Neurology

Transient Ischaemic attacks are discussed with predominant emphasis on clinical features; pathogenesis and treatment, followed by a brief review of the current role of plasmaphoresis and visual evoked responses in neurology.

Transient Ischaemic Attacks

Definition

In 1978 the WHO defined transient ischaemic attacks (TIA) as a temporary and focal episode of neurological dysfunction of presumed vascular origin typically lasting 2-15 minutes and occasionally as long as 24 hours. The particular emphasis in this definition is on the episodes being temporary, focal and of presumed vascular origin.

The episodes should clear without residue and the distribution should be either in the carotid or vertebrobasilar territories.

The following symptoms do not constitute transient ischaemic attacks when they occur in isolation: lightheadedness, syncope, confusion, vertigo, dysarthria or double vision.

The carotid territory

The internal carotid artery has three major branches: the ophthalmic artery; the middle cerebral artery; the anterior cerebral artery.

Internal carotid territory disease is caused by lesions in any of these three vessels.

The ophthalmic artery: lesion causes amaurosis fugax or transient blindness or possibly total blindness in one eye. This can be demonstrated clinically by asking the patient to cover one eye at a time while keeping the other eye open. One can then determine whether the lesion is mono-ocular or binocular.

If the lesion involves the anterior or middle cerebral arteries the pathology occurs in the ipsilateral cerebral hemisphere.

Clinically, headache may occur immediately after the TIA due to compensatory post ischaemic vasodilation. The headache occurs on the side of the involved cerebral artery, ie ipsilateral.

On the contralateral side the patient may develop homonymous hemianopia, dysphasia, motor or sensory loss. If the motor loss occurs predominantly in the leg or shoulder, the anterior cerebral artery is involved. If the loss is predominantly face and arms - motor and sensory - the vessel involved is the middle cerebral artery. These patients rarely lose consciousness.

The vertebrobasilar territory

The major vessels involved are the two vertebral arteries, the basilar, the two posterior cerebral arteries, the anterior cerebellar artery and the posterior superior and posterior inferior cerebellar arteries.

Ischaemia may involve any part of the brain stem - including the long tracts, the cranial nerves, the occipital cortex and the cerebellum.

A vertebrobasilar TIA may cause: Vertigo and ataxia related to ischaemia of the vestibular pathway ie. vestibular nucleus, vestibular tract and connections to the cerebellum, eyes, cervical spine and temporal lobes.

- Motor or sensory loss occurring in a patchy distribution on the same side or opposite sides depending on which tracts are involved.
- Horner's syndrome due to sympathetic tract involvement in the brain stem.
- Hemianopia or binocular transient or total visual loss due to basilar artery ischaemia creating simultaneous ischaemia to the occipital lobes and visual pathways via posterior cerebral artery ischaemia.
- Any cranial nerves may be involved eg. 5th - sensory loss ipsilateral - 7th lower motor neurone ipsilateral facial weakness; 9th - Dysphasia, dysphagia, dysarthria.
- Headache and vomiting due to postischaemic vasodilatation at base of brain
- Syncope due to involvement of reticular activating system of midbrain.
- Drop attacks due to bilateral pyramidal tract ischaemia.

A comparison of the clinical presentations of carotid and vertebrobasilar territory lesions is shown in **Table 1.**

Carotid system: All features are contralateral ie. weakness, numbness and paraesthesias, speech deficit is usually dysphasia because of cortical involvement.

Visual loss is ipsilateral amaurosis fugax or contralateral homonymous hemianopia. Any combination of the above may occur.

Vertebrobasilar system: The weakness can be on either side or shifting; there may be associated ataxia and balance dysequilibrium and similarly numbness and parasthesias may be bilateral or shifting.

There is often dysarthria and dysphagia and the vision loss is usually complete or partial and involves both homonymous fields.

TABLE I CLINICAL FEATURES OF TIA

Symptom	Carotid System	Vertebrobasilar System
Motor Defect	Weakness - unilat. opposite side	Weakness - bilateral or shifting ataxia, imbalance, dysenquilibrium
Sensory Defect	Numbness & Parasthesia opposite side	Numbness & Parasthesia bilateral or shifting
Speech defect	Dysphasia Dysarthria	Dysarthria
Vision Defect	Amaurosis Fugax -same side occas. homonymous hemianopia – opposite side	Blindness, complete or partial in both homonymous fields Diplopia
Other	Combinations of above	Combinations of above

Update

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Consciousness loss is important in this group and any combination of the above may occur.

