GUILLAIN-BARRE SYNDROME

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STATEMENTS

1. **Guillain-Barré Syndrome (GBS) is the most frequent cause of acute peripheral paralysis.**

2. **GBS is secondary to an acute immune-mediated polyneuropathy**

3. **GBS can be differentiated in various clinical and electrophysiological sub-types**

4. **Its gravity includes respiratory failure, cardio-vascular autonomic dysfunction, and long-term disability**

INCIDENCE

1. **INCIDENCE: 0.5–2.0 cases/100 000/year**
2. **SEX RATIO (F/M): < 1.0**
3. **AGE RATIO (O/Y): > 1.0**
4. **OUTBREAK: NO SEASONAL VARIATION**
5. **PRECEDING SYMPTOMS: 70-90%**

MISSIONS

- **DIAGNOSTIQUER**
  - Eliminer un syndrome medullaire aiguë
  - Eliminer une méningoradiculite
  - Eliminer une autre cause de paralysie aiguë périphérique
  - Eliminer une maladie systémique, une néoplasie, une carence, une pathologie métabolique (porphyrie)

- **ANTICIPER UNE IRA**

ACUTE FLACCID WEAKNESS

SENSORIMOTOR PARALYSIS

1. ± MRI
2. CSF ANALYSIS
3. BLOOD TESTS (ESR)
4. EMG (Axonal PN, Demyelinating PN)

PURE MOTOR PARALYSIS

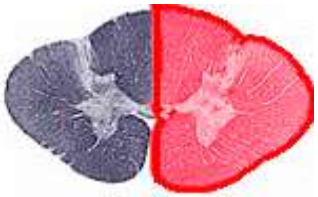
1. BLOOD TESTS (K+)
2. CSF ANALYSIS
3. EMG (Myopathy, NMJ, Neuropathy)

SPINAL CORD SYNDROMES

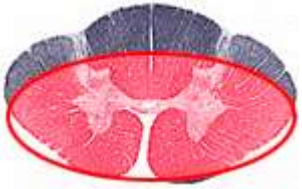
Complete transection

ALS

Posterior spinal artery



Brown Séquard



Anterior spinal artery

Poliomyelitis

Syringomyelic

Subacute combined degeneration

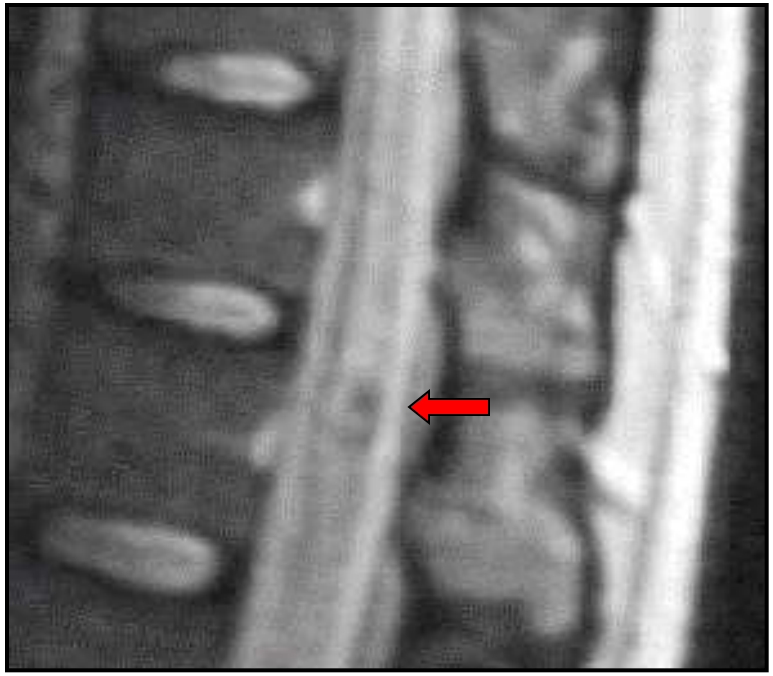
ACUTE SENSORIMOTOR HYPOREFLEXIC PARALYSIS

Pyramidal signs

Sensory level

Cauda-equina syndrome

SPINAL CORD MRI



ACUTE SENSORIMOTOR HYPOREFLEXIC PARALYSIS

	ESR NORMAL	ESR INCREASED
CSF NORMAL	TOXIC (Thallium, arsenic…) METABOLIC (Gly, Vit …) VASCULITIS (SLE…) PRIMARY GBS	VASCULITIS (SLE…)
INCREASED CSF CELLS	MENINGORADICULITIS	MENINGORADICULITIS
INCREASED CSF PROTEIN	PRIMARY GBS CANCER, LYMPHOMA, VASCULITIS, DIPHTERIA, HIV.	CANCER, LYMPHOMA, VASCULITIS, DIPHTERIA, HIV.

PURE MOTOR HYPOREFLEXIC DEFICIT

	SIGNS	K+	CSF	EMG
PERIODIC PARALYSIS	EXERCISE	↑↓	↔	MYOPATHY
MYASTHENIA GRAVIS	VARIATION EYE MVT	↔	↔	NM JUNCTION
BOTULISM	FOOD POISONNING PUPILL	↔	↔	NM JUNCTION
POLIO MYELITIS	TRAVEL DIARRHEA	↔	↑ CELLS	ANTERIOR HORN CELLS
PORPHYRIC NEUROPATHY	CONFUSION PAIN	↔	↔	POLY NEUROPATHY
PRIMARY GBS	INFECTION ASCENDANT	↔	↑ PROTEIN	POLY NEUROPATHY

CRITERES DIAGNOSTIQUES

Criteria for the diagnosis of typical Guillain-Barré syndrome (GBS) (adapted from Asbury [7])

Features required for diagnosis:

- progressive weakness in both arms and both legs;
- areflexia.

Features strongly supporting diagnosis:

- progression of symptoms over days to 4 weeks;
- relative symmetry of symptoms;
- mild sensory symptoms or signs;
- cranial nerve involvement, especially bilateral weakness of facial muscles;
- recovery beginning 2–4 weeks after progression ceases;
- autonomic dysfunction;
- absence of fever at onset;
- high concentration of protein in cerebrospinal fluid, with fewer cells than $10 \times 10/L$;
- typical electrodiagnostic features;
- pain (is often present).

Features excluding diagnosis:

- diagnosis of botulism, myasthenia, poliomyelitis, or toxic neuropathy;
- abnormal porphyrin metabolism;
- recent diphtheria;
- purely sensory syndrome, without weakness.

Van Doorn et al – Press Med - 2013

DIAGNOSTICS DIFFERENTIELS

Features that should raise doubt about the diagnosis

- Marked persistent asymmetry of weakness.
- Bladder or bowel dysfunction at onset.
- Persistent bladder or bowel dysfunction.
- Sharp sensory level.
- Severe pulmonary dysfunction with limited limb weakness at onset.
- Severe sensory signs with limited weakness at onset.
- Fever at onset of neurological symptoms.
- Increased number of mononuclear cells in CSF ($> 50 \times 10^6$/L).
- Polymorphonuclear cells in CSF.

Pas de syndrome confusionnel
Pas de syndrome inflammatoire
ps d'hypercellulorachie

Van Doorn et al – Press Med - 2013

Differential diagnosis of Guillain-Barré syndrome (GBS)

Intracranial/spinal cord:

- brain stem encephalitis, meningitis carcinomatosis/ lymphomatosis, transverse myelitis, cord compression.

Anterior horn cells:

- poliomyelitis, West Nile virus.

Spinal nerve roots:

- compression, inflammation (e.g. Cytomegalovirus), CIDP, meningitis carcinomatosis/lymphomatosis.

Peripheral nerves:

- drug-induced neuropathy, acute intermittent porphyria, critical illness polyneuropathy, vasculitic neuropathy, diphtheria, vitamin B1 deficiency (Beri-beri), heavy metal or drug intoxication, tick paralysis, metabolic disturbances (hypokalaemia, hypophosphatemia, hypermagnesia, hypoglycemia).

