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ABSTRACTS*

**Benign epilepsy syndromes in infants
and young children**

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Epilepsies with onset in the first two years of life are usually associated with brain damage and run an unfavorable course from both the seizure and the neurodevelopmental points of view.

In the past two decades, a number of both generalized and focal epilepsies with an excellent outcome have been reported.

– These include, among the **generalized epilepsies**, the *benign myoclonic epilepsy of infants* [1], with onset before age 3 years, expressed only by brief but sometimes frequently repeated myoclonic seizures with bursts of fast spike-waves on a normal interictal EEG without other types of seizure except possibly febrile convulsions. Neurodevelopment is normal and seizures disappear usually before adolescence. However, late epilepsy can develop in a few cases and mild or moderate behavioral anomalies and school difficulties may be present in up to 50% of cases.

– Among the **focal epilepsies**, several syndromes have been recognized. All are marked by clusters of brief seizures with focal onset, occurring before age 1 or 2 years in infants with normal development and normal interictal EEG, and disappearance of seizures before age 2 or 3 years. Generalized seizures are associated in some patients. Many of these focal seizures are part of genetic, dominantly inherited syndromes. These include :

a) the syndrome of *familial benign infantile convulsions* [2] dominantly transmitted, with linkage to two different loci (19q, 16) that occurs after the age of 4-6 months and always disappear before age two years and respond well to antiepileptic agents in most cases. Mutations of potassium channels are the molecular base of both forms.

b) a similar syndrome that sometimes has a neonatal onset and is termed for that reason *neonatal-infantile familial seizures* syndrome is due to mutations of a sodium channel gene mapping to chromosome 2q [3]. These

cases have the same benign course but later epilepsy can occur in 10-15% of cases. In these forms, the interictal EEG is normal but seizures are associated with paroxysmal discharges. A variant may be characterized by the presence of small vertex spikes on sleep (interictal) EEG but its individuality is dubious.

c) The *syndrome of infantile convulsions and choreo-athetosis* characterized in the first years of life by neonatal seizures that present the same features as the familial benign cases. Months or years later episodes of paroxysmal dyskinesia, kinesigenic or not, usually choreic in type occur. The dyskinesia responds to carbamazepine and may disappear before adult age [4] ; this form has been found to map to centrometric region of chromosome 16. The same linkage can be responsible for infantile convulsions apparently not followed by dyskinesia.

– **Other benign infantile seizures** that do not belong to genetic syndromes or at least are not dominantly inherited. They include :

a) *Nonfamilial partial benign infantile seizures* that may be partial complex or secondarily generalized [5-6] and seem to be common in some Asian countries. Except for the absence of obvious genetic character and perhaps the occurrence in cluster, they do not differ from familial cases.

b) *Cases of infantile seizures associated with viral gastro-intestinal infections* that occur without associated fever and have been occasionally reported from western countries.

The **diagnosis** of benign infantile seizures is easy when a history of similar seizures in parents is elicited. However, these are often forgotten or may not have existed. The diagnosis rests on the characteristics of the seizures and normal neurological examination, EEG and neurodevelopment in other cases. Making the diagnosis is extremely important to avoid to wrongly give in such cases the poor prognosis that is attached to other infantile convulsions.

REFERENCES

1. Dravet C, Bureau M. Benign myoclonic epilepsy in infancy. In : Roger J et al., editors. *Epileptic Syndromes in Infancy Childhood and Adolescence*, 3rd ed., London : John Libbey, 2002 : 69-79.
2. Vigeveno F, Bureau M. Idiopathic and/or benign localization-related epilepsies in infants and young children. In : Roger J et al., editors. *Epileptic Syndromes in Infancy Childhood and Adolescence*, 3rd ed., London : John Libbey, 2002 : 153-60.

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3. Berkovic SF, Heron SE, Giordano L et al. Benign familial neonatal-infantile seizures characterization : new sodium channelopathy. *Ann Neurol* 2004 ; 55 : 550-7.
4. Szepetowski P, Rochette J, Berquin P et al. Familial infantile convulsions and paroxysmal : a new neurological syndrome linked to the pericentric region of human chromosome 16. *Am J Hum Genet* 1997 ; 61 : 889-98.
5. Watanabe K, Yamamoto N, Negoro T. Benign complex partial epilepsy in infancy. *Pediatr Neurol* 1987 ; 3 : 208-11.
6. Watanabe K, Negoro T, Aso K. Benign partial epilepsy with secondarily generalized seizures in infancy. *Epilepsia* 1993 ; 34 : 635-8.

Severe Epilepsy Syndromes of Infancy

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These syndromes exhibit common features including : Impaired cognitive and neurological development and reduction in developmental potential + Severe epileptiform EEG abnormalities + Frequent disabling seizures + Detectable brain lesion. These include : Epileptic encephalopathies with burst suppression, West syndrome, severe myoclonic epilepsy of infancy (Dravet syndrome), myoclonic epilepsy (status) in nonprogressive encephalopathy, migrating partial epilepsy, folinic acid responsive seizures with neonatal onset [1] or with infantile onset [2], and infantile refractory grand mal syndrome-IRGMS [3-4]. Advances in clinical neurophysiology have allowed the identification of several syndromes based on our increasing understanding of those syndromes and the differences between them. Advances in molecular biology are extending this knowledge even further (including, for example, X-linked West syndrome and Dravet syndrome).