Pathogenesis

There are five major categories of disorder that may contribute to transient cerebral events **(see Table II).** The two most important are abnormalities of blood vessel wall and embolic phenomena.

The blood vessel wall may have atheromatous lesions (which can be extra or intracranial) or non atherosclerotic lesions such as dissection or inflammatory vasculitic lesions.

The most common sources of emboli causing TIA's are the internal carotid arteries. The emboli are often made of platelets and arise from ulcers, or stenosis or stumps of occluded vessels within thrombosis distal to the occlusion. Intracranial arteries or other extracranial arteries are less common sources of emboli. Occasionally the heart is the source of small emboli to the brain.

Less commonly, haemodynamic causes may result in TIA's. Any form of decrease in cerebral blood flow due to drop in blood pressure will result in syncope or a blackout or dizzyness. Usual causes are bradyarrhythmias, orthostatic hypotension and autonomic abnormalities. If this is an associated focal intracerebral vascular stenosis then a generalised decrease in cerebral blood flow may manifest initially as a transient focal cerebral ischaemic episode.

Alteration in blood coagulation eg. hypercoagulation, thrombocytosis and hyperviscosity, will usually cause a cerebral thrombosis; however focal cerebral "sluggish" flow will cause a TIA.

Miscellaneous vascular lesions causing TIA are varied. The most common is the contraceptive pill but other causes may occur eg. migraine, haemorrhagic telangiectasia and cerebral angiography. Non-vascular causes may look alarmingly like TIA's eg. focal epilepsy, mass lesions including tumors or metabolic causes.

Treatment – conservative

It is most important to define the territory. This has already been discussed. Then exclude mimicking irreversible diseases and do a general examination in the usual way especially looking for bruits, cardiac disease, hypertension, ECG abnormalities, atheromatous risk factors and treat reversible causes eg. hypertension.

Having defined the territory, the approach depends on the area involved.

If the lesion is vertebrobasilar, surgery is useless and medical therapy alone is indicated. Exclude other causes eg. cervical spondylosis with vertebral artery compression.

TABLE II

PATHOGENESIS OF TRANSIENT ISHAEMIC ATTACKS

(1) ABNORMALITIES OF BLOOD VESSEL WALLS
- (a) Extracranial atherosclerosis
- (b) Intracranial atherosclerosis
- (c) Non-atherosclerotic vasculopathies
- (d) Carotid artery dissections (spontaneous and traumatic)
- (e) Inflammatory disorders (infectious and collagenoses)

(2) EMBOLIC PHENOMENA
- (a) Cardiac
- (b) Stumps of occluded vessels
- (c) Arterio-arterial

(3) HAEMODYNAMIC
- (a) Alteration in blood circulation
- (b) Bradyarrhythmias
- (c) Orthostatic hypotension
- (d) Autonomic abnormalities
- (e) Vasospasm

(4) ALTERATION IN BLOOD COMPOSITION
- (a) Hypercoagulability
- (b) Thrombocytosis
- (c) Hyperviscosity
- (d) Hyperfibrinogenaemia

(5) MISCELLANEOUS
- **(a) Vascular**
  - (i) Migraine
  - (ii) Haemorrhagic telangiectasia
  - (iii) Oral contraceptive pill
  - (iv) Complications of cerebral angiography
- **(b) Non Vascular**
  - (i) Epilepsy
  - (ii) Mass lesions of brain
  - (iii) Metabolic

Use antiplatelet or anticoagulant therapy. Our particular choice in this situation is antiplatelet therapy. We feel that Aspirin and Persantin have had better results in this potentially haemorrhagic part of the brain.

If the territory is carotid two choices are presented.

If the patient is over 70 years of age; if there is a poor anaesthetic risk for any reason, (medical or otherwise) or if no further facilities are available for non invasive tests or more specifically for angiography or good vascular surgery the safest approach to treatment is medical **(see Table III).**

The choice lies between antiplatelet drugs and anticoagulants. This is a controversial field with many studies to define the best form of therapy.

In the first three months after the TIA, the Mayo Clinic group advocated the use of anticoagulants. After six months they found that the complication rate of the drug was worse than its efficacy. However, most authors do not use anticoagulants and advocate the use of antiplatelet drugs ab initio.