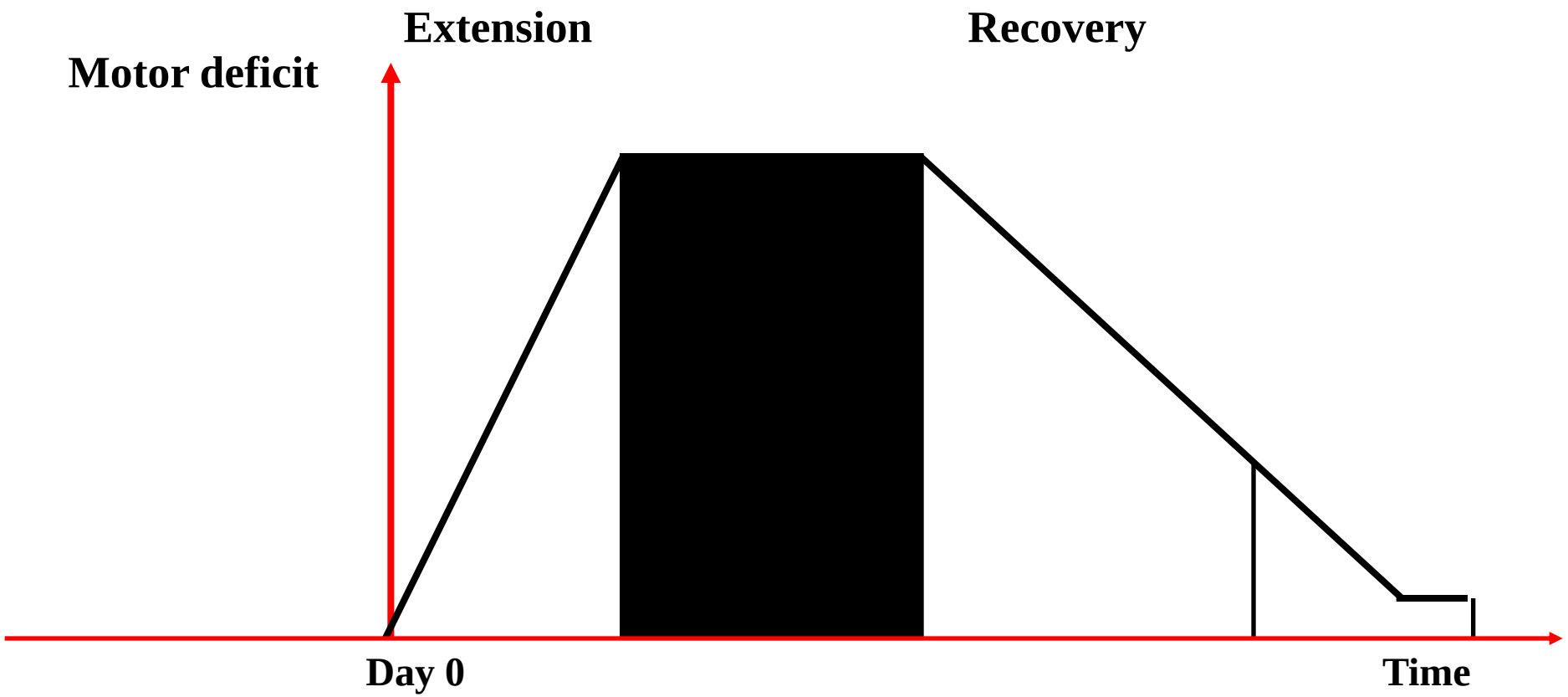
Neuromuscular junction:

- myasthenia gravis, botulism, organophosphate poisoning.

Muscle:

- critical illness polyneuromyopathy, polymyositis, dermatomyositis, acute rhabdomyolysis.

GUILLAIN-BARRE SYNDROME COURSE



SUBTYPES

1. **Acute inflammatory demyelinating polyneuropathy (AIDP)**
2. **Acute motor axonal neuropathy (AMAN)**
3. **Acute motor and sensory axonal neuropathy (AMSAM)**
4. **Miller Fisher syndrome (MFS)**

PATHOPHYSIOLOGY

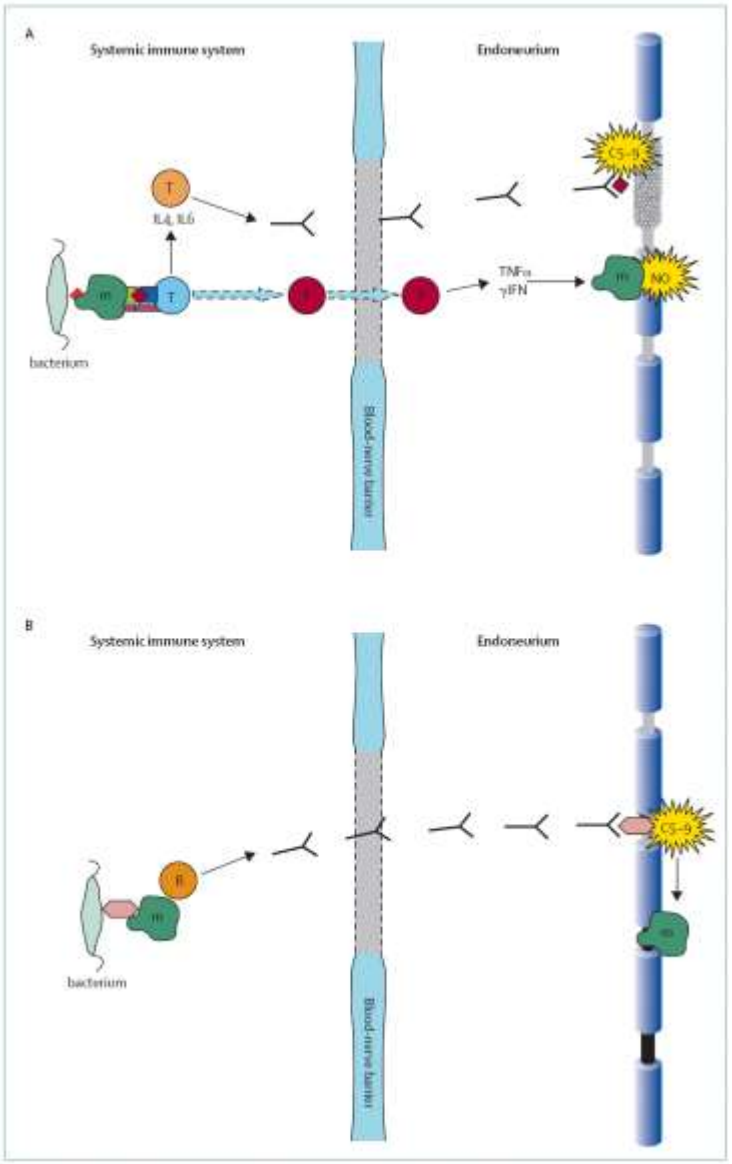


Figure 3: Immune mechanisms in (A) AIDP, and (B) AMAN, AMSAN, and Fisher's syndrome

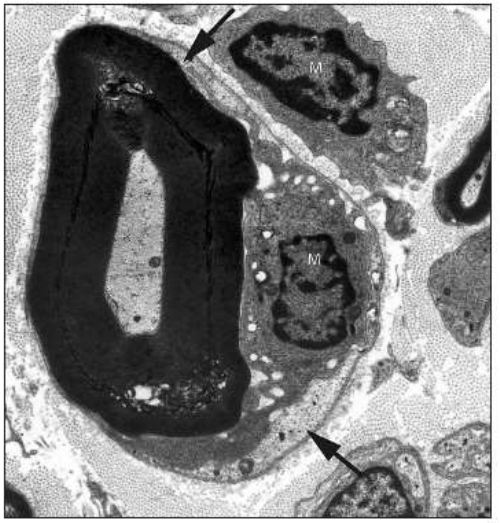


Figure 1: Nerve fibre from patient with AIDP

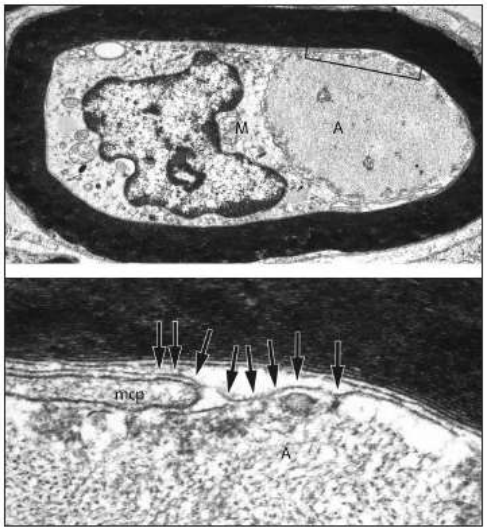


Figure 2: Nerve fibre from patient with AMAN

Hughes and Cornblath - Lancet - 2005

ANTIGANGLIOSIDE ANTIBODIES

	Antibodies
Acute inflammatory demyelinating polyradiculoneuropathy (AIDP)	Unknown
Acute motor and sensory axonal neuropathy (AMSAN)	GM1, GM1b, GD1a
Acute motor axonal neuropathy (AMAN)	GM1, GM1b, GD1a, GalNac-GD1a
Acute sensory neuronopathy	GD1b
Acute pandysautonomia	
Regional variants	
Fisher's syndrome	GQ1b, GT1a
Oropharyngeal	GT1a
Overlap	
Fisher's syndrome/ Guillain-Barré-syndrome overlap syndrome	GQ1b, GM1, GM1b, GD1a, GalNac-GD1a