REFERENCES

1. Torres OA, Miller VS, Buist NM, Hyland K. Folinic acid-responsive neonatal seizures. *J Child Neurol* 1999 Aug ; 14 (8) : 529-32.
2. Ramaekers VT, Hausler M, Opladen T, Heimann G, Blau N. Psychomotor retardation, spastic paraplegia, cerebellar ataxia and dyskinesia associated with low 5-methyltetrahydrofolate in cerebrospinal fluid : a novel neuro-metabolic condition responding to folinic acid substitution. *Neuropediatrics* 2002 Dec ; 33 (6) : 301-8.
3. Kanazawa O. Refractory grand mal seizures with onset during infancy including severe myoclonic epilepsy in infancy. *Brain Dev* 2001 Nov ; 23 (7) : 749-56.
4. Doose H, Lunau H, Castiglione E, Waltz S. Severe idiopathic generalized epilepsy of infancy with generalized tonic-clonic seizures. *Neuropediatrics* 1998 Oct ; 29 (5) : 229-38.

Lennox-Gastaut Syndrome, Doose's Syndrome, Dravet's Syndrome and Febrile Seizures Plus : How Can We Distinguish ?

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The term Lennox-Gastaut syndrome (LGS) is often loosely used to denote severe epilepsy syndromes of childhood, featuring several types of seizures including falls, often medically intractable. Such a broad definition includes in fact several types of epilepsy whose outcome and therapy may be different. Currently, the LGS is defined as an epilepsy syndrome characterized by multiple types of seizures including a nucleus of brief tonic and/or atonic seizures, atypical absences, and, less characteristically, myoclonic attacks, associated with an interictal EEG pattern of diffuse, slow (< 2.5 Hz) spike-waves complexes (443). Several authors consider that the presence of runs of fast (10 Hz) rhythms associated with the tonic attacks or occurring with minimal or without associated clinical manifestations, especially during non-REM sleep, are an additional necessary criterion. Episodes of non-convulsive status epilepticus are a frequent occurrence. Mental retardation is a very frequent but not an absolutely constant feature. The clinical and etiological heterogeneity of the LGS probably accounts for the many different clinical patterns, variably overlapping with one another and with other syndromes that can be encountered, depending on the individual combination of seizure types and EEG abnormalities. Myoclonic-astatic epilepsy and transitional forms between the myoclonic epilepsies and LGS will be discussed, focusing on diagnostic issues and therapeutic strategies.

Dravet's syndrome (severe myoclonic epilepsy) was initially mistakenly considered as a form of the Lennox-Gastaut syndrome because of the occurrence of repeated falls. However, it is clearly different in its clinical and EEG features and in its treatment and thus should be distinguished from the other syndromes that can be associated with myoclonic seizures. The differential diagnosis varies with the stage of the disorder. Dravet's syndrome does not present primarily as a myoclonic syndrome, but rather as febrile convulsions of long duration and frequently repeated, in the first year of life. During the initial phase, the diagnosis of febrile convulsions is difficult to avoid. Indeed, the initial attacks are febrile convulsions. Some clinical nuances, however, may attract attention, such as a low degree of fever often below 38°C, a prolonged duration of the seizures beyond 15 or 30 minutes, and a unilateral localization. The diagnosis usually becomes obvious during the second year of life, with the appearance of brief seizures of multiple types. A more difficult issue may be the differentiation from progressive degenerative disease, especially during periods of non-convulsive status when ataxia and regression become evident.

GEFS+ cannot be considered a syndrome, in the

commonly used sense of the term. GEFS+ is a term used to refer to a great variety of epileptic seizures and epilepsy syndromes present in the same family. The presence of FS+ in more than one member of the family can be considered as a distinguishing feature. When dealing with an individual patient, with no family history of seizures, differential diagnosis from common febrile seizures is impossible. Similarly, in individual patients, differential diagnosis from Dravet's syndrome may be difficult. Dravet's syndrome can be considered as part of the GEFS+ spectrum when other members of the family fulfil the general criteria of GEFS+.

Selection of Pediatric Patients for Epilepsy Surgery

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Criteria for epilepsy surgery in children include : Epilepsy syndrome not expected to remit, truly intractable patient, and for focal or lateralized resection : localization of a single epileptogenic zone that is resectable (e.g. focus within a lobe, a lobe, or a hemisphere). The work-up includes initial preadmission screening to determine epilepsy syndrome and true intractability, determine *semiology* (confirm with LTM), review the interictal EEG, MRI, psychologic status, and social status. Phase I involves in patient video-LTM recordings to confirm localization and semiology. In a minority of patients Phase II is needed and this involves insertion of intracranial, usually subdural electrodes (or depth electrodes and recently in some centers laminar electrodes which have the goal to obtain horizontal as well as vertical cortical recordings). In Phase II extraoperative cortical stimulation and subsequent intraoperative corticography and activation are often performed. Tailored resection can take advantage of the reorganization that can occur with early and congenital lesions before surgery and in many cases after surgery (plasticity). Specific clinical examples and videos to illustrate the above points will be included in the review.