In our unit we use the antiplatelet drugs from the onset having had bad experiences with Warfarin in the elderly. Our regimen is Aspirin once daily (300mg) and Persantin three times daily, (100mg). Aspirin alone, especially in men, is probably just as effective.

Treatment – surgical

There is one group of patients in whom surgery becomes an important form of therapy: If the territory of the TIA is carotid; if the patient is under 70 years of age; if he is a good anaesthetic risk and if good facilities are available for the investigation and surgical therapy of carotid stenosis, it becomes important to exclude an operable lesion.

This should be done in the following way: listen for bruits (absence of bruit doesn't exclude a lesion); look for all the risk factors; do EEG to exclude epilepsy; do non invasive flow studies.

If the flow study results are positive indicating a focal lesion of the relevant internal carotid artery - do a CT scan to exclude a large cerebral infarct or haemorrhage. If a cerebral vascular lesion is present, angiography should be delayed four to six weeks to prevent worsening of the stroke by the contrast medium.

Table III

APPROACH TO THERAPY – CONSERVATIVE

Examine clinically for risk factors or reversible aetiology eg. hypertension, bruits, heart disease, arrhythmias, polycythaemia, diabetes

Define Territory

Vertebrobasilar

- medical Rx only anti-platelets or anticoagulants
- exclude other causes eg. cervical lesions

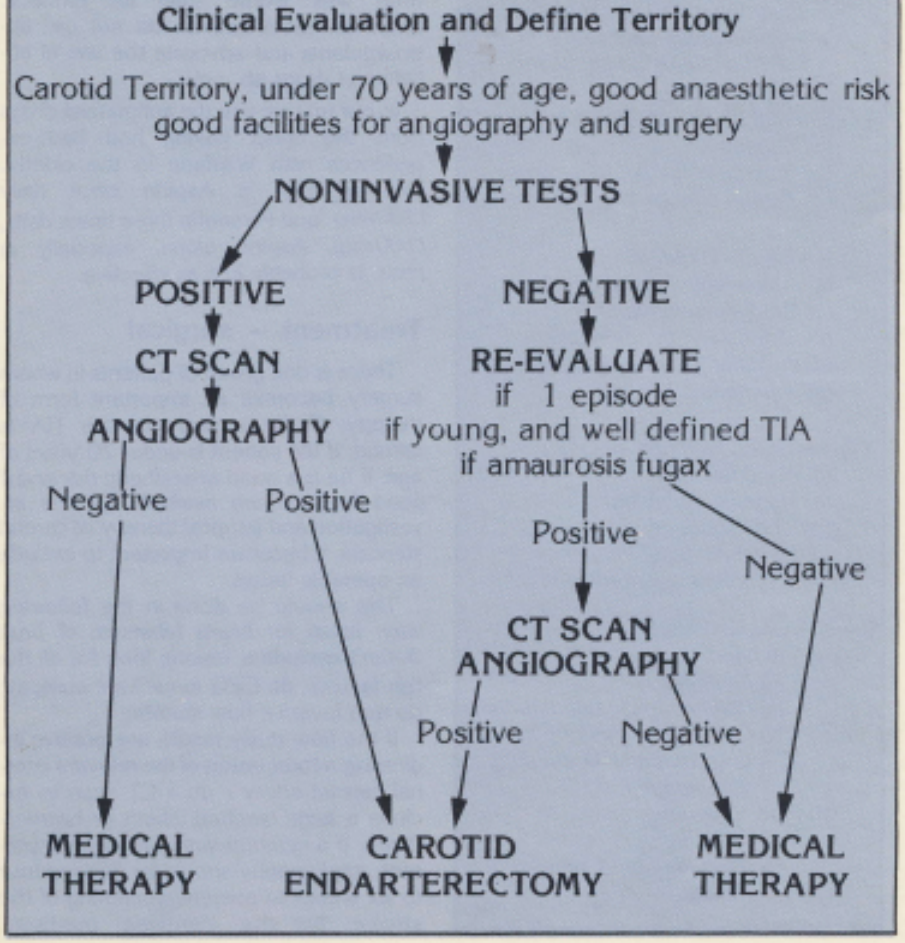
Carotid

Over 70 years of age or poor anaesthetic risk
- Rx medical

No facilities for angiography or safe surgery
- Rx medical

Table IV

APPROACH TO THERAPY – SURGICAL



Angiography should then be carried out. If a lesion is demonstrated, do endarterectomy. If no lesion is present then utilise medical therapy.