Table 1: **Classification of Guillain-Barré syndrome and related disorders and typical antiganglioside antibodies, by pathology**

Hughes and Cornblath - Lancet - 2005

ADMISSION

1. **ASCENDANT WEAKNESS (70%)**
   - **Flaccid symetric areflexic weakness**
   - **Pure motor deficit: 18%**

2. **SENSORY SYMPTOMS (50 à 80 %)**
   - **Paresthesia, pain**
   - **Superficial and deep sensory impairment**

3. **CRANIAL NERVES**
   - **VII: 24-55%; IX-X: 6-46%; III-IV-VI: 5-13%**
   - **XII: 1 - 13%**

4. **DYSURIA (10 - 30%)**

SCALES

Disability grade

Table I Guillain-Barré syndrome disability scale

0. Healthy
1. Minor symptoms or signs of neuropathy but capable of manual work/*capable of running*
2. Able to walk without support of a stick (*5 m across an open space*) but incapable of manual work/*running*
3. Able to walk with a stick, appliance or support (*5 m across an open space*)
4. Confined to bed or chair bound
5. Requiring assisted ventilation (*for any part of the day or night*)
6. Death

The original scale is shown in regular print (Hughes *et al.*, 1978) and subsequent modifications in *italics* (Plasma Exchange/Sandoglobulin Guillain-Barré Syndrome Trial Group, 1997).

MRC sum score

Functions assessed
- Upper extremity: wrist flexion, forearm flexion, shoulder abduction
- Lower extremity: ankle dorsiflexion, knee extension, hip flexion

Score for each movement
- 0–No visible contraction
- 1–Visible muscle contraction, but no limb movement
- 2–Active movement, but not against gravity
- 3–Active movement against gravity
- 4–Active movement against gravity and resistance
- 5–Active movement against full resistance

Maximum score: 60 (four limbs, maximum of 15 points per limb) [normal]

Minimum score: 0 (quadriplegia)

Kleyweg et al. - Muscle Nerve - 1991

SEVERITY AT ADMISSION

1. SWALLOWING IMPAIRMENT

- **In 6 to 46%**

2. RESPIRATORY DYSFUNCTION

- **Respiratory symptoms in 40 to 60%**
- **Vital capacity < 1 L in 16%**

3. CV AUTONOMIC DYSFUNCTION

- **in about 15%**
- **Correlated with weakness**

ANTICIPATING ACUTE RESPIRATORY FAILURE IN GUILLAIN-BARRE SYNDROME

MECHANICAL VENTILATION

1. **Required in 20 to 30%**
2. **Median time from admission to MV: 2 days**
3. **Median MV duration: 21 days**
4. **Up to 1/3 weaned from MV within 3 weeks**

MECHANISMS

IX-X

Bulbar dysfunction

Aspiration

Hypoxaemia

↓ cough

Atelectasia

Phrenic

Accessory

Diaphragm

T8-T12

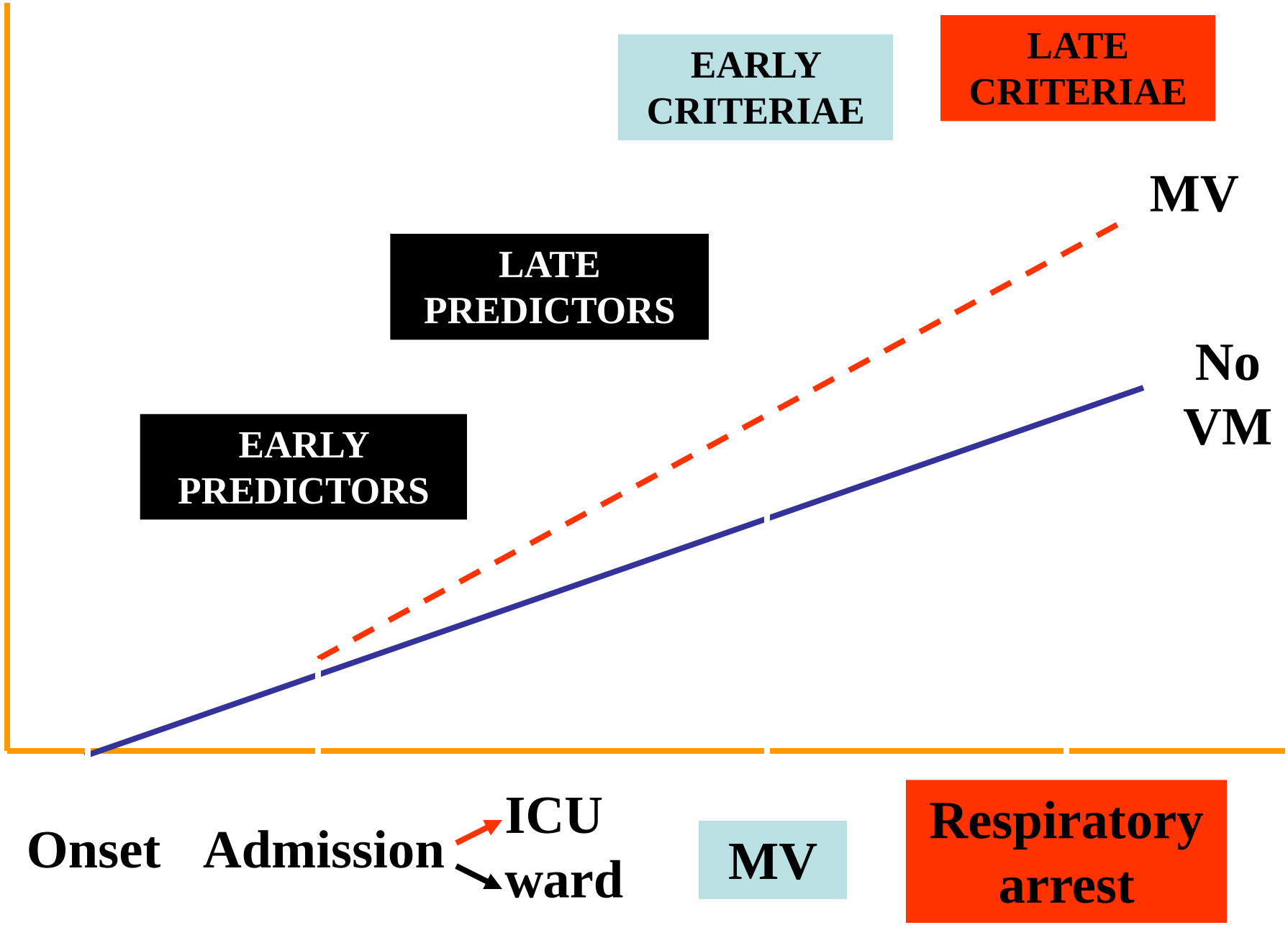
Abdominal

↓ CV

↓ Pi_{max}

↓ Pe_{max}

Hypoventilation


EARLY CRITERIAE
LATE CRITERIAE
MV
LATE PREDICTORS
No VM
EARLY PREDICTORS
Onset
Admission
ICU
ward
MV
Respiratory arrest

CRITERIA FOR INTUBATION

MAJOR CRITERIA

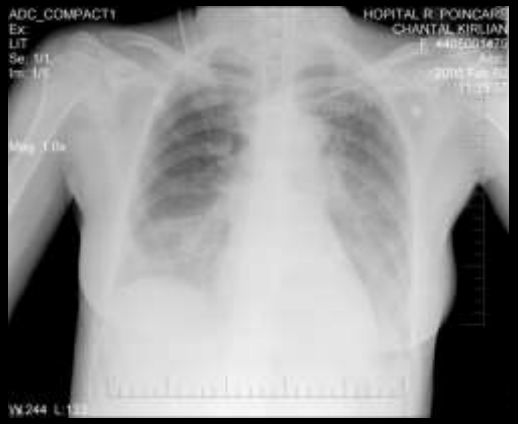
1. **Signs of respiratory distress**
2. **VC< 15 ml/kg, Pi_{max} ou Pe_{max} < 25 cm H_2O**
3. **$PaCO_2$ > 6,4 kPa**
4. **PaO_2 < 7.5 kPa (FiO_2= 0,21)**