MCI and Prodromal Alzheimer's Disease

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The concept of MCI has been introduced to fill up the gap between two discrete cognitive states : the state associated with aging and the one that characterizes dementia. Thus, MCI does correspond to a clinical entity reality, useful for a large proportion of patients consulting memory clinics. Some of these patients with MCI will convert to dementia – approximately 15% per year – but some will not. As these patients tend to progress to clinically probable Alzheimer's disease (AD) at a considerably accelerated rate, this condition has been considered as suitable for therapeutic intervention that are ongoing.

The concept of MCI presents 2 main advantages. First, it provides a diagnosis entity for those individuals that have not already reached the threshold of dementia. Second, it allows to shift attention toward the early stages of diseases where treatment might be more efficient and useful, especially those aimed at slowing the disease process. Per contra, there is an ambiguity in the concept that concerns the content, the tenor of one believes that it covers :

- At first glance, it copes with different pathological entities, even though the precise nature of these entities remains unclear besides the well-known degenerative disorders of the CNS. This heterogeneity in the diseases responsible for MCI may hamper the choice of diagnostic criteria (memory impairment alone or cognitive changes as well), the knowledge of evolution (some patients aggravate whereas other are stable or even improved !) and the therapeutic approaches (symptomatic or disease related ?);

- In fact, MCI is considered more and more as a diagnosis category for prodromal AD. Two arguments plead for this interpretation : 1) the choice of memory impairment as the main criterion for MCI ; 2) The fact that up to 80% of subjects with MCI will convert to AD in approximately 6 years. If so, the question is to know whether it is possible today to recognize the disease in its prodromal phase. Unfortunately, there is no reliable biological marker for AD that may help to identify the disease with assurance. Brain imaging may be more useful but the real value at this stage remains to be established, given a certain degree of overlap with results in normal elderly. Indeed, the best way to identify prodromal AD is to characterize the pattern of memory deficits of patients, because it has been clearly defined : 1) low free recall ; 2) weak efficacy of cueing in cued recall ; 3) high proportion of extra-list intrusions (Tounsi et al.). It is therefore possible to identify AD before dementia if one uses specific memory tests that investigate the 3 vulnerable stages (encoding, consolidation and retrieval) that may account for deficit in delayed recall.

To conclude, what is useful for a given individual ? Is it to diagnose MCI, a syndrome of unknown aetiology, or to detect the disease which is responsible for most of the cases, i.e. incipient AD ? The question is opened...

New Antiplatelet Strategies in Stroke Prevention

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Stroke prevention is based on the management of vascular risk factors such as hypertension, tobacco smoking, diabetes... and on the use of antithrombotic drugs : oral anticoagulants and antiplatelet drugs. Obviously antithrombotic treatments addresses only ischemic strokes but they carry a risk of intracranial bleeding and the stronger the antithrombotic effect, the higher the risk of bleeding. The optimal use of antithrombotic drugs depends of the etiopathogenic subtype of ischemic stroke :

atherothrombotic (20%), small artery diseases (25%), cardiogenic embolism (20%), unusual causes (5%) and cryptogenic (30%). Specific randomized trials of anti-thrombotic drugs have been performed only in two groups : atherothrombotic and cardiogenic embolism.

Among antiplatelet drugs effective in stroke prevention, the oldest and most widely studied is aspirin and the most recent still ongoing numerous studies is clopidogrel. A new class of antiplatelet drugs, oral GP II b/III a receptor antagonists, was developed a few years ago and raised much hope. Unfortunately all studies devoted to the secondary prevention of vascular events have been stopped because of increased bleeding and mortality. There has thus been no new effective antiplatelet drug in the last 10 years. New strategies mainly concern new indications and associations of antiplatelet drugs. These will be reviewed according to the subtype of ischemic stroke.

1. Atherothrombotic brain infarction (ABI)

In primary prevention, aspirin is the only drug studied but, in contrast to its 40% reduction in myocardial infarction, aspirin does not reduce the risk of cerebral infarction in low-risk populations. It does however have a preventive effect in patients with vascular risk factors.

In secondary prevention, numerous studies and meta-analysis (ATC 2002) have shown that antiplatelet drugs decrease by 25% the risk of major vascular events (stroke, myocardial infarction and vascular death). This applies to aspirin (75-300 mg), ticlopidine (500 mg), clopidogrel (75 mg) and the combination of dipyridamole (400 mg) + aspirin (50 mg) and possibly to triflusal, a drug very similar to aspirin which has only been studied in one small trial so far.

The most recently published trial is MATCH which compared aspirin 75 mg vs placebo on top of clopidogrel in 7599 patients with a non cardio-embolic TIA or stroke, less than 3 months old, with one additional vascular risk factor : myocardial infarction, angina, another previous ischemic stroke, diabetes or peripheral arterial disease. After a mean follow-up of 17.5 months there was a non significant 6.4% decrease in the composite vascular endpoint counterbalanced by an increase in major bleedings, particularly gastrointestinal.

