection for the central nervous system, skin, skeletal muscle and the eyes. It is most common in the Indian subcontinent, Central and South America, Spain and Eastern Europe[1] .Its incidence is rising in the non endemic areas because of rising rates of immigration from endemic countires[2]. Clinical manifestations of the disease are varied and depend upon topography, number, and size of the lesions, as well as status of host's inflammatory reaction against the parasite. In brain, the common sites of involvement are cerebral parenchyma, meninges and ventricles. Brainstem and cerebellum are infrequently affected, and are usually part of disseminated form of cysticercosis. We report here 3 cases of isolated cysticercus lesions in brainstem who had acute presentation.

## CASE 1

A – 22 year old right =handed man presented with three days history of headache followed by drooping of left eyelid. There was no history of vomiting, blurring of vision, fever or trauma. On examination patient was normotensive general physical & musculoskeletal examination was unremarkable. Neurological examination was normal except left sided partial ptosis with unilateral dilated pupil which was sluggishly reactive to light, & there was restriction of adduction in left eye.

Routine Investigations like hemogram, blood sugar and other biochemistry were normal .X-ray of chest and soft tissues of thigh did not reveal any abnormality. ELISA for cysticercal antigen in CSF and serum was positive. Serological tests for tuberculosis and HIV were negative. C.T. scan brain showed a ring enhancing lesion in the left mid brain with hyperdense nodule within it and perilesional edema (fig. 1). M.R.I. brain confirmed it to be cysticercus lesion.

The patient was primed with oral steroids (Prednisolone 40 mg per day) & received albendazole (15 mg/kg/day). The neurological deficit started improving within seven days of treatment and complete recovery was seen after 15 days of treatment. Follow up CT scan after eight weeks showed complete resolution of lesion (Fig. 2).

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*Fig.1: Ring enhancing lesion in left mid brain.*

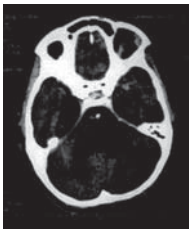

*Fig. 2 : Resolution of the lesion.*

## CASE 2

A-9 year old right handed child presented with one day history of headache followed by drooping of right eyelid. There was no history suggestive of fever or raised intracranial pressure. General physical & neurological examination was unremarkable except right sided ptosis with dilated pupil which was sluggishly reactive to light. Routine hemogram and blood chemistry was normal and ELISA for cysticercal antigen in CSF and serum was positive C.T. scan brain showed a ring enhancing lesion in the right mid brain with hyperdense nodule within it and perilesional edema. M.R.I brain also confirmed, the cysticercal lesion. Similarly this patient was also primed with steriods & given albendazole. He had complete recovery withih 3 weeks. Follow up CT after six weeks showed complete resolution of lesion.

## CASE 3

A 18year old right-handed female presented with two days history of headache followed by deviation of angle of mouth

toward right side, along with restriction of lateral movement of left eye. there was no history suggestive of fever or raised intracranial pressure. General physical examination was unremarkable & neurological examination revealed left lower motor neuron type of seventh nerve palsy along with left sixth nerve palsy. Routine hemogram & blood chemistry was normal & ELISA for cysticercal angtigen in CSF and serum was positive. C.T. scan brain showed a ring enhancing lesion in the left pons with hyperdense nodule within it and perilesional edema (Fig.3). MRI brain also confirmed, the cysticercal lesion.

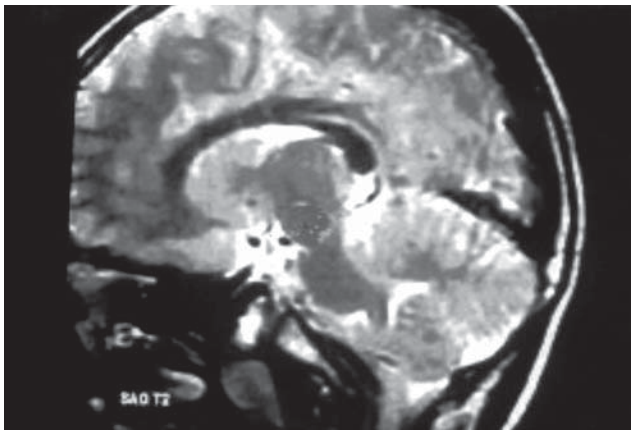


*Fig.3: Ring enhancing lesion in pons.*

The patient was put on oral steroids with albendazole. They neurological deficit started improving within two weeks of treatment and follow up CT scan after eight weeks showed complete resolution of lesion (Fig.4).

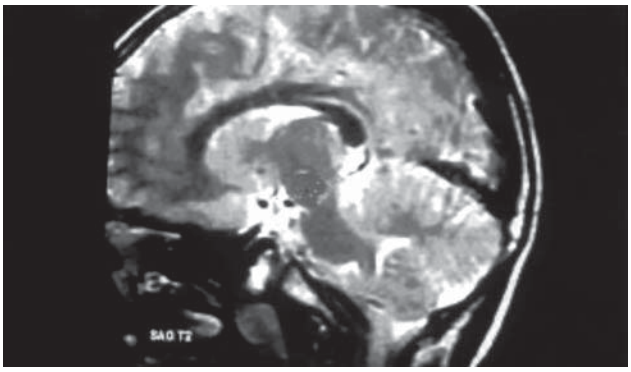


*Fig.4: Resolution of the lesion*

## DISCUSSION

Cysticercosis, caused by taenia, is mainly a disease of gastrointestinal tract that is found predominantly in the third world countries. Ramamurthi and Balasubramanian[3] found the incidence if cysticercosis to be 1.25% of all intracranial space occupying lesion in south India. Wani et al[4] reported an incidence of 2.5% among space occupying lesion. The common clinical features are seizures, raised intracranial tension and dementia. Uncommon presentation like pure motor hemiparesis,ataxic hemiparasis, homonymous hemianopia, cerebellopontine angle syndrome. Painful cervical radiculopathy have been reported in literature[5,6,7.]

Focal neurological deficit is because of involvement of arterial system in subarachniodal from the disease. The literature survey revealed involvement of brainstem along with multiple intracebral lesions[8]. However, there are few documented cases of solitary lesion in the brainstem[9,10,11,12]. The possible mechanism for deficit in these patients may be the lesion itself and the perilesional edema. The rapid improvement could be because of reduction inperilesional edema. The diagnosis of NCC by clinical features alone is difficult because of the varied clinical presentation. the neuroradiological features depends upon the stage of disease. The diagnosis in our cases are based on clinical data, neuroradiological features finding of specific antigen in CSF. The other common causes of acute cranial nerve palsies like diabetes mellitus, vasculitis due to intracranial infections and vascular aneurysms were ruled out. Immunoassays like ELISA and Western blot techniques are more often used these days as an adjuvant in the diagnosis because they are more specific. Purpose of our case reports is to make physicians /neurologist aware of these uncommon presentation of a treatable disease like cysticersosis so that a correct diagnosis can be made especially in tropical countries where diagnostic facilities are limited because of a paucity of resources.