If the flow study results are negative: reassess the patient clinically; if multiple TIA's have occurred in the same territory; if amaurosis has occurred particularly associated with a contralateral hemisensory or motor loss; if the patient is young with a clearly defined transient lesion and no other cause, do CT scan and angiography with the same responses to positive and negative results as defined above **(see Table IV).**

In conclusion, I would like to point out that TIA's represent a clinical pattern with wide aetiological diversity. In all cases the aetiology of the lesion and the cerebral territory involved must be clearly assessed.

Only one aetiology is surgical ie. a single clearly defined stenosis or ulcer of the internal carotid artery just above the carotid bulb. If this condition is present, surgery can and should be carried out with reasonably good results.

PLASMAPHORESIS

This has become a very popular form of treatment in recent years. The principle involves removing blood, centrifuging blood and separating cell constituents, then returning packed cells with a plasma or electrolyte solution.

Aims

The aims of plasmaphoresis are to:

- Remove abnormal plasma constituents, eg. immune complexes or antibodies;
- Decrease excessive amounts of normal plasma constituents (eg. acute phase proteins).
- Restore plasma factors noted to be deficient or reduced in disease eg. complement components in SLE.

Role in Neurology

In neurology there are three major uses of plasmaphoresis. These include Guillain Barre Syndrome, Myasthenia Gravis and Polymyositis. All these are neuroimmunological disorders.

In Guillain Barre syndrome antimyelin antibodies occur; in myasthenia antireceptor site antibodies to the muscles are found; polymyositis is another form of autoimmune disease.

Guillain Barre Syndrome

Recently, 15 cases of Guillain Barre Syndrome were studied in the Johannesburg Hospital. Improved recovery time was noted if plasmaphoresis was started early prior to structural change, especially prior to the patient requiring respirator therapy.

We have found that if the patient is already on a respirator or has had the

disease for a long time, plasmaphoresis does not help at all.

The disease has an unpredictable natural history and many patients improve rapidly on their own. Therefore it is difficult to analyse what our results mean. World literature has also shown that this form of therapy is unpredictable. It may improve recovery time but it will not change the pattern of the disease or alter the ultimate prognosis of a particular patient.

Myasthenia Gravis

34 cases of Myasthenia Gravis have plasmaphoresed at the Johannesburg Hospital. Plasmaphoresis appears to be most helpful in crises and in patients with sudden rapid deterioration.

In patients going for thymectomy fewer problems appear to occur post thymectomy, if plasmaphoresis is used.

The role of plasmaphoresis both as a primary form of therapy and as maintenance therapy is not clearly established.

The disease group has a cyclical natural history and results are difficult to analyse. Plasmaphoresis is being used in many parts of the world. its exact place has not yet been clearly defined. Like steroids and immunosuppressive drugs there is a place for this form of therapy in diseases that are antibody mediated.

Complications of Plasmaphoresis

a) Adverse reactions for foreign proteins with plasma replacement.
b) Effects on intrinsic mechanisms eg. reticuloendothelial function being interfered with.
c) Decreased K + Ca +
d) A/V shunt is often needed and this may lead to infection.
e) Hepatitis and adverse reactions result from blood transfusion and using plasma products. In these circumstances saline can be used but the problem of depleting the patient of essential proteins and other plasma constituents then arises.
f) Mild anaemia invariably follows plasmaphoresis as does postural hypotension due to volume depletion.

Conclusion

Plasmaphoresis is a form of therapy in its infancy. It is an expensive form of therapy, very time consuming and has many complications. It is an adjunct to treatment of immune diseases where steroids and immune suppression were used in the past.

There are no conclusive results to show whether Plasmaphoresis has an important role to play or not. If facilities are available, it may be a useful form of therapy. However, no patient should be moved specifically to a distant centre for this form of therapy.