There are 4 major ongoing randomized clinical trials (RCT) of antiplatelet drugs in ABI prevention :

- CHARISMA is a double blind RCT of clopidogrel vs placebo on top of aspirin 160 mg in 15 000 patients with ABI, myocardial infarction or peripheral arterial disease.
- PROFESS is a double-blind RCT comparing dipyridamole + aspirin vs clopidogrel in about 15 000 patients with ABI or TIA.
- ESPRIT is an open RCT comparing oral anticoagulants vs aspirin (30-325) vs aspirin + dipyridamole in non cardioembolic ischemic stroke or TIA.
- ARCH is an open RCT comparing warfarin (INR 2-3) vs aspirin (75-325) + clopidogrel 75 in patients with a symptomatic 4 mm aortic arch plaque.

2. Small artery diseases of the brain

No specific study of antiplatelet drugs has been performed in this large subtype of stroke but patients with lacunar infarcts have been included in trials of ABI, representing up to 54% of the patients in MATCH. Subgroup analysis suggest that antiplatelet drugs are effective but it will be important to have the results of the first study specifically dedicated to this variety of stroke : SPS 3, comparing clopidogrel and placebo on top of aspirin.

3. Cardiac sources of emboli (OAC)

Oral anticoagulants (OAC) are the drugs of choice for preventing stroke in atrial fibrillation (AF) which accounts for 50% of all cardiogenic emboli as well as in other high-risk sources of emboli. The relative risk reduction (RRR) with warfarin over placebo in primary as well as in secondary prevention is 62 % (48-72%).

The only antiplatelet drug so far studied in AF is aspirin which shows a RRR over placebo of 21%. In the 4 studies which directly compared aspirin and OAC, the RRR was 49% for OAC over aspirin. OAC are thus much more effective than aspirin in the primary and secondary stroke prevention in patients with AF but they carry a higher hemorrhagic risk and are far more inconvenient. This explains the ongoing trials of antiplatelet drugs in high risk AF patients : ACTIVE W, an open RCT comparing OAC vs clopidogrel (75 mg) + aspirin (75-100 mg) and ACTIVE A, a double-blind RCT comparing aspirin (75-200 mg) vs aspirin (75-100) + clopidogrel (75 mg) with a target of 14000 patients.

4) Cognitive impairment and dementia

This is a new area for antiplatelet drugs but since 1) there is a relationship between vascular risk factors and dementia, 2) vascular dementia is the second most frequent cause of dementia, it is tempting to speculate that antiplatelet drugs could have a preventive effect on cognitive decline and dementia.

In conclusion, antiplatelet drugs play an important role in the prevention of ischemic strokes. They are the antithrombotic drugs of choice in the prevention of ABI ; they are the second choice (if OAC are contraindicated) in the prevention of cardiac emboli. They are used – but without firm evidence – in small artery diseases and in cryptogenic strokes. Because of its cost effectiveness, aspirin remains the most widely used but ongoing studies should help to better determine the efficacy of associations of antiplatelet drugs.

Cerebral Venous Thrombosis (CVT)

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CVT is a fascinating condition which differs in all respects from arterial stroke. Although uncommon, it is more frequent than classically though accounting for 0.5% of all strokes and it can occur at all ages from the newborn to the very old, with a slight preponderance in young women because of pregnancy and oral contraceptives.

Its causes and risk factors encompass numerous con-

ditions, including all surgical, gynaecological, obstetric and medical causes of deep vein thrombosis as well as a number of local, infective and non infective, causes. Despite the continuous description of new causes, such as various varieties of congenital thrombophilia, the proportion of cases of unknown etiology remains around 25%. In such cases, a long follow-up with repeated investigations is required.

CVT presents with a huge variety of signs and of modes of onset. The five most frequent signs are headache, papilloedema, focal deficits, seizures and altered consciousness which can occur in isolation or in combination. The mode of onset is predominantly subacute over a few days but it can also be sudden or more progressive, particularly in the frequent cases with isolated intracranial hypertension. Given this wide variety, the clinician must therefore consider CVT in all recent brain syndromes, and perform the appropriate investigations. MRI + MRA is the best tool both to detect the parenchymal lesions and to diagnose the thrombosed sinuses. It should thus be performed as first line investigation when CVT is suspected. If MRI is not possible, CT scan with venous angioCT is a good alternative. Conventional angiography may still be required particularly in isolated cortical vein thrombosis.

The prognosis of CVT is much better than classically thought, with a 30 days mortality < 10% in recent series and 3.8% in the 624 patients included in the international CVT study (ISCVT). Although many factors of poor prognosis have been identified the outcome remains largely unpredictable. Sequelae occur in about 15-20% of cases in recent series.

By contrast to arterial stroke, Heparin (or LMWH) is the treatment of choice, even in cases with haemorrhagic lesions. It should be associated with symptomatic measures (anticonvulsants, analgesics, and measures to reduce intracranial hypertension) and whenever possible, with the treatment of the cause. If the patient deteriorates despite this antithrombotic, symptomatic and etiologic treatment and if there is no other cause of deterioration than the thrombosis itself, a local clot extraction or thrombolysis may be attempted. Afterwards, according to the cause, oral anticoagulation with INR 2-3 is performed for at least 6 months.