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***ERRATA*** ***The name of Prof. N.S. Neki, Professor of Medicine Government Medical College, Amritsar has been inadvertently missed in the list of peer reviewers published in October-December 2007 issue page 316. Prof. Neki has peer reviewed several articles in the quarterly issues of the year 2007.***

***Error is regretted.***

***Editor***

# DIAGNOSTIC CHALLENGES IN CEREBROSPINAL FLUID ANALYSIS

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***Abstract :*** *The brain is surroundded and enclosed by a large volume of fluid known as cerebrospinal fluid (CSF). CSF is very vital as it gives important information about bleeding, in flammation and infection in brain, which is not available by other methods. the description of patterns of CSF data cannot, of course, yield a definitive diagnosis in the absence of clinical information. Nevertheless, in contrast to single variable analysis of patterns, it can yield answers to clinical questions that aid differential diagnosis, suggestions for further specific analysis and sensitive controls for analysis. Innovative approaches to treatment of diagnostically challenging neurological diseases are being widely tested. All the currently available measurements, including CSF cytology, biochemistry, immunology and molecular markers suffer from poor sensitivity and specificity and often correlate poorly with each other. Thus, the need of the hour is a better understanding of not only the CSF but the newer diagnostic challenges posed and strategizing future diagnostics against all the challenges faced.*

The brain and spinal cord are subjected to a varied number of physical processes quite different from those faced by other organs in the body as they lie in rigid body compartments of the skull and spinal canal. These physical processes depend on the fact that the brain is surrounded by and enclosed in a large volume of a fluid known as Cerebro Spinal Fluid (CSF). The analysis of CSF is very vital as it gives important information about bleeding, inflammation and infection in the brain, which is not available by other methods.

The description of patterns of CSF data cannot, of course, yield a definitive diagnosis in the absence of clinical information. Nevertheless, in contrast to single estimation variable analysis, the analysis of patterns can yield answers to clinical questions that aid differential diagnosis, and provides clue to suggestions for further specific analysis and sensitive controls for analysis (part of analytical quality assessment). CSF analysis can give detailed information about differentiation between acute inflammatory processes (viral v/s bacterial meningitis, encephalitis), detection of micro organisms (as cause of an inflammatory process), detection of an intracranial hemorrhage, early detection of a chronic inflammatory process or a polyspecific immune response, early detection of a post surgery infection, organic cause of psychiatric symptoms, differential diagnosis of dementia, detection of tumors or for efficiency of therapy.

All parts of the nervous system may be involved by infection: muscles (infectious polymyositis due to trichinosis, cysticercosis, certain viral infections), peripheral nerves (mononeuritis or mononenuritis multiplex due to leprosy, borreliosis), plexus ( post infectious or post-vaccinnial Parsonage-Turner syndrome) spinal and/or cranial roots (radiculitis with or without associated meningitis i.e. menigo-radiculitis due to neuroborreliosis, varicella zoster, herpes simplex type 2, HIV, schistosomiasis), meninges (bacterial, viral, fungal, spirochetal meningitis), spinal cord (myelitis due to herpes viruses, HIV, HTLV-1, Mycoplama pneumoniae,Toxocara), cerebellum (post infectious cerebellitis due to varicella zoster), brain stem (rhombencephalitis) and the brain (encephalitis). The involvement of the brain also maybe diffuse or focal as in brain abscesses or in herpetic encephalitis.

Once the topographic diagnosis is made, the etiologic diagnosis will rely on blood analysis (inflammatory markers, leucocytosis, eosinophilia, serology), CSF analysis (pleocytosis, culture, PCR, intrathecal immune response), imaging of the target organ and in some cases, nerve or brain biopsy. Routine cerebrospinal fluid analysis includes estimation of total protein, albumin, immunoglobulins, glucose, lactate, cell count, cytological staining, bacterial culture and sensitivity and C reactive protein.

Changes in volume of blood, CSF or brain compartments produces compensatory changes in the other compartiments which results in increased CSF pressure. Physiology explaining rise in CSF pressure in various diseases is: increased tissue volume in brain tumor and abscess, increased blood volume in hypercapnia, hypoxia and venous sinus occlusion, cytotocic oedema in ischemia, trauma, toxins and metabolic diseases, vasogenic oedema in infection, brain tumours and inflammation and interstitial oedema in hydrocephalus with transependymal flow.

## CSF CYTOLOGY

The timely detection of meningococcal meningitis epidemics is crucial, lowering the meningitis threshold obviously being necessary. Prevention strategies should be initiated as quickly as possible, full coverage of serogroup A (and W 135); a serogroup A containing meningococcal conjugate vaccine being one of the three highest priorities for new vaccine development. Nevertheless, bacterial meningitis can be diagnosed and treated even in rural areas employing simple diagnostic methods, the lack of laboratory facilities forcing the medical community to such simple methods as CSF turbidity, CSF leukocyte count or CSF- serum glucose ratio.

Usual CSF **cytological findings** in various different types of meningitis are – *acute bacterial meningitis* several hundreds,

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usually a few thousand but occasionally less than 100 cell seen, polymorphonuclear cells predominating; *Tuberculous meningitis* 25-100, rarely more than 500 cells, *Cryptococcal meningitis* 0-800 cells, average 50 with lymphocytic predominance: *viral meningitis* 5 to few hundred, lymphocytic predominance but there may be more than 80% polymorphs in the first few days; *Syphilitic meningitis* average of 500 cells, usually lymphocytes, rarely polymorphs. *Cysticercosis meningitis* has an increased mononuclear and polymorphoneuclear cellular infiltration with 2-7% eosinophils; *Sarcoid meningitis* has 0 to fewer than 100 mononuclear cells; *Tumour* - 0 to several hundred mononuclear cells & malignant cells. Pleocytosis is also seen in various other diseases like *brain infarction, subarachnoid bleed, cerebral vasculitis, acute demyelination* and *brain tumours.*

## CSF IN TOTAL PROTEINS

Total protein level of CSF ranges between 15-50mg/dl. While an elevated protein level lacks specificity, it is an index of neurological disease reflecting a pathological increase in permeability of endothelial cells. Increase in protein level to 5g/dl and above is seen in meningitis, blood stained CSF, and cord tumors with spinal block. Polyneuritis (Guillain barre syndrome), diabetic radiculopathy and myxoedema may increase level to 1 to 3 g/dl. Levels below 0.15g/dl occur most often with CSF leaks due to previous lumbar puncture or traumatic dural fistulas.