MINOR CRITERIA

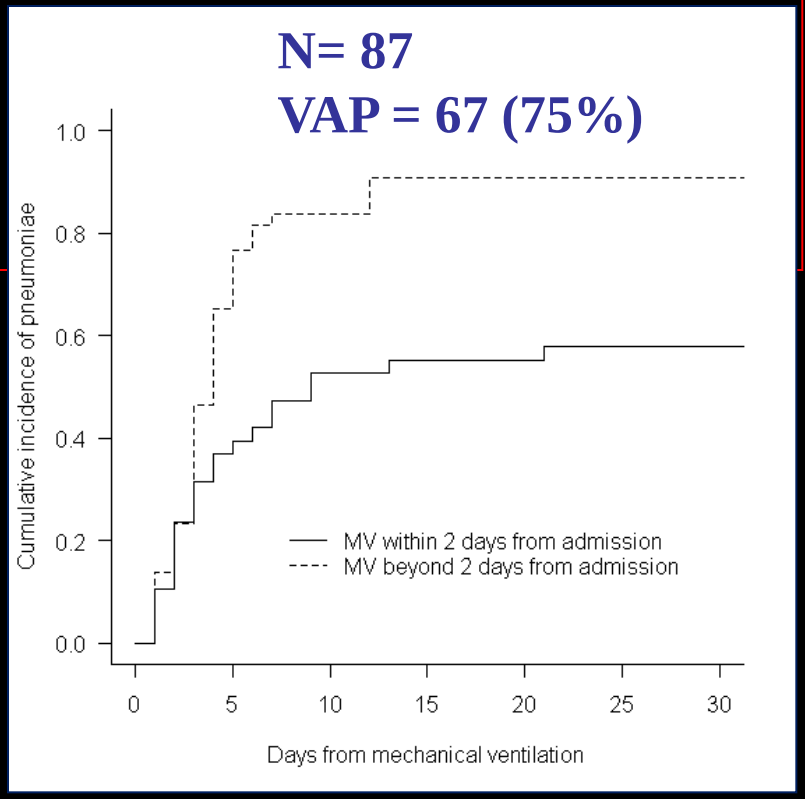
1. **Expectoration inefficient**
2. **Severe bulbar dysfunction**
3. **Atelectasis**

Ropper *Neurology* 1985 - Wijdicks *Neurology* 1998

THE RISKS



- **RESPIRATORY AND CARDIAC ARREST**
- **ASPIRATION**
- **ARDS**



Orlikowski et al - ICM - 2007

BLOOD GASES « FAUX-AMIS »

1. **Presence of hypercapnia or hypoxemia indicates a severe respiratory muscle weakness and misgives an impeding respiratory arrest**

2. **Conversely, absence of blood gases abnormality does not rule out severe respiratory muscle weakness**

HYPOXEMIA

- **Can be induced by increased $PaCO_2$**
  - **physiological law**
  - **Check that decrease in PAO_2 is explained by increase in PaO_2**
- **Pneumoniae, atelectasia…**
  - **Check the chest x Ray**
- **Pulmonary embolism**
  - **To be suspected if chest x ray is normal**
  - **Frequent in this patient**

EARLY PREDICTORS

n = 722

INABILITY	OR	95% CI	p
PROGRESSION < 7 days	2.51	(1.7 – 3.8)	< 0.0001
STAND	2.53	(1.4 – 3.3)	< 0.0005
RISE ELBOW	2.99	(1.8 – 4.9)	< 0.0001
RISE HEAD	4.34	(2.7 – 6.7)	< 0.0001
COUGH	9.09	(4.0 – 20.00)	< 0.0001
CYTOLYSIS	2.09	(1.4 – 3.2)	< 0.0005

Sharshar et al-Crit Care Med-2003

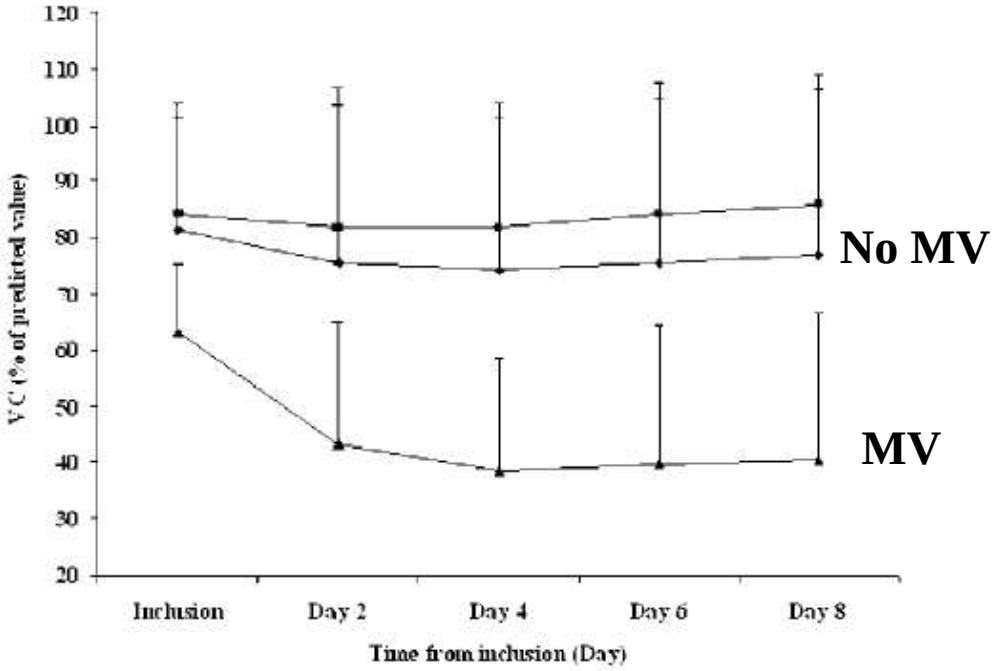
EARLY PREDICTORS

n= 196

Inability	OR	95% CI	p Value
PROGRESSION < 7 days	5.0	(1.4 – 5.7)	< 0.003
HEAD	5.0	(1.9 – 12.5)	< 0.0011
VC < 60%	2.86	(2.4 – 10.0)	< 0.0001

Sharshar et al-Crit Care Med-2003

CHANGE IN VC WITH TIME



REPEAT THE MEASUREMENT OF VITAL CAPACITY

OTHER PREDICTORS

1. **30 to 50% fall in VC**
   or VC < 20 ml/kg
2. **30% fall in Pi_{max} or Pe_{max}**
   or Pi_{max} ou Pe_{max}< 30 to 40 cmH_2O
3. **Bulbar dysfunction**