Clinical Approaches to Neuropathies

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Polyneuropathy consists of the triad of sensory changes in a glove and stocking distribution, distal weakness, and hyporeflexia. Certain types of neuropathy may show widespread sensory symptoms, and others may begin with more prominent proximal weakness. Positive sensory symptoms result from ectopic impulse generation and autoexcitation of myelinated afferent fibers. In general, but not always, normal muscle stretch reflexes

speak against peripheral neuropathy. Acute pandysautonomic neuropathy characteristically shows severe post-ganglionic sympathetic and parasympathetic dysfunction, with relative or complete sparing of motor and sensory function. Milder autonomic dysfunction also accompanies most peripheral neuropathies, but manifests clinically detectable symptoms only in a few conditions, such as diabetes, amyloidosis, Guillain-Barré's syndrome, porphyria, and familial dysautonomia. Such autonomic disturbances usually result from acute demyelination or damage to small myelinated and unmyelinated fibers.

A detailed history often reveals general medical conditions such as diabetes, alcoholism, renal disease, malignancies, sarcoidosis, periarteritis nodosa, amyloidosis and infectious processes such as diphtheria and leprosy. Inflammatory neuropathies include Guillain-Barré's syndrome and chronic inflammatory demyelinating neuropathy. Metabolic neuropathies result from nutritional deficiencies or the toxic effects of drugs or chemicals. The family history is essential in establishing the type of inherited conditions associated with polyneuropathy. Sometimes a patient's own account may not provide sufficient information, necessitating independent examination of family members. For some patients with an unequivocal diagnosis of polyneuropathy, extensive studies may fail to uncover the exact etiology. Hereditary and immune mediated polyneuropathy account for most cases. In one study, intensive evaluation permitted classification of 76% of 205 patients with initially undiagnosed neuropathy; the final diagnoses included inherited disorders in 42%, inflammatory-demyelinating polyradiculoneuropathy in 21%, and neuropathies associated with systemic disorders in 13%.

Anatomic diagnosis depends on clinical and electrodiagnostic evaluation, but few specific patterns of peripheral nerve involvement characterize a given disorder. Nerve conduction and electromyographic studies delineate the extent and distribution of the lesions, and differentiate two major pathologic changes in the nerve; axonal degeneration and demyelination. An index based on multiple electrophysiologic measures against standard norms may provide a better overall estimation as reported in the assessment of diabetic polyneuropathy. Electrical studies alone rarely distinguish clinical types of neuropathies or establish the exact etiology in a given case. Arriving at a specific diagnosis and establishing a course of therapy depend heavily on clinical, electrophysiologic and histologic assessments.

Despite the unpredictable nature of traumatic injuries, certain individual nerves are predisposed to isolated damage. These include the long thoracic, suprascapular, musculocutaneous and axillary nerves in the shoulder girdle, and the lateral femoral cutaneous, femoral and sciatic nerves in the pelvic girdle. Injuries resulting from acute or chronic repetitive external pressure produce compressive neuropathy, whereas chronic distortion or angulation of the nerve from an internal source causes entrapment neuropathy.

Entrapment syndromes develop at the common sites of chronic or recurrent constriction of the radial, median, ulnar, common peroneal and tibial nerves. Certain types of peripheral nerve disorders may develop occupationally. For example, instrumentalists may suffer from symptoms of cervical radiculopathies, thoracic outlet syndrome, and median, ulnar, and digital neuropathies. A number of different nerve lesions also result from stretch, ischemia, compression or laceration during a surgical procedure. Unusual sites of involvement may suggest rare anomalies such as congenital ring constrictions of peripheral nerves.

Focal weakness of an arm may follow segmental herpes zoster affecting the same limb. Neurophysiologic investigation has localized the lesion at the root, plexus or peripheral nerve level. In one series, 21 of 40 patients had the evidence of denervation, suggesting widespread subclinical motor involvement. Another study found no correlation between the degree of post-herpetic neuralgia and electrophysiologic abnormalities, with the inference that pain has little to do with the damage to the large-diameter sensory fibers in this condition. Topical application of aspirin dissolved in chloroform induces prompt relief of pain for 2-4 hours.

In one study involving 169 athletes, one third of 190 sports injuries occurred while playing football. The most common injuries included, in addition to burners and stingers representing cervical radiculopathies, median, axillary, ulnar, suprascapular and peroneal mononeuropathies. Bodybuilders also develop rare mononeuropathies of the upper limb most commonly involving thoracodorsal, dorsoscapular, suprascapular and medial pectoral nerves. Acute focal neuropathies also affect weight lifters who develop usually sudden, painless weakness in a muscle supplied by a terminal motor nerve branch.

Many instrumental musicians suffer from entrapment neuropathies, most commonly carpal tunnel syndrome and ulnar neuropathy. The available information regarding ulnar neuropathy suggests that violinists and violists tend to develop symptoms depending on their playing position. Ulnar neuropathy may initiate or sustain a hand dystonia by inducing a central disorder of motor control. Conservative treatment, which provides relief for a substantial percentage of patients, consists of modification in playing technique or time, splinting, and medication. Surgical decompression is an effective alternative. The specific diagnoses most likely to require surgery include trigger digits, carpal tunnel syndrome, ulnar nerve entrapment, rheumatoid arthritis and Dupuytren's contracture. Nerve conduction and electromyographic studies help confirm the diagnosis, establish the extent and type of pathology, detect coexisting peripheral nerve disorders and determine the efficacy of therapy.