## CSF GLUCOSE

Concentration of glucose in CSF depends on its concentration in the blood. Normal range of glucose concentration in CSF is between 2-5 and 4.5mmol/l in patients with normal blood glucose level. Hyperglycemia 4 hours prior to lumbar puncture results in parallel increase in CSF glucose. Decreased CSF glucose level is characteristic of acute purulent meningitits and is the usual finding in tuberculous and fungal meningitits; it is normal in viral meningitis, although reduced to 25% in mumps cases, and in some cases of herpes simplex and zoster meningoencephaitis. CSF glucose also decreases in other inflammatory meningitis including cysticercosis, amoebic meningitis, acute syphilic meningitis, granulomatous arteritis and other vasculitis.

## MICROBIOLOGICAL AND SEROLOGICAL REACTION

Use of appropriate stains and cultures is essential in cases of suspected infection. DNA amplification techniques using the polymerase chain reaction have improved diagnostic sensitivity.

## DIAGNOSIS OF VARIOUS NEUROLOGICAL DISEASES ON THE BASIS OF CSF EXAMINATION

### *Bacterial meningitis*

A prolonged increase of glutamate levels in the CSF may predict poor clinical outcome in patients with bacterial meningitis, possibly because of the sustained neurotoxic effects of this excitatory neurotransmitter. CSF cortisol levels in patients with bacterial meningitis are highly elevated and correlate with disease severity. Moreover, our findings also suggest that intrathecal cortisol may serve as a valuable marker in discriminating between bacterial and aseptic meningitis. Bacterial meningitis is a severe, comparatively frequent disease especially in tropical countries. The causative agent is usually identified by culture, which takes one or two days. Since the prognosis of the patient depends on the early onset of an apt therapy a more rapid diagnosis is highly desirable. Fluorescence in situ hybridization (FISH) is a quick test used for the diagnosis of bacterial meningitis. FISH allows specific visualization of bacteria by the fluorescent microscope by implementing fluorescently marked probes, which hybridize to specific complementary sequences on the bacterial ribosomal RNA. FISH has recently been introduced for the quick detection ( 3 hours) of pathogens directly in clinical samples like blood cultures, sputa and pyloric biopsies.

### *Neoplastic meningitis*

CSF cytology is used as a diagnostic gold standard for neoplastic meningitis Positive CSF cytology and the presence of multifocal neurological deficits are compatible with the diagnosis of neoplastic meningitis.

Serious doubt about the validity and reliability of the technique have recently been raised. Whereas, false-positive studies are rare or nonexistent in cases of solid tumour neoplastic meningitis; false-negative results are common, particularly when small CSF volumes (<10 $cm^3$ )are submitted,or when specimens are not processed by the cytology laboratory immediately, when CSF is obtained from a site distant from the location of active CSF disease (i.e., from the lumbar region in patients with cranial nerve or cerebral signs and symptoms or from a ventricular reservoir in patients with predominantly spinal disease), or when a second CSF specimen is not obtained after an initial specimen is cytologically negative.

### *Multiple sclerosis*

Increased CSF Ig (predominantly IgG but IgM and IgA may also increase) is found in more than 90% patients of multiple sclerosis. Linked to the elevation of IgG is the finding of oligoclonal bands in the cathodal region of electrophoresis CSF osteopontin levels are higher in patients with active disease.

### *Syphilis*

CSF examination is recommended in patients with syphilis with ophthalmic symptoms. CSF mononuclear pleocytosis (more than 5 cells per vol.) and increased protein support the

diagnosis of neurosyphilis. CSF-VDRL is more sensitive in meningovascular syphilis than asymptomatic neurosyphilis and tabes dorsalis. False positive CSF-VDRL may also occur if blood contaminates CSF as it occurs in a traumatic lumbar puncture.

### *CNS viral infections*

CSF by PCR is virtually diagnostic of viral CNS infection (in asymptomatic immunocompetent individuals the CSF does not amplify viral nucleic acid). False positive tests are very rare when the test is performed by a reliable laboratory.

### *Acute poliomyelitis*

CSF shows pleocytosis polymorphonuclear cells predominating during the acute stage. CSF protein is mild to moderately increased. CSF polio virus specific IgM antibody test enables an accurate immunological diagnosis.

### *Cerebral malaria*

Protozoan infections like malaria and African trypanosomiasis are major killers in tropical countries. Every year, more than 1 million people, primarily children, die from malaria due to severe anaemia, multi-organ system failure or cerebral complications Cerebrospinal fluid analysis has diagnostic and prognostic values which are routinely applied for trypanosomiasis, but not for cerebral malaria. The use of toxic drugs in trypanosomiasis emphasises the need for standardized criteria to determine CNS involvement in this disease. However, in cerebral malaria, clinical diagnosis is not specific enough, leading to false diagnosis and over diagnosis. Systematic lumbar puncture and standardized data collection could improve treatment strategies in both diseases. In children with cerebral malaria, central nervous system TNF alpha production is associated with subsequent neurologic and cognitive morbidity.

### *Creutzfeldt- Jacob disease*

Creutzfeldt-Jakob disease (CJD) is a spongiform encephalopathy that affects about 1 in $10^6$ inhabitants per year. In 1994, a variant of CJD (vCJD) was described in the United Kingdom; further studies are indicated to establish causal relation with bovine spongiform encephalopathy (BSE). In a recent WHO publication a call has been made for addressing surveillance and diagnosis of not only BSE but also CJD and vCJD in Third world countries. To assist the clinical diagnosis of CJD and vCJD various cerebrospinal fluid (CSF) biomarkers are available.

The 14-3-3 protein assay involves Western blot followed by immunodetection. A commercial ELISA is used to measure tau and amyloid-beta in CSF. Transport conditions of the CSF samples have no effect on the detection of the biomarkers. Elevation of IgG to total CSF protein ratio, sometimes with oligoclonal bands has been reported to occur in up to 20% cases. Immunoassays that detect the class of 14-3-3 proteinase inhibitor proteins released into CSF from damaged neurons have proved extremely useful in diagnosis in difficult cases.

### *Alzheimer's disease*

CSF pressure, cell count, sugar and protein are with in normal limits. Presence of Ubiquitin and tau protein levels in CSF have been reported to be raised in Alzheimers disease, also the level of A Beta 4 are reduced and of this in combination with tau has been suggested as a diagnostic marker.