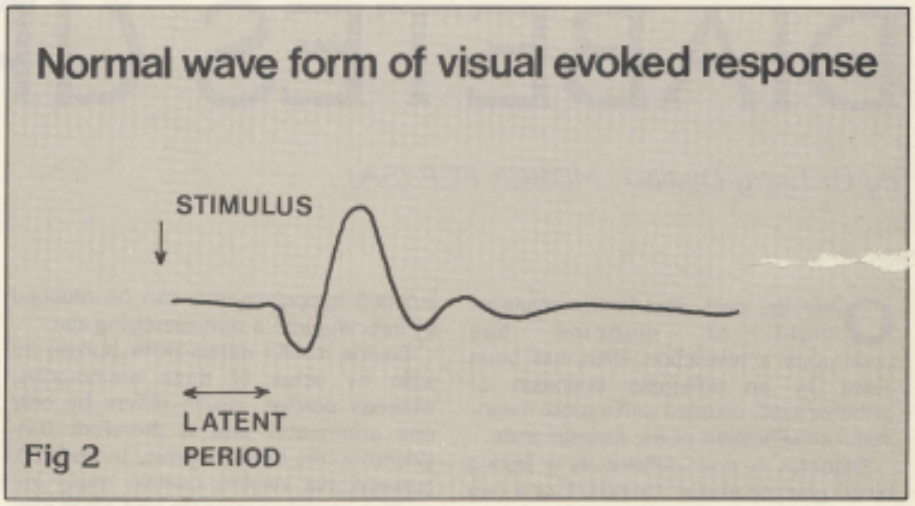


Fig 2

VISUAL EVOKED POTENTIALS (VEPS)

Finally I wish to discuss a new form of investigation which has aroused a great deal of comment and interest in recent years.

This is a form of investigation which is extremely expensive and utilises a great deal of expensive equipment ie. the visual evoked response (VER) or VEP.

The principle behind this is that when the visual system is stimulated by light, minute signals can be elicited in the occipital cortex. These signals could not be analysed properly previously because they were swamped by the EEG patterns. Recently, by using averaging computers, the EEG pattern can be eliminated because the wave patterns cancel each other out when superimposed by an averaging computer.

At the same time the small signals can be superimposed on each other, averaged out and recorded as a single wave pattern.

VEP's are recorded in the following manner. The patient sits and looks at a chequer board pattern on a screen. A lead is placed over the inion to record the signals over the occipital cortex. This signal is then amplified and averaged via the computer.

The visual field triggers the computer at the same time so that it is time locked. Then a plotter plots out the final wave form. **(See Fig. 1).**

The wave pattern consists of a stimulus, a latent period and a slow wave pattern (Fig. II). The most important measurement is the latency, which is the time taken for the response to occur after the stimulus. The shape and height of the wave form is also significant.

Clinical applications of VEP's

In neurology the most important role is in multiple sclerosis because it is a helpful way of diagnosing subclinical forms of optic neuritis. Patients with Multiple Sclerosis have a very high incidence (up to 80% of optic nerve involvement – this is frequently subclinical and the patient is unaware of this. An abnormal VER in the presence of a suspicious clinical picture may be very helpful. This disease is becoming more frequent in South Africa. We have well over 200 South African born patients with Multiple Sclerosis on our records today.

Other forms of Evoked Responses

Other forms of evoked response that are in use today include:

- Auditory evoked response; the stimulus is a click in the ear and the recording is made over the temporal lobe in much the same way as described for visual responses.
- Somatosensory evoked responses which depend on stimuli picked up over the cortex and cervical region from a stimulus delivered to the hand or leg. □

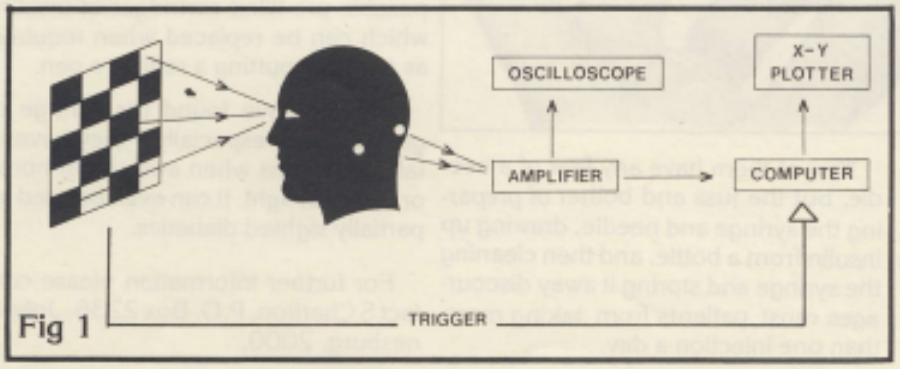


Fig 1