In one study, 9 of 520 patients who underwent liver transplantation developed mononeuropathy involving the peroneal nerve, radial nerve and cutaneous branch of the femoral nerve. In another study, 10% of liver transplant recipients developed focal peripheral nerve lesions,

most commonly involving the ulnar nerve. The operative procedures during hip arthroplasty may injure a number of nerves travelling in the vicinity for different reasons such as compression, traction, and ischemia. These include the peroneal division of the sciatic nerve, femoral nerve and gluteal nerve, and superior gluteal nerve.

The diagnosis of a focal nerve lesion depends on elucidation of weakness and atrophy of all muscles supplied by the nerve distal to the lesion. Sensory findings, that usually appear earlier, provide less reliable localizing signs than motor deficits, particularly in the upper limbs, where sensory dermatomes overlap considerably. Electrodiagnostic studies help localize and characterize a focal lesion if conducted as an extension of a physical examination in a proper clinical context. Electromyographic examination delineates the exact distribution of denervated muscles in localizing a focal nerve lesion. In demyelinating or other neuropathic conditions, a reduced recruitment of motor units despite the preservation of the axons signals a conduction block. The pattern of distribution here also helps elucidate the zone of involvement.

Nerve conduction studies may provide the evidence of conduction abnormalities, which usually precede axonal degeneration in a compression neuropathy. Stimulation above and below the suspected site of lesion will document not only the slowing of conduction velocity, but also changes in amplitude and area of the muscle or nerve action potential as indices of functional block. Such a pattern of abnormalities often helps differentiate an entrapment syndrome from a diffuse neuropathy. This distinction, however, may blur in certain types of polyneuropathy that, in early stages, mimic a localized pathology at the common sites of compression.

Electrophysiologic evaluations play an important role in determining the outcome of mononeuropathies produced by a single episode of limb trauma. In an axonal injury, amplitude loss begins on days 3-5 for compound action potentials and days 5-7 for sensory nerve action potentials. With complete axonal degeneration, conduction studies alone cannot provide conclusive evidence for or against neurotmesis, or loss of continuity. In clinically suspected cases of transection, failure to demonstrate evidence of reinnervation in 2-3 months calls for surgical exploration for suture or grafting. In studies of finger amputation, and toe-to-digit transplantation, early surgical intervention prevented retrograde degeneration, improving recovery of function.

Bilateral Subthalamic Stimulation for Parkinson's Disease Using Stereotactic MRI and Electrophysiological Guidance

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Bilateral subthalamic deep brain stimulation (STN-DBS) has become a widely used technique in the treatment of Parkinson's disease (PD).

Between October 1999 and September 2004, 52 patients with severe PD and disabling levodopa-induced dyskinesia (LIDs) underwent STN-DBS. Only 46 of them completed the three months assessment. Patients' age ranged from 31 and 78 years old. Before surgery the mean SEM UPDRS III motor subscore was 56.6 ± 4.2 , mean motor fluctuations and LIDs scores were 5.1 ± 0.3 and 6.5 ± 0.6 respectively. They received a mean daily levodopa and pergolide equivalent agonist dose of 1082 ± 113 mg and 2.3 ± 0.5 mg respectively. Patients underwent bilateral STN implantation of DBS electrodes using a T1 volumetric stereotactic MR (3D-SteMR), a multiplanar T2 SteMR for direct visualization of the STN coupled with an electrophysiological recording and stimulation guidance. Three months after surgery, motor signs were assessed using the UPDRS III under continuous bilateral stimulation in the "OFF" drug conditions. LIDs and motor fluctuations were assessed using the UPDRS IV subscores.

RESULTS : All patients improved under STN stimulation. There was a dramatic improvement of all PD features with an 87% reduction of motor fluctuations and 80% of dyskinesias. Mean UPDRS III subscore improved by 75% Levodopa and pergolide equivalent daily doses were decreased by 90% and 38% respectively (all results were significant with a $p < 0.001$).

COMPLICATIONS : One patient had an infection of the left connecting cable. Another had a hemispheric right frontal bleeding with transient hemiparesis and somnolence. Hematoma was surgically removed and electrodes kept in place with a general improvement of 60% in motor function.

CONCLUSION : Bilateral STN-DBS is a safe and effective approach in the treatment of advanced PD.

Tics and Gilles de la Tourette's Syndrome Diagnosis and Management : Update

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Tics are sudden brief, intermittent movements (motor tics), or sound (vocal or phonic tics). They typically consist of simple or coordinated, repetitive or sequential movements, gestures, and utterances that mimic fragments of normal behavior. Tics may be voluntarily suppressed by few minutes, although these suppression leads to rising tension and disquiet, which is inevitably followed by the "release" of bout of tics. The ability of patients to suppress their tics, helps to distinguish tics from others hyperkinetic disorders such as chorea, dystonia, myoclonus. Tics are attenuated by intense concentration, pleasurable pastimes, sexual arousal and alcohol, and tend to be worse at time of anxiety, anger, or self-consciousness. Tics may disappear or persist during all stage of sleep. Tics are more evident in public places and social gathering than, for example, in the doctor consulting rooms. Another characteristic of tics are their sug-

gestibility : the patient may incorporate a new – suggested – tic in his repertoire of tics. Motor and phonic tics occur in bouts over the course of the day, may change character within the same person and typically wax and wane in severity over the course of the weeks to months.