### *Acquired immunodeficiency syndrome (AIDS)*

Central nervous system (CNS) opportunistic complications in patients with HIV infection include CNS toxoplasmosis, cryptococcal and tuberculous meningitis, cytomegalovirus (CMV), herpes encephalitis, and progressive multifocal leuco-encephalopathy (PML). Some of these conditions can be diagnosed relatively easily by the examination of the cerebrospinal fluid (CSF) such as cryptococcal meningitis. For other conditions, CSF findings may suggest the diagnosis such as in the case of tuberculous meningitis. In the presence of CNS toxoplasmosis with cerebral oedema surrounding the lesions; performing a spinal tap is contraindicated.

The interpretation of CSF findings in those with HIV infection is complicated by the fact that HIV itself may cause CSF abnormalities, even in the absence of HIV encephalitis or AIDS dementia complex. CNS tuberculosis generally occurs in patients with still a relatively good immune function (CD4 count less than 350), while all other opportunistic infections only occur at very low CD4 count: CNS toxoplasmosis (less than 100), cryptococcal meningitis (less than 100), CMV encephalitis (less than 00) and PML (less than 50).

### *Human African Trypanosomiasis(HAT)*

The detection of trypanosomes in blood, lymphatic gland juice and/or cerebrospinal fluid, remains the unique and certain criterium of human African trypanosomiasis diagnosis. However, the study of CSF modifications is necessary to establish and assess efficacious treatment. The white blood cells count (WBC) and protein level are used as an indicators to determine the in CSF stage of the disease and evaluate the efficacy of treatment.

### *Neuroborreliosis*

A combination of basic CSF variables and Borrelia burgdorferi (Bb) specific IgG and IgM antibody index (AI) values are used for the diagnosis of early neuroborreliosis. Combined analysis of Bb-specific Al values and basic CSF variables give the highest sensitivity of 80% and specificity of 98%.

### *Lymes disease*

Presence of CSF pleocytosis and PCR testing of CSF are helpful in diagnosis.

### *Rhinocerebral mucormycosis*

It is a severe opportunistic infection caused by moulds belonging to the *mucoraceae* family. These organisms are saprophytic in the respiratory and digestive tracts in 2% of normal individuals. However, conditions such as diabetes mellitus, hematological cancers, renal insufficiency, organ transplantation and chemotherapy can predispose to disease. The CSF analysis shows pleocytosis and high concentration of protein.

### *Paracoccidioidomycosis (PCM)*

It is a chronic granulomatous infectious disease, endemic in

subtropical areas of Central and South America. The diagnosis of the central nervous system (CNS) involvement with paracoccidioidomycosis is frequently difficult. A definitive diagnosis is usually made by the isolation of the P. brasiliensis from CNS biopsy or necropsy material. The presence of antibodies anti-gp43 in CSF of patients with CNS involvement in PCM may indicate disease.

### *Guillain barre syndrome*

In the first week of neurological symptoms the CSF protein may be normal but then becomes elevated on subsequent examination. In 10% cases, CSF protein remains normal throughout the illness. Transient oligoclonal IgG bands and elevated myelin basic protein may be detected in some patients.

### *Subarachnoid hemorrhage*

Cerebrospinal fluid adrenomedullin concentration correlates with hyponatremia and delayed ischemic neurological deficits after subarachnoid hemorrhage.

### *Dementia*

Measuring proteins in cerebrospinal fluid (CSF) has gained wide acceptance for the differential diagnosis of dementia. Median Abeta 42 level increases in dementia and decreases in Alzheimers. S-100B protein increases during follow-up in both the diseases.

### *Neurocysticercosis(NCC)*

It is a parasitic disease of the nervous system caused by the larva of taenia solium. The diseasis is an important public health problem in developing countries. The diagnostic criteria for NCC are related to the clinical and epidemiological data , neuroimaging studies and the reactivity of immunosorbent assay (ELISA) for NCC in the serum and CSF.

## CONCLUSION

Innovative approaches to treatment of diagnostically challenging neurological diseases are being widely tested. Unfortunately ,research on diagnostic strategies and outcome measures on which any advances in treatment ultimately depends, has not been avidly pursued. All the currently available measurements, including CSF cytology, biochemistry, immunology and molecular markers suffer from poor sensitivity and specificity and often correlate poorly with each other. Although CSF cytological examination, performed according to a rigorous, research supported –protocol, may be the optimum diagnostic and outcome measure at this time, additional research is a prerequisite for any further advances in the diagnosis of challenging CSF's.

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### *Drug Profile*

***VORICONAZOLE***

***Voriconazole*** is a triazole antifungal agent, chemically, it is designated as (2R,3S)-2(2,4-diffuorophenyl)-3-(5-fluoro-4-pyrimidinyl)-1(1H-1,2,4- triazol-1-yl)-2-butanol.

***Indications:*** The Drug is indicated for use in the treatment of . (a) invasive aspergillosis; (b) fluconazole- resistant serious invasive candida infections (including C. Krusel); (c)esophageal candidiasis; (d) Serious fungal infections caused by scedosporim apiosermum (a sexual form of pseudallescheria boydia)

***Mecanism of Action*** : Voriconazole is a triazole antifungal agent; its primary mode of action is by inhibition of fungal Cytochrome P-450-mediated 14 alpha-alamosterol demethylation - an essential step in fungal ergosterol biosynthesis. The accumulation of 14 alpha-methyl sterols correlates with the subsequent loss of ergosterol in the fungal cell wall and may be responsible for the antifungal activity of voriconazole. The drug has been shown to be more selective for fungal cytochrome P- 450 enzymes than for various mammalian cytochrome p-450 enzyme systems.

***Dosage and Administration***: The pharmacokinetics of orally administered voriconazole is not affected by renal impairment. Therefore, no adjustment is necessary for oral dosing for patients with mild to severe renal impairment.

Table 1 A: Recommended Dosing Regimen in Adults and Adolescents (12 to 16 years of age)

| Dose Regimen | Intravenous | Oral (tablets) | |
|---|---|---|---|
| | | Patients 40 Kg and above | Patients less than 40 Kg |
| Loading Dose (for the first 24 hrs) | 6 mg/kg every 12 hrs | 400 mg every 12 hrs. | 200 mg every 12 hrs. |
| Maintenance Dose (after first 24 hrs) | 4 mg/kg twice daily | 200 mg twice daily | 100 mg twice daily |

Voriconazole is haemodialysed with a clearance of 121 ml/min. A four hour haemodialysis session does not remove a sufficient amount of Voriconazole to warrant dose adjustment.After intravenous administration, cyclodextrin can accumulate in the kidneys, unlike after oral administration. Accumulation of the intravenous vehicle, hydroxypropyl B cyclodextrin may occurs in patients with moderate or severe renal insufficiency ( creatinine clearance <50 mL/min). Oral voriconazole should be administered to these patients, unless an assessment of the benefit/risk to the patient, justifies the use of intravenous voriconazole. Serum creatinine levels should be closely monitored in these patient, and if increase occurs, consideration should be given to changing to oral voriconazole therapy.