Chevrolet et al Am Rev Respir Dis 1991

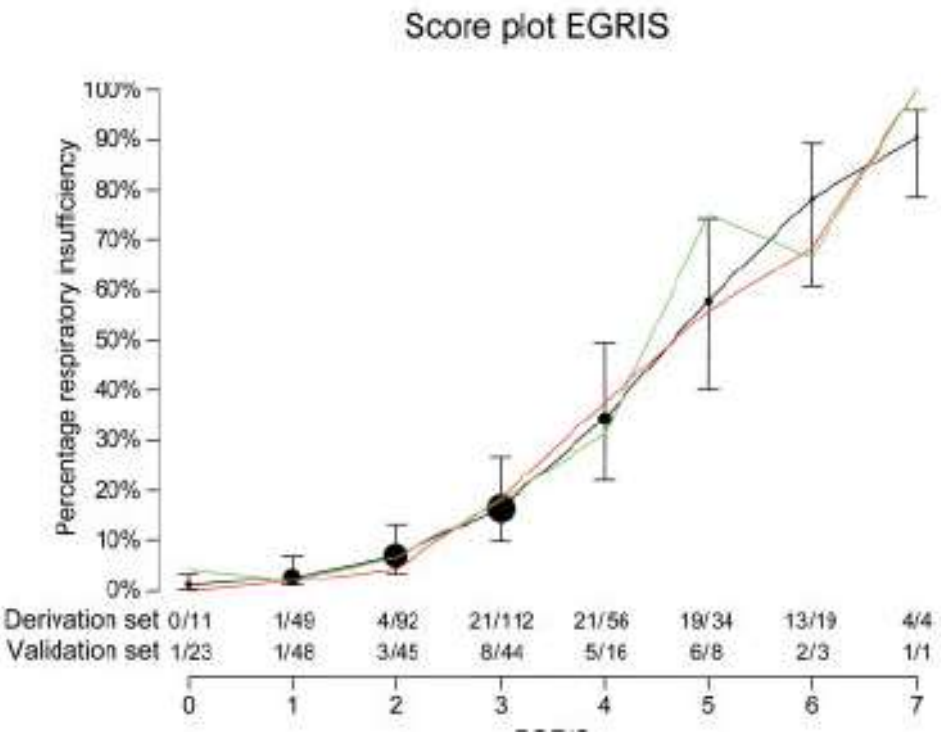
Hahn et al Arch Neurol 2001

OTHER PREDICTORS

TABLE 2: EGRIS

Measure	Categories	Score
Days between onset of weakness and hospital admission	>7 days	0
	4–7 days	1
	≤3 days	2
Facial and/or bulbar weakness at hospital admission	Absence	0
	Presence	1
MRC sum score at hospital admission	60–51	0
	50–41	1
	40–31	2
	30–21	3
	≤20	4
EGRIS		0–7

EGRIS = Erasmus GBS Respiratory Insufficiency Score; MRC = Medical Research Counsel.

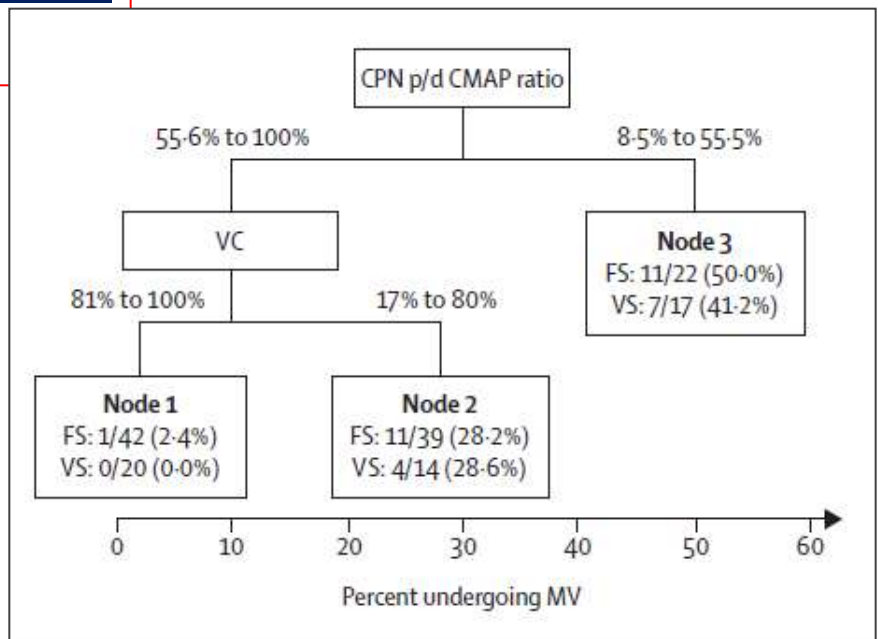


Walgaard et al – Ann Neurol - 2010

ELECTROPHYSIOLOGY

- **Phrenic ENMG**
  - **Not helpful (*Durand – Neurology – 2005*)**
- **Standard ENMG**
  - **Demyeliting form at higher risk (*Durand– Eur J Neurol 2003*)**
  - **No risk if no conduction block on common peroneal nerve + VC >80% (*Durand – Lancet Neurology – 2006*)**

Durand et al – Lancet Neurology - 2006



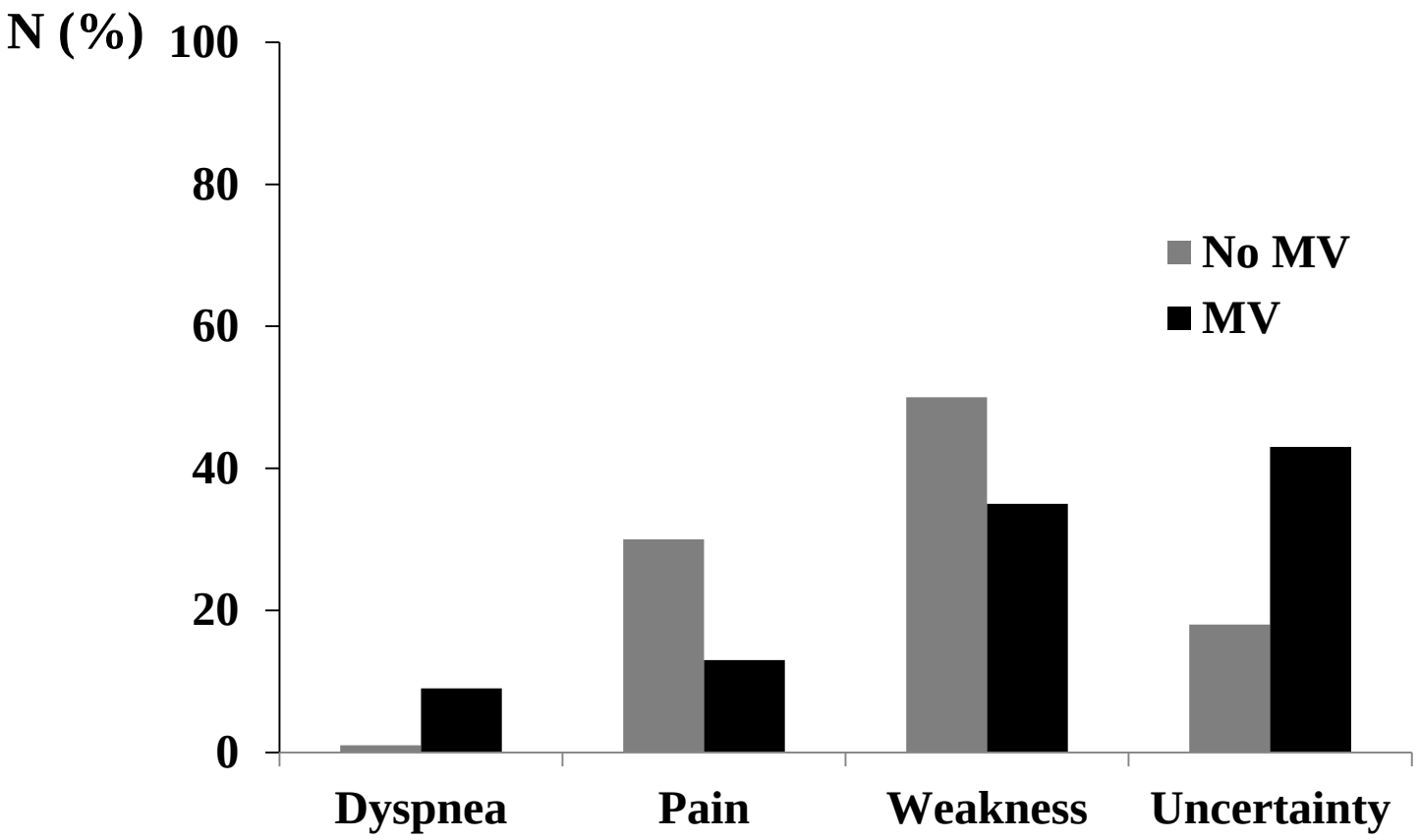
CORTISOLEMIA

Variable	no MV (Group 2)	MV > 24h (Group 3)	P*
n	60	17	
[Cortisol]T0 (ng/ml)	20.4 ± 9.6	28.5 ± 12.1	0.01
[Cortisol]T60 (ng/ml)	42.4 ± 14.8	53.1 ± 16.8	0.05