Gilles de la Tourette's disease, the most common cause of tic is defined by the association of motor and phonic tics, coprolalia, and variable and complex behavioral abnormalities including abnormal repetitive behavior, obsessive-compulsive behavior, self-mutilation behavior and various psychopathologies.

The management of tics may be difficult, as no long-term effective treatment is available, and requires a multidisciplinary approach, including educational intervention and behavioral therapies, pharmacological therapies (mainly based on dopamine antagonist drugs). In most severe cases preliminary results suggest that deep brain stimulation applied within the limbic territories of the basal ganglia can significantly improve tics and self-mutilation.

History of Neurosciences in Lebanon

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The history of neurosciences in Lebanon may represent a shortcut of their evolution in the countries of Europe and North America. In a period of less than half a century, including the first and second World War, the French mandate, and the beginning of independence, the most essential parts of the academic and hospital structures were placed in position. After that period, progress improved swiftly. At the present time, the new technological and therapeutic acquisitions are applied in a delay becoming shorter, with regard to the country of origin.

PSYCHIATRY

The psychiatry was the first branch of neurosciences to be separated from internal medicine.

In 1896, a Swiss Quaker, Theophilus Waldemeier, founded the first mental hospital of the Middle East, and named it "The Lebanon Hospital for Mental and Nervous Disorders". It was better known locally as Asfourieh. Since its foundation, this hospital worked in close cooperation with the American University of Beirut (AUB) born in 1863. The earlier psychiatrists were Scotch (Dr Watson Smith, Dr Ferguson Miller and Dr Robert Miller). The first Lebanese psychiatrist was Dr Antranig Manoukian who started his work in 1939. The hospital contracted with many of the Middle East countries to treat their mental cases, and for the training of young psychiatrists and mental health personnel. The staff of this hospital gradually grew to include famous psychiatrists like Dr Jean Hayeck, Dr Antoine Shakh-toura, Dr Joseph Haykal, Dr Ala'el-Dine Drooby and

Dr Fuad Antoun. In 1974, negotiations were started to sell the premises, and a new hospital was built in Aramoun. Unfortunately, it was destroyed during the war in 1982, and that was the end of the institution.

Meanwhile, another psychiatric institution was established by a Lebanese Capuchin friar, Father Jacques Haddad. As early as 1925, an "Asylum for the Poor and Disabled" was entrusted to the newly formed Franciscan Sisterhood of The Cross, headed by Mother Marie. In 1929, Dr Georges Stephan was the physician of the place, which became progressively the "Psychiatric Hospital of the Cross" in 1951, in cooperation with the French Faculty of Medicine, born in 1881. The precursors were Dr Maurice Potet and Dr Albert Brousseau in 1943, followed by Lebanese psychiatrists Dr Henri Ayoub and Dr Edouard Azouri in 1951.

The electroshock treatment was used since 1948. The Sakel insuline therapy was used between 1951 and 1958. The first neuroleptic drug, phenothiazine, was used in 1951, nearly at the same time of its discovery in France.

At the present time, the Lebanese group of psychiatrists is about 60 members, almost all trained in Europe or North America, and representing the majority of the current methods, going from drug therapy to the different forms of psychotherapy or psycho-analysis.

NEUROLOGY

The birth of neurology as a distinct specialty is more recent.

There was some precursors who were teaching and practising neurology while they were responsible for another branch of internal medicine. Between 1934 and 1950, Dr Yves Poursines was pathologist and consultant of neurology in the French Faculty and in the Hôtel-Dieu de France Hospital, built in 1922. In the American University, before 1948, a virologist from Rochester, Dr Howard Slavin, was in charge of neurology teaching.

In 1946, and upon the suggestion of Dr Miller, then Dean of AUB Medical School, Dr Fuad Sabra decided to travel to New York to further his training in neurology at the Montefiore Hospital and at Columbia University. After a full year of training, he returned to Beirut in 1947 to establish the first division of neurology in AUB. In 1948, Dr Sabra set up the first EEG laboratory in the Middle East.

He was followed in 1962 by Dr Edmond Rahme, and in 1964, by Dr Riad Khalifeh, the first Lebanese to obtain the American Board of Neurology.

In 1967, Dr Jean Rebeiz returned from Boston and established the first Neuropathology laboratory in the country. In 1968, he was also the first author to describe the "Corticodentatonigral Degeneration With Neuronal Achromasia", better known as "Cortico-basal Degeneration".

At Hôtel-Dieu de France, the first neurologist was Dr Joseph Hajjar, who arrived in 1952, coming from Marseille and London. He started EEG in 1955, and the first electromyography in the country in 1957. He per-

formed some carotid angiographies using the primary technique, through a surgical denudation. Very soon after, in 1954, Dr Sami Tohme introduced the percutaneous angiography and the pneumoencephalography as routine in the French hospital. He was followed by Dr Raymond Chemaly in 1965, holding the first French Stateboard of Neuropsychiatry.

After the sixties, the number of neurologists increased, reaching 124.

In January 1995, Dr Mohamad Mikati, who was the first epileptologist in the country, started the first epilepsy program in the region. This program included basic and clinical research and inpatient video-EEG long-term monitoring for diagnosis and presurgical workups of epilepsy.