***Precautions***: (1) Pregnancy- teratogenic effects on the foetus. (2) Women of childbearing potential should use effective contraception with increased dose during co- administration of voriconazole with oral contraceptive. (3) The excretion of voriconazole in breast milk has not been investigated. Voriconazole should not be used by nursing mothers unless the benefit clearly out weights the risk.

***Undesirable Effects*** : The most frequently reported adverse events in the therapeutic trials include fever, rash, vomiting, nausea, diarrhoea, headache, sepsis, peripheral edema, abdominal pain and respiratory disorder. The treatment- related adverse events which may often need discontinuation of voriconazole therapy include (i) elevated liver emzymes, (ii) rash, (iii) visual disturbances .(colour vision change, photophobia, decrease in visual field– 20% cases). (iv) dematological reaction like photosensitivity.

# VIRAL ENCEPHALITIS: IMAGING FEATURES

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***Abstract :*** *Encephalitis commonly referred to as brain fever, implies inflammation of the brain. Since meningeal inflammation often accompanies this inflammatory process, term meningoencephalitis is sometimes used. Symptoms of encephalitis include sudden fever, headache, vomiting, weak muscles, impaired judgement and irritability. Encephalitis is usually caused by viral infection of the brain tissue but can also be caused by other factors such as exposure to certain bacteria, fungi, parasites, harmful chemicals or heavy metal poisoning. Herpes simplex encephalitis (HSE) is the commonest sporadic acute viral encephalitis all over the world. With few exceptions (for example, HSE), no specific therapy is available for most forms of viral encephalitis. The brain damage caused by acute encephalitis is due to a combination of intracellular viral growth and the host inflammatory response. Acute viral encephalitis is caused by direct viral infection of neural cells with associated perivascular inflammation and destruction of gray matter. Acute encephalitis constitutes a medical emergency. Early diagnosis is important for appropriate management. Magnetic resonance imaging of brain is the investigation of choice and the diagnosis may be confirmed by the polymerase chain reaction test for the virus in the cerebrospinal fluid. Mortality and morbidity may be high and long term sequelae are known among survivors. The emergence of some of the zoonotic encephalitis like Japanese encephalitis and Dengu encephalitis have posed an important public health problem in India. Encephalitis resulting from viral infection manifests as either acute viral encephalitis or postinfectious encephalomyelitis. Postinfectious encephalomyelitis follows infection with various viral or bacterial agents; the primary pathologic finding is demyelination of white matter, a non-infective inflammatory encephalitis that may require to be treated with steroids. In emergency cases, the presence of focal neurological signs and focal seizures will distinguish encephalitis from encephalopathy.*

***Keywords****: Viral, Encephalitis, Imaging, MRI, CT*

## VIRAL CAUSES

More than 100 different viruses can cause acute encephalitis. In India the most frequently reported causes are herpes simplex virus type 1 (HSV-1), arthropod-borne viruses (arboviruses) like Japenese encephalitis, Dengue, and Rabies caused by animal bites. In children herpes simplex virus type 2 (HSV-2), cytomegalovirus and measles are common sources of encephalitis. HIV is a common cause in all age groups.

**Table 1.** ***Common viral causes of acute encephalitis in India***[1]

| Cause | Characteristics of infection |
|---|---|
| Herpes simplex virus type 1 | Common year-round; commonest cause of sporac encephalitis in adults |
| Herpes simplex virus type 2 | Common year-round; commonest cause of sporac encephalitis in infants and children |
| Cytomegalovirus | Affects primarily immunosuppressed persons, particula children |
| HIV | Occurs year-round; affects all age groups |
| Measles | Occurs in winter and spring; commonly children |
| Japanese Encephalitis | Occur in summer; all age groups |
| Dengue | Occcur in winter; all age groups |
| Rabies | Occurs year-round; all age groups |
| Mumps | Occurs in winter and spring; parotitis, orchitis, common children |
| Rubella | Occurs in winter and spring; rash, lymphadenopatl common in children |
| Varicella | Chickenpox or herpes zoster; all age groups |

## OTHER DIAGNOSTIC CONSIDERATIONS

Differential diagnosis of encephalitis encompasses a large number of viruses as well as nonviral pathogens and noninfectious causes (table 2).

Patients with bacterial infection of the CNS usually appear more acutely ill than those with viral infection. However, meningitis caused by Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenzae type b may be insidious in onset. CNS infection caused by less virulent bacteria, such as Mycobacterium tuberculosis, Treponema pallidum, Borrelia burgdorferi, Bartonella henselae (cat-scratch disease) and Bartonella quintana also may be clinically indolent. Parameningeal bacterial infections (e.g., brain abscess, subdural empyema) may have features similar to those of viral CNS infections.

Other sources of encephalitis include noninfectious disorders such as metabolic derangement (e.g., hypoglycemia, electrolyte disturbances, uremia, hepatic encephalopathy, inborn errors

**Table 2.** ***Nonviral and noninfectious causes of encephalitis***

Bacterial
Bartonella henselae
Bartonella quintana
Borrelia burgdorferi
Brucella species
Leptospira interrogans
Listeria monocytogenes
Mycobacterium tuberculosis
Mycoplasma pneumoniae
Rickettsia rickettsii
Treponema pallidum
Brain abscess or subdural empyema
Partially treated bacterial meningitis

Protozoal
Naegleria fowleri
Acanthamoeba species
Cysticercosis
Echinococcus species
Plasmodium falciparum
Trypanosoma species

Fungal
Blastomycosis
Coccidioidomycosis
Cryptococcosis
Histoplasmosis

Noninfectious
Central nervous system hemorrhage
Collagen vascular disease
Exposure to certain toxins or drugs
Inborn errors of metabolism
Malignant disease