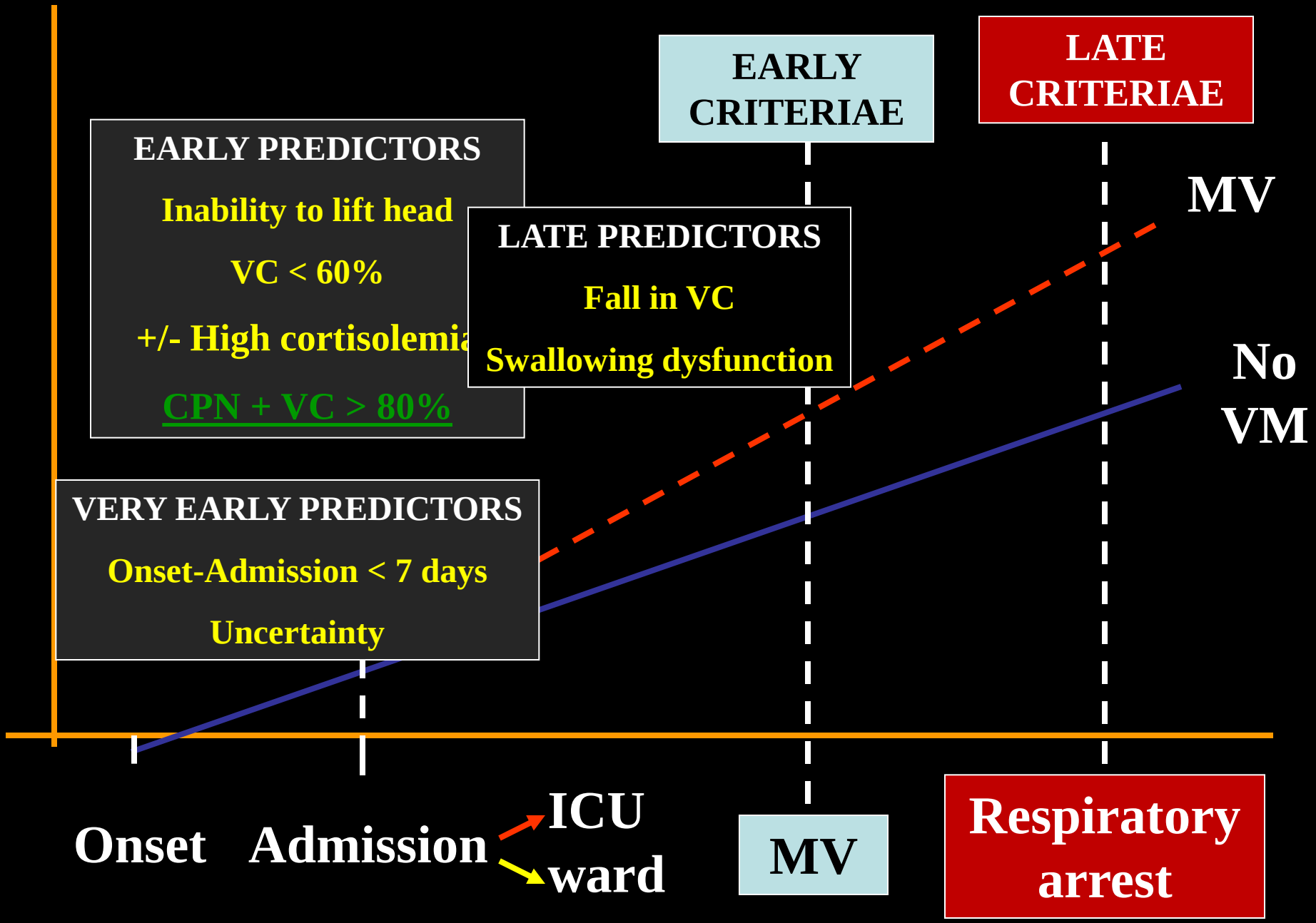
[Cortisol]T0 correlated with occurrence of dysautonomia

Strauss et al – CCM - 2009

FEAR



Marcadet et al - Submitted


EARLY CRITERIAE
LATE CRITERIAE
EARLY PREDICTORS
Inability to lift head
VC < 60%
+/- High cortisolemia
CPN + VC > 80%
LATE PREDICTORS
Fall in VC
Swallowing dysfunction
MV
No VM
VERY EARLY PREDICTORS
Onset-Admission < 7 days
Uncertainty
Onset
Admission
ICU
ward
MV
Respiratory arrest

ADMISSION IN ICU

1. **Progression less than 7 days**
2. **Inability to lift head above the bed**
3. **Bulbar dysfunction**
4. **VC less than 60% or 20 ml/Kg**

   Pi_{max} ou Pe_{max}< 30 to 40 cmH_2O
5. **VC fell by 30%**

   Pi_{max} or Pe_{max} fell by 30%
6. **CV autonomic dysfunction**

The absence of these criteria does not exempt to assess regularly weakness, bulbar function and respiratory function

OTHER ABNORMALITIES

HYPONATREMIA

1. **Hyponatremia < 133 mmol/L : 31%**
2. **Pseudohyponatremia due to IvIg: 46%**
3. **Hyponatremia: worst outcome ?**

LIVER DYSFUNCTION

1. **Cytolysis: 25%**
2. **Secondary to CMV: 25%**
3. **Predictors of MV**

Colls Int Med J 2003; Oomes et al Neurology 1996;

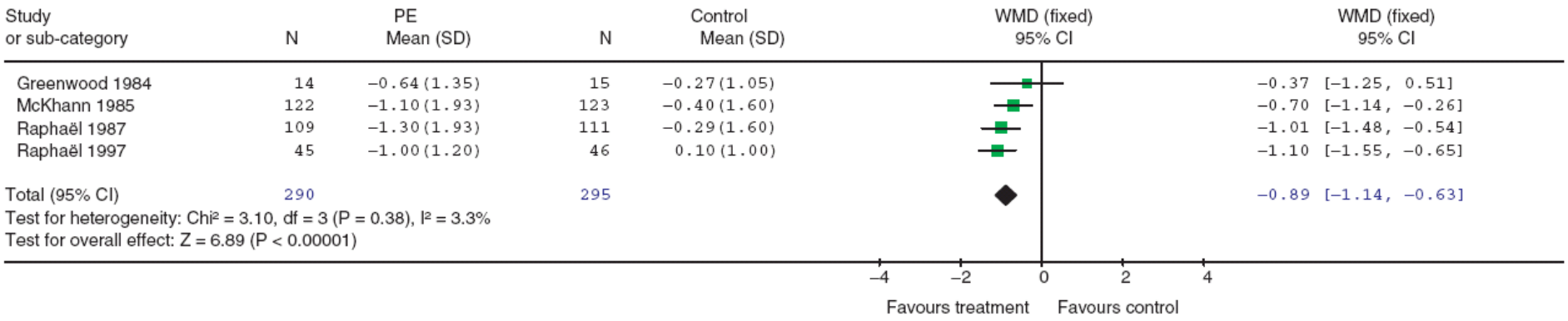
Sharshar et al Crit Care Med 2003

TREATMENT

1. **Specific treatment**
    1. **Plasma exchange (PE) NO IF INFECTION**
    2. **High-dose intravenous immunoglobulin (IvIg)**
2. **Supportive therapy**
    1. **Thrombosis prophylaxis**
    2. **Pain relief**
    3. **Psychological support**
    4. **CV support: atropine …**
    5. **Bladder catheter, nutrition, physiotherapy…**
    6. **Intercurrent diseases**
    7. **Early non-invasive mechanical ventilation**

PLASMA EXCHANGE

Plasma exchange vs no treatment: DG at 4 weeks

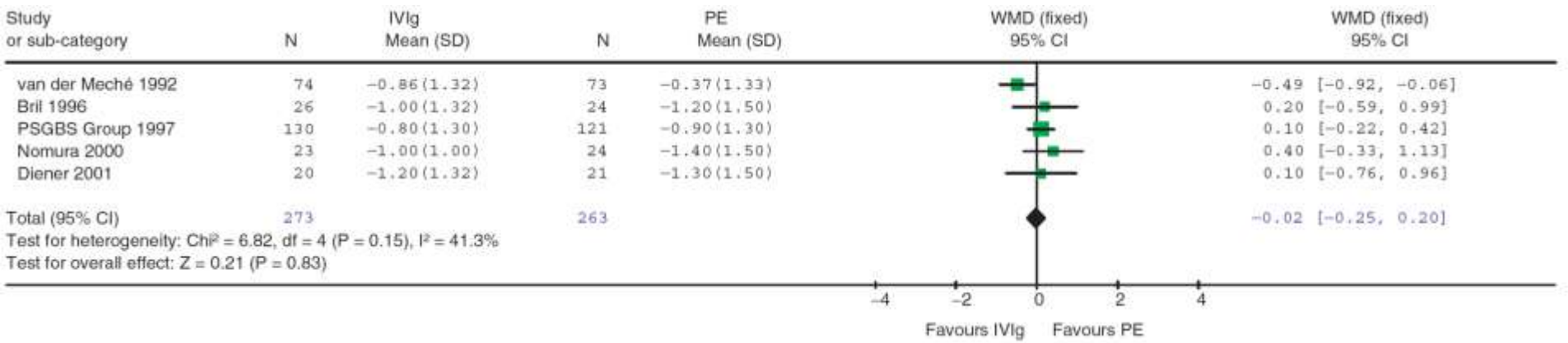


Hughes et al - Brain - 2007

1. **Benefit irrespective of severity**
2. **Tested against placebo**
3. **Tested up to 4 weeks after GBS onset**