One of the most exciting new therapeutic experience was also the use of thrombolysis, by intra-arterial route in 1996, and intravenous since 1999.

NEUROSURGERY

The neurosurgery came to the scene in third position, during the second half of the twentieth century.

Before that, it was very infrequent to open a skull or a back. This was done by general surgeons, since the third decade of the century. At that time, a patient needing neurosurgery had to travel to the western countries.

Dr Fuad Sami Haddad, in AUB, fell in love with neurology, as he said himself, after learning it with the visiting professor Dr Howard Slavin. He began teaching neurophysiology at AUB in 1948. Two years later, Dr Wilder Penfield, passing through Beirut, and finding out that there was no trained neurosurgeon in the Middle East, suggested to Dr Haddad to do neurosurgery. In 1954, Dr Haddad came back to AUB, holding the Canadian FRCS and the American Board of Neurosurgery.

In 1955, he founded the Lebanese Society of Neurology, Neurosurgery and Psychiatry. Its membership included eleven psychiatrists, three neurologists and one neurosurgeon.

In 1961, the second Lebanese neurosurgeon arrived in Beirut. Dr Gedeon Mohasseb, holding the French Agregation, established the second neurosurgical unit in the country, at Hôtel-Dieu Hospital. He added a new dimension to neurosurgery by introducing novel procedures, among others the trans-sphenoidal approach to the pituitary gland, the thalamotomy for Parkinson's disease, and the ventriculo-peritoneal shunting.

After these two pioneers, the following team included Dr Sami Nassar, Dr Kamal Refka and Dr Salim Ghostine.

Later on, the number of neurosurgeons increased. The total number is now 110.

Talking about the latest procedures, the stereotaxis for the tumors was introduced by Dr Nabil Okais in Hôtel-Dieu in 1994, the surgery for epilepsy by Dr Youssef Comair in AUB in 1997, and the deep brain stimulation for Parkinson's disease in 1999 by Dr Paul Bejjani and Dr Georges Nohra in N.-D. des Secours Hospital in Byblos, and by Dr Youssef Comair in AUH.

NEURORADIOLOGY

The neuroradiology had a parallel evolution.

The first period could be qualified as related to crafts, the procedures being performed by the neurologists and the neurosurgeons themselves, after they had been trained for that. These techniques were carotid angiography, pneumo-encephalography, ventriculography and myelography, with manual seriography. They were very painful for the patient, tiring and time consuming for the specialist, and not always satisfactory.

In 1967, the first neuroradiologist, Dr Naim Atallah, came to the AUH, and the catheterization and automatic seriography became a routine procedure. The same happened in Hôtel-Dieu with Dr Pierre Zalzal in 1973. Now, there is, at least, 22 angiography units in the country.

The third period of the neuroradiology was the revolution brought about by the CT scan, the first one being established in Hôtel-Dieu Hospital in February 1980 by Dr Sami Tohme. The MRI was retarded because of the war, and we had to wait for the first one until September 1991, when it was brought to the Lebanese Hospital (Geitaoui) by Dr Naim Atallah.

The number of these machines grew up very quickly, reaching, at the present time, 64 scanners, 25 MRI, and 2 PET-scan

ANCILLARY SPECIALTIES

The other specialties were developed following the arrival of the qualified specialists.

The EEG was first in AUH in 1948, with Dr Fuad Sabra, then in Dr Joseph Hajjar clinic in 1955, and in the Hôtel-Dieu Hospital in 1959, with Dr Sami Tohme. At the present time, almost every hospital and every neurologist has an EEG.

The EMG was first in the private clinic of Dr Hajjar in 1957, then in AUH in 1969, in Hôtel-Dieu in 1991 with Dr Salam Koussa, and in Saint-Georges Hospital in 1993 with Dr Antoine Aouad. Now, it is present in many hospitals and private clinics.

The neuropathology had its first laboratory in AUH with Dr Jean Rebeiz in 1967. Later on, Dr Gerard Abadjian developed in Hôtel-Dieu the diagnosis of brain tumors in 1991 after a special training in France with Dr Daumas-Duport, and the pathology of muscular diseases in 2001.

The electron microscope was introduced in 1966 in AUB by Dr Adel Afifi, but was stopped after the war in the seventies, and Dr Afifi went to the USA. Another electron microscope was set up in the French Faculty of Medicine, with Father Johan De Witt in 1973. It was stolen during the war in 1975.

ACADEMIC SOCIETIES

The golden age of the development of the Lebanese Society of Neurology, Neurosurgery and Psychiatry was during the sixties. Because of the increasing number of specialists, the society was split into three divisions in 1970, with a common board. In 1992, the number of participants and the divergence of their interests led to the separation into three different societies.

RESIDENCY PROGRAM

The great number of qualified specialists certainly improved the teaching of neurosciences in the faculties. At the end of the eighties, a Residency Program was started for the three branches of neurosciences in the main universities. A complementary training program is also available in many French and American centers and in other countries. A part of our former residents are working in Lebanon, some of them continue their career in Europe or the USA.

CONCLUSION

At the end of this review, it is encouraging to see how the medical branches concerned by the nervous system, have achieved their itinerary from birth to a prominent level of quality. It is our duty to take up the challenge and to go behind the progress.