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## TABLE – 3 IMAGING FEATURES OF ENCEPHALITIS

| S. No. | Type Of Infection | Location | T1 ↓=Hypointense ↑=Hyperintense | T2/FLAIR ↓=Hypointense ↑=Hyperintense | T1+C | Diffusion Restriction | T2* GRE | MRS ↓=decreased ↑=increased | Comments |
|---|---|---|---|---|---|---|---|---|---|
| 1 | HSV-1 | Limbic System (Temporal & Inferior Frontal Lobes) | ↓ | ↑ | + | + | + | ↓NAA/Cr ↑Cho/Cr | Involvement may initially appear unilateral but is typically followed by less severe contralateral disease. This 'sequential bilaterally' is highly suggestive of herpes encephalitis |
| 2 | HSV-2 | Diffuse & Nonfocal involvement, Initially periventnicular white matter withrelative sparing of the basal ganglia, thalami, and posterior fossa structures | ↓ | ↑ | + | + | - | nonspecific | No predilection to temporal & frontal lobes unlike HSV-1,Disease may progress to parenchymal calcification & cystic encephalomalacia |
| 3 | CMV | Periventricular White Matter | ↓ | ↑ | + | + | - | nonspecific | Subependymal enhancement is an infrequent finding but, if present, is a valuable diagnostic due |
| 4 | Measles(SSPE) | Posterior parietal, occipital and temporal regions, basal ganglia, corona radiata and subcortical and deep white matter | ↓ | ↑ | - | - | - | nonspecific | Nonspecific involvement in Acute & Subacute Measles Encephalitis<br><br>Basal ganglion involvement is noted in patients of SSPE who have severe disease and of longer duration |
| 5 | Varicella | Multifocal Areas of Cortex | ↓ | ↑ | -/+ | + | - | nonspecific | A highly contagious disease with a generalized skin eruption; it usually occurs in childhood and is usually of little consequence in healthy children. However, may cause more serious disease, including encephalitis,in immunocompmomised patients |
| 6 | Zoster | Brainstem/cortical GM, cranial nerves | ↓ | ↑ | -/+ | + | - | nonspecific | Represents a reactivation of a latent varicella-zoster virus infection, usually in adulthood. can may have several CNS manifestations. Can be the causative agent in encephalitis, neuritis, and myelitis; it typically appears in patients with the characteristic skin eruption (shingles) |
| 7 | JE | Bilateral thalami, brainstem, cerebellum spinal cord, cerebral cortex | ↓ | ↑ | + | + | + | Absent NAA +Lactate +Choline +Creatinine | In a patient presenting with encephalitic illness from an endemic zone of JE with demonstration of lesions in the basal ganglia, thalami and brainstem should help in differentiating JE from atypical HSE. |
| 8 | Rabies | Brainstem, hippocampi, hypothalamus , WM, GM. | ↓ | ↑ | -/+ | + | - | nonspecific | T1-Hyperintense bilateral BG is a rare but characteristic finding in appropriate clinical setting. Paralytic rabies can show Medulla and spinal cord T2- hyperintensity. |
| 9 | Dengue | Nonspecific involvement | ↓ | ↑ | -/+ | + | +(In cases of JE coinfection) | nonspecific | There is paucity of radiological change in dengue encephalopathy/encephalitis, which is in contrast to JE where thalamic, basal ganglia and brainstem abnormalities are common The MRI abnormalities includes oedema, ,scattered focal lesions and cerebral haemorrhage |
| 10 | HIV-1 | Cerebral WM, brainstem, thalamus, BG | ↓ | ↑ | - | - | - | ↓NAA ↑Cho ↑Myoinisotol | Cortical atrophy is the most frequent MR finding and is usually the only early alteration. The frontal lobes are the most common sites. White matter lesion in HIV encephalopathy are usually bilateral in asymmetrical manner. Gray matter is typically spared and mass effect is absent. The lesions do not enhance. A diffuse pattern of periventricular white matter hyperintensity suggests HIV encephalitis in contradistinction to the multifocal pattern produced by progressive multifocal leukoencephalopathy (PML) |
| 11. | PML (caused by JC virus) | Periventricular and/or subcortical white matter | ↓ | ↑ | - | - | - | ↓NAA ↓Creatinine ↑Cho ↑Myoinisotol(occasional) ↑Lipids/Lactate | Mimicks HIV encephalopathy.A multifocal distribution pattern is seen, which may be unilateral but is more often bilateral and asymmetric. There is an absence of mass effect and lesion rarely enhance. |
| 12. | CJD (Creutzfed Jakob Disease) Slow virus disease caused by Prion infection | Corpus striatum, thalamus, cortical gray matter and occipital lobes | ↓ | ↑ | - | + | - | ↓NAA | Symmetric abnormal, hyperintense T2 signal intensity within the corpus striatum is a relatively constant MR imaging feature. Diffusion-weighed images have been shown to be more sensitive in depicting involvement of the cortical gray matter or deep gray matter when compared with T2-weighted/FLAIR images. The hyperintensity seen on the diffusion-weighted images could be related to regions of restricted diffusion related to the intracellular vacuolation |

of metabolism), malignant disease, collagen vascular disease, and intracranial hemorrhage. Exposure to certain drugs or toxins may also cause encephalitis.

## IMAGING FEATURES

Imaging is frequently nonspecific[2]. MRI with contrast is the investigation of choice. CT is frequently negative in early disease and underestimates the actual extent of the disease process.

Abnormal T2 hyperintensity of gray matter (GM) and deep grey nuclei is the best diagnostic clue in appropriate clinical setting. Concomitant white matter involvement are seen sometimes. Large, poorly delineated areas of involvement are common and patchy hemorrhages can be noted on T2*GRE images. Most of the cases show restricted diffusion on Diffusion Weighted (DW) images reflecting presence of cytotoxic edema. Contrast enhancement is noted in most cases secondary to meningeal involvement. MR spectroscopy shows reduced NAA/Cr ratio and increased Cho/Cr ratio in cases of HSV-1 Encephalitis and presence of lactate in JE. No specific abnormality is noted on MR perfusion studies.

## DIFFERENTIAL DIAGNOSIS

Encephalitis is one of the important differentials of intraaxial brain masses[3]. These lesions include primary neoplasms (high- and low-grade), secondary (meta-static) neoplasms, lymphoma, tumefactive demyelinating lesions, abscesses, and **encephalitis.** Application of a diagnostic algorithm that integrates advanced MR imaging techniques (perfusion imaging, diffusion-weighted imaging, and MR spectroscopy) with conventional MR imaging findings may help the practicing radiologist make a more specific diagnosis for an intraaxial tumor. Intraaxial brain masses are a significant health problem and present several imaging challenges. The role of imaging is no longer limited to merely providing anatomic details. Sophisticated magnetic resonance (MR) imaging techniques allow insight into such processes as the freedom of water molecule movement, the microvascular integrity and hemodynamic characteristics, and the chemical makeup of certain compounds of masses.

## SPECIFIC VIRAL SYNDROMES

***Acute Infecnous Encephalitis/Herpes Simplex-1 Encephalitis***

HSV-I is a fulminant haemorrhagic meningoencephalitis involving the limbic system as a result of reactivation of latent viral infection, which spreads along the branches of the cranial nerves. HSV-1 is the cause of 95 percent of all herpetic encephalitis and the most common cause of fatal sporadic encephalitis. Clinical symptoms include an altered sensorium, a diminished level of consciousness, focal neurologic deficit and fever. CSF findings are non-specific.