IMMUNOGLOBULIN

Plasma exchange vs IvIg: DG at 4 weeks

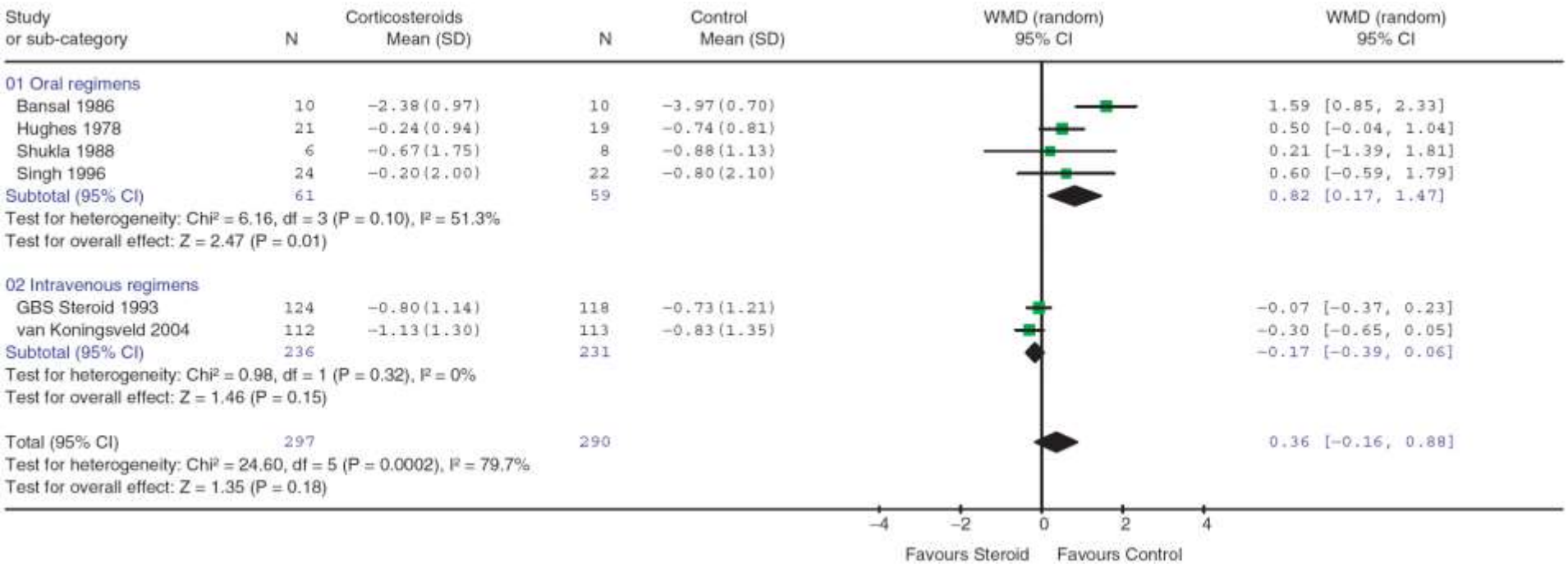


Hughes et al - Brain - 2007

1. **Tested against PE**
2. **Tested in mild or severe GBS**
3. **Tested within 2 weeks after GBS onset**

CORTICOSTEROIDS

Corticosteroids vs placebo or no treatment: DG at 4 weeks



Hughes et al - Brain - 2007

CONTRAINDICATIONS

PE

1. **Infection**
2. **Hypotension**
3. **Haemorrhage**
4. **Clotting deficiency**

IvIg

1. **IgA deficiency**
2. **Allergy**
3. **Renal failure**

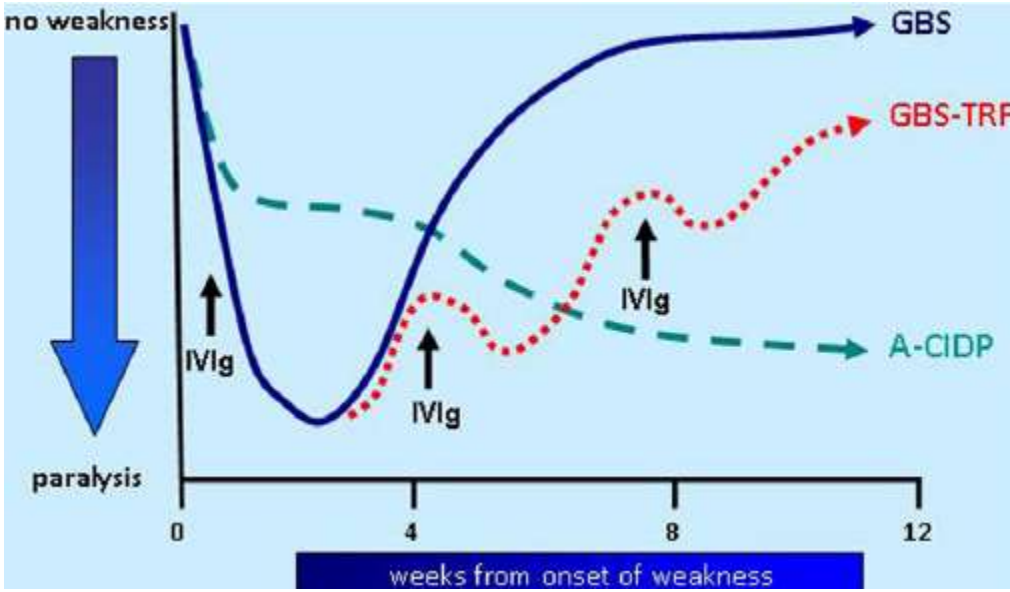
ALGORITHMS

Disability Stage	Walking (DG < 4)	Bedbound (DG =4) MV (DG = 5)
Initial*	2 PE	4 PE or IvIg**
Deterioration	2 additional PE	No additional treatment
Relapse	No treatment or do initial treatment	No treatment or do initial treatment

*As soon as the diagnosis is confirmed

** 0.4g/kg/ daily for 5 days

EVOLUTION



Differences between GBS-TRF and acute onset CIDP (A-CIDP) [45]

GBS-TRF patients:

- more frequent cranial nerve dysfunction;
- more rapid onset of weakness;
- more severe weakness;
- only one or two TRF's;
- first TRF sooner compared to deterioration in A-CIDP;
- TRF('s) occur(s) $<$ 2 months from onset.

A-CIDP patients:

- no ventilatory support;
- more demyelinating features on EMG;
- when three or more exacerbations;
- when deterioration occurs $>$ 2 months from onset.

Van Doorn et al – Press Med - 2013

Raymond Poincaré

THANK YOU

MORBIDITY

n = 114

RESPIRATORY		
1.	Tracheobronchitis	33 (29%)
2.	Pneumonia	27 (24%)
3.	Pneumothorax	6 (4%)
INFECTION		
1.	Bacteremia	21 (15%)
2.	Catheter	3 (3%)
3.	Urinary tract	75 (66%)
THROMBOSIS		
1.	Deep venous thrombosis	5 (4%)
2.	Pulmonary embolism	3 (3%)
OTHERS		
1.	Hyponatremia (< 130 mmol/L)	28 (25%)

Henderson et al Neurology 2003

RISK FACTORS OF MORBIDITY

n = 114

Characteristic	OR	95% CI	p Value
Background illness	**2.8**	**(0.8 - 9.1)**	**0.10**
Plasma exchange	**3.4**	**(1.1 – 10.5)**	**0.03**
Prolonged MV	**12.4**	**(3.7 – 41.3)**	**< 0.0001**

Henderson et al Neurology 2003

ADMISSION IN ICU

1. **Progression less than 7 days**
2. **Inability to lift head above the bed**
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PUZZLE

Pathogen agent

1. C. jejuni
2. CMV
3. Others

Subtypes

1. AIDP
2. AMAN
3. AMSAM
4. MFS

Clinic

1. Sensorimotor
2. Pure motor
3. Cranial nerves

Severity

1. Aspiration
2. Intubation
3. Dysautonomia

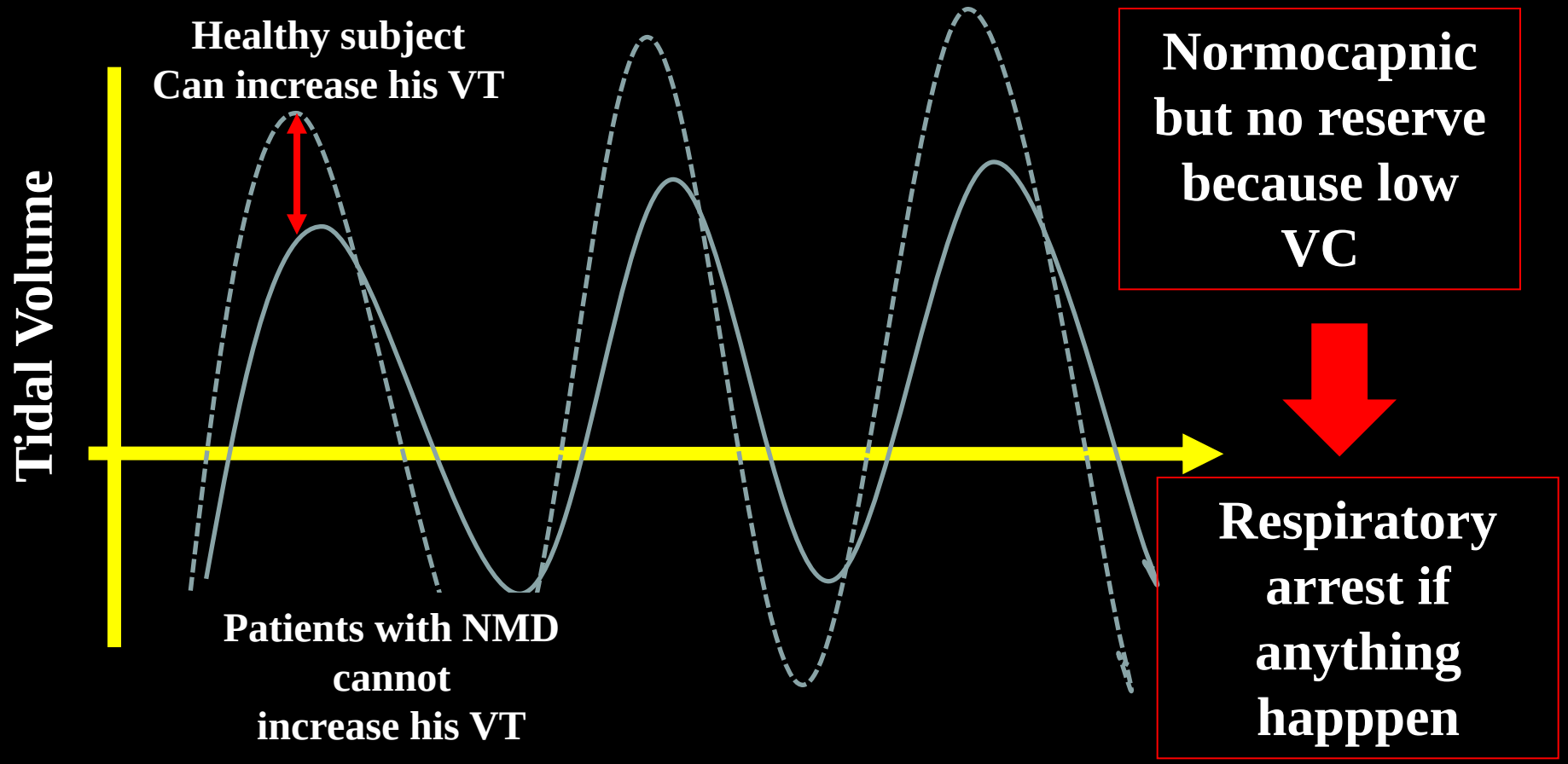
Anti-Ganliosides

1. Ant-GM1
2. Anti-GM2
3. Anti-G1QB

Outcome

1. Recovery
2. Sensory sequellae
3. Motor sequellae

WHY NORMOCAPNIC IS NOT « SAFE »



ACUTE FLACCID WEAKNESS

SENSORIMOTOR PARALYSIS

1. ± MRI
2. CSF ANALYSIS
3. BLOOD TESTS (ESR)
4. EMG (Axonal PN, Demyelinating PN)

PURE MOTOR PARALYSIS

1. BLOOD TESTS (K+)
2. CSF ANALYSIS
3. EMG (Myopathy, NMJ, Neuropathy)

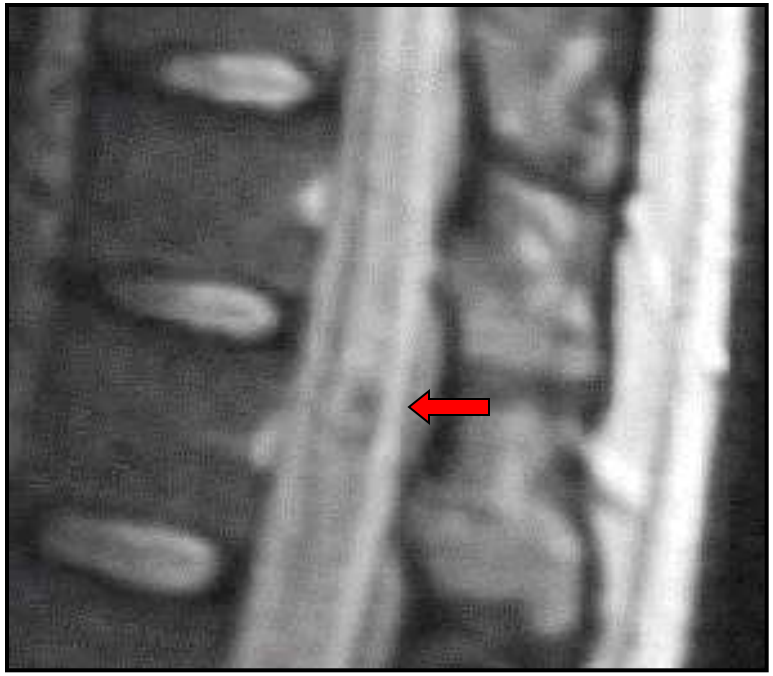
ACUTE SENSORIMOTOR HYPOREFLEXIC PARALYSIS

Pyramidal signs

Sensory level

Cauda-equina syndrome

SPINAL CORD MRI



TRACHEOSTOMY

Prolonged MV > 21 days

1. **Elder patients**
2. **Preexisting pulmonary disease**
3. **Pulmonary function d_{int}/d_{12} ratio < 1**
    1. **PF score = CV + Pimax + Pemax**
    2. **Sensitivity = 70%, specificity: 100%**

Lawn and Wijdicks Muscle Nerve 1999, 2000

ACUTE SENSORIMOTOR HYPOREFLEXIC PARALYSIS

	ESR NORMAL	ESR INCREASED
CSF NORMAL	TOXIC (Thallium, arsenic…) METABOLIC (Gly, Vit …) VASCULITIS (SLE…) PRIMARY GBS	VASCULITIS (SLE…)
INCREASED CSF CELLS	MENINGORADICULITIS	MENINGORADICULITIS
INCREASED CSF PROTEIN	PRIMARY GBS CANCER, LYMPHOMA, VASCULITIS, DIPHTERIA, HIV.	CANCER, LYMPHOMA, VASCULITIS, DIPHTERIA, HIV.

PURE MOTOR HYPOREFLEXIC DEFICIT

	SIGNS	K+	CSF	EMG
PERIODIC PARALYSIS	EXERCISE	↑↓	↔	MYOPATHY
MYASTHENIA GRAVIS	VARIATION EYE MVT	↔	↔	NM JUNCTION
BOTULISM	FOOD POISONNING PUPILL	↔	↔	NM JUNCTION
POLIO MYELITIS	TRAVEL DIARRHEA	↔	↑ CELLS	ANTERIOR HORN CELLS
PORPHYRIC NEUROPATHY	CONFUSION PAIN	↔	↔	POLY NEUROPATHY
PRIMARY GBS	INFECTION ASCENDANT	↔	↑ PROTEIN	POLY NEUROPATHY

DEFINITION