HSV-I encephalitis has a particular predilection for the limbic system. Infection is therefore often localized to interomedial temporal lobes (fig.1A), the orbital surface of the frontal lobes and insular cortex. There is sparing of the basal ganglia. Involvement may initially appear unilateral but is typically followed by less severe contralateral disease. This '**sequential bilaterality**' is highly suggestive of herpes encephalitis (see fig 1A). Hemorrhagic changes are common finding(fig 1B).

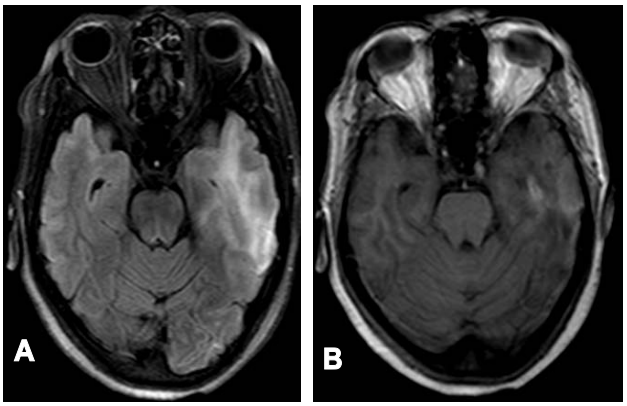


*Figure 1: ( A ) FLAIR image shows hyperintensity in left temporal lobe. Subtle signal changes are also seen in right temporal lobe. (B) T1-weighted image showing hyperintensity in left temporal lobe suggestive of subacute hemorrhage.*

***Herpes Simplex Type-2 Encephalitis***

HSV-2 is a major cause of neonatal encephalitis along with other TORCH agents (toxoplasmosis, other entenoviral infections, rubella, cytomegalic inclusion disease, herpesvinuses, mumps, measles). The neonate typically becomes infected during birth, infection spreads from the mother to the child. Infection may lead to death or severe neurologic sequelae such as seizures, microcephaly, microphthalmia, ventniculomegaly, and multicystic encephalomalacia. Neumoimaging in this group of patients has not revealed the predilection for this virus to involve the temporal lobes, as seen in patients without AIDS, and imaging findings are typically diffuse.

***Varicella-ZosterVirus***

The varicella-zoster virus can cause two seemingly different but actually closely related disorders, namely, varicella (chickenpox) and herpes zoster infection (shingles). Both disorders result in similar histopathologic findings. Varicella is a highly contagious disease with a generalized skin eruption; it usually occurs in childhood and is usually of little consequence in healthy children. However, varicellia may cause more serious disease, including encephalitis, in immunocompromised patients. Herpes zoster represents a reactivation of a latent varicella-zoster virus infection, usually in adulthood. Varicella may have several CNS manifestations: cerebellar ataxia, meningoencephalitis, transverse myelitis, and aseptic meningitis. Herpes zoster can be the causative agent in encephalitis, neuritis, and myelitis. Neumoimaging findings are usually unremarkable. CT/MRI show multiple lesions in the deep white matter; haemorrhage may be seen.

***Measles Encephalitis***

Measles is an acute, highly contagious infection caused by the rubeola virus, an enveloped RNA virus of the paramyxovirus family. There are three CNS syndromes related to measles infection acute measles encephalitis (AME),

subacute sclerosing panencephalitis (SSPE) and subacute measles encephalitis (SME).

AME is probably an autoimmune process and presents as fever during convalescence from measles. It is characterized by absence of the measles virus and by the presence of demyelination, necrosis, vascular damage and haemorrhage. No specific imaging feature has been described for it in literature.

SSPE is an invariably fatal neurodegenerative disease, developing as a sequel to early childhood measles infection. Following the original measles infection, the virus becomes altered and remains dormant intracellularly only to manifest as SSPE a decade or so later. Myoclonic attacks then develop and become increasingly more frequent, dementia follows and within months or a few years, the child is comatose and void of higher mental function.

SME usually occurs as an opportunistic infection in immunodeficient individuals with a latent period of 1 to 7 months. The prominence of congnitive and motor dysfunction is similar to that of SSPE but it has a subacute onset with more rapid evolution. The presence of seizures rather than myoclonus is the distinctive features of SME.MRI findings are non-specific.

### *Acquired Immune Deficiency Syndrome (AIDS) and its related CNS Infections*

The retrovirus designated human immuno-deficiency virus (HIV) causes AIDS. Two HIV subtypes are recognized : HIV – I and HIV- 2. HIV-1 is the most widespread type and accounts for most AIDS cases. CNS involvement is both an early and a common feature of HIV infection.

HIV is a neurotropic virus that can directly involve both the peripheral and the central nervous system. The HIV virus itself is the most common CNS pathogen in AIDS patient followed by Toxoplasma gondii and Cryptococcus neoformans. The CNS infections in AIDS include.

- HIV encephalitis – most common (60%)
- Toxoplasamosis – commonest opportunistic infection (20-40%)
- Cryptococcosis (5%)
- Progressive multifocal leukoencephalopathy PML (1-4%).

### *Others*

- Tuberculosis (2-18%)
- Neurosyphilis (1 to 3%)
- Varicella Zoster (< 1%)
- CMV encephalitis

### *HIV Encephalitis*

The most common neurologic complication seen in AIDS patients is subacute encephalitis. Clinical presentation includes a progressive dementia associated with motor and / or behavioural dysfunction.

The effects of cerebral HIV infection are clearly more evident on MR than CT. Cortical atrophy is the most frequent MR finding and is usually the only early alteration. T2- weighted images reveal hyperintense lesions in the periventricular white matter and centrum semiovale that correspond to foci of demyelination and vacuolation. The frontal lobes are the most common sites. White matter lesion in HIV encephalopathy are usually bilateral in asymmetrical manner. Gray matter is typically spared and mass effect is absent. The lesions do not enhance. Fluid attenuated inversion recovery images are particularly useful in the detection of white matter disease. A diffuse pattern of periventricular white matter hyperintensity suggests HIV encephalitis in contradistinction to the multifocal pattern produced by progressive multifocal leukoencephalopathy (PML).

### *Progressive Multifocal Leukoencephalopathy (PML)*

PML occurs in about 5 percent of patients with AIDS. Before the era of AIDS, PML was primarily associated with other immuno- deficient disorders, including renal transplantation, autoimmune disease, tuberculosis (TB), sarcoidosis, Whipple's disease, nontropical sprue and lymphoproliferative disorders. Patient treated with chemotherapy are also at increased risk for PML. Currently, PML appears to have a stronger association with AIDS than with any other immunosuppressive disorder and 55 to 85 percent of recent PML case are attributable to AIDS.

PML is a progressive demyelinating disorder arising from CNS infection with a paporvavirus. The aetiologic agent is a human polyomavirus, the JC virus..

Clinical presentation of PML includes memory loss, visual deficit, personality changes, cognitive and speech disturbances, altered mental status, and motor and / or sensory abnormalities with a progressive neurologic decline.

### *Cytomegalovirus (CMV) Encephalitis*

In adults, CMV is a frequent pathogen in the AIDS population and in other immunocompromised patients, occurring not only in the CNS but throughout the body. CMV more often presents outside the CNS, involving the respiratory tract, liver, gastrointestinal tract, genitourinary tract, and/or haematopoietic system. Neurologic manifestations of CMV include acute or chronic meningoencephalitis, cranial neuropathy, vasculitis, retinitis, myelitis, brachial plexus neuropathy and peripheral neuropathy.

In addition to atrophy. MR may demonstrate increased signal on T2-weighted images in the periventricular white matter, which may be patchy and is less often confluent. Infrequently, subependymal enhancement is evident and, if present, is a valuable diagnostic due.

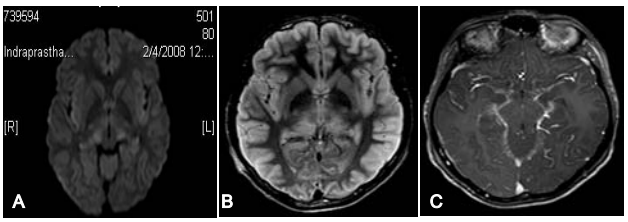


*Figure 2: (A) Diffusion-weighted scan showing restricted diffusion in bilateral thalami. (B) Corresponding FLAIR images showing bithalamic hyperintensity. (C) T1-weighted contrast enhanced image showing mild meningeal (basal cistern) enhacement.*

### *Japanese Encephalitis (JE )*

Epidemic of Japanese encephalitis ( JE ) occur in all countries throughout Asia. It usually appears in summer and is often severe with rapid progression to coma. The characteristic neurologic findings during the acute stage are extrapyramidal signs such as tremor, dystonia and rigidity. Seizures are more common in children than adults. It is important to distinguish JE from other types of encephalitis, particularly HSE, because antiviral therapy for HSE is very effective in the acute stage. Specific antiviral therapy is not available for JE, its treatment being supportive.

Diffuse meningoencephalitis affecting both gray and white matter of the cerebral hemispheres, basal ganglia, brainstem, cerebellum and thalamus has been reported[4]. Diffuse inflammatory changes are also found in the spinal cord, particularly in the anterior and lateral column.

### *Rabies*

Rabies encephalitis is an acute CNS infection caused by a type of RNA virus of the rhabdovirus family. The disease is also known as hydrophobia or aquifuga Transmission to humans is mainly through bites of infected rabid dogs, cats, bats, and other wild animals. Human rabies may present in one of two forms: encephalitic and paralytic. In paralytic rabies, the medulla and the spinal cord are mainly involved by extensive neuronal damage and inflammation, whereas in the encephalitic form, it is the brain stem and the cerebrum, particularly the limbic system. Involvement of the basal ganglia and the thalamus is usually seen late in the disease.

Because the disease has a rapidly fulminant course, imaging of these patients is uncommon and difficult. Hence, the imaging findings in naturally acquired rabies have received little attention in the literature. A CT/MRI may show involvement of the basal ganglia, periventricular white matter, hippocampus, and brain stem[5]. Pontine hemorrhages have also been reported. Diffuse cerebral edema may be seen in advanced cases.

### *Dengue*

Dengue virus belongs to the family Flaviviridae, which also includes yellow fever, Japanese encephalitis (JE) and West Nile encephalitis viruses. The yellow fever infection presents with liver dysfunction and JE with encephalomyelitis. The dengue virus infection may manifest with both hepatic and neurological involvement. Neurological involvement in dengue can be attributed to metabolic alteration such as liver failure, electrolyte imbalance and renal impairment as well as hypotension. Bleeding and coagulation abnormalities in dengue haemorrhagic fever and dengue shock syndrome can also contribute to altered sensorium. The neurological complications of dengue virus infection include encephalitis, myelitis, Guillain Barre (GB) syndrome and myositis.

There is paucity of radiological change in dengue encephalopathy/encephalitis, which is in contrast to JE where thalamic, basal ganglia and brainstem abnormalities are common[6]. The MRI abnormalities includes oedema,scattered focal lesions and cerebral haemorrhage.

### *Prion Infections : Creutzfeldt - Jakob Disease (CJD)*

Creutzfeldt-Jakob disease is a human spongiform encephalopathy. Like Kuru and Scrapie results form an infection by a slow unconventional virus known as Prion. Dementia is usually the predominant feature of this disease, presenting in people between the ages of 40 and 80 years. The dementia may be accompanied by sensory abnormality, confusion and cerebellar ataxia. Prognosis is poor with a mean survival of less than 1 year from the onset of symptoms.

MR imaging clues in the diagnosis of Creutzfeldt – Jakob disease include progressive atrophic change of the brain or symmetric deep gray or cortical hyperintense lesion on the T2 – weighted images or diffusion images that lack gadolinium enhancement. Spectroscopy shows diminished levels of NAA.

### *Acute Disseminated Encephalomyelitis (ADEM)*

Acute disseminated encephalomyelitis is caused by immune response to a preceding viral infection or vaccination. Patients usually present with neurologic signs and symptoms 5 days to 2 weeks later. Both humoral and cell mediated immunity are implicated as the cause of pathologic changes. A hypersensitivity reaction to a myelin protein is thought to cause demyelination. Perivenous demyelination is the hallmark of the disease.

The disease primarily involves white matter, but change may also be apparent in gray matter and brainstem. CT may show low density in the periventricular white matter and MRI may show hyperintensity in the white matter on T2 weighted images and some of the lesions may exhibit contrast enhancement.

The *differential diagnosis* include multiple sclerosis, vasculitis and embolic infarction. In later stages of the disease, encephalomalacia, ventriculomegaly and atrophy may be seen.

## SUMMARY

Encephalitis affects persons in all age-groups and can result from a myriad of infectious and noninfectious causes. Depending on the cause, the outcome may be benign or in some cases fatal History taking and physical examination can provide clues to the cause, but the diagnosis is usually established on the basis of CSF analysis, viral culture, MRI, and serologic testing, when indicated. MRI can help in the in the diagnosis of HSV-1 encephalitis,Japanense encephalitis, HIV encephalitis and Creutzfeld Jakob's disease in appropriate clinical setting. However most of the time imaging is meant to rule out other possible causes in an acutely ill febrile patient showing focal neurological deficits and seizures. MRI is helpful in the assessment of complications and prognosis.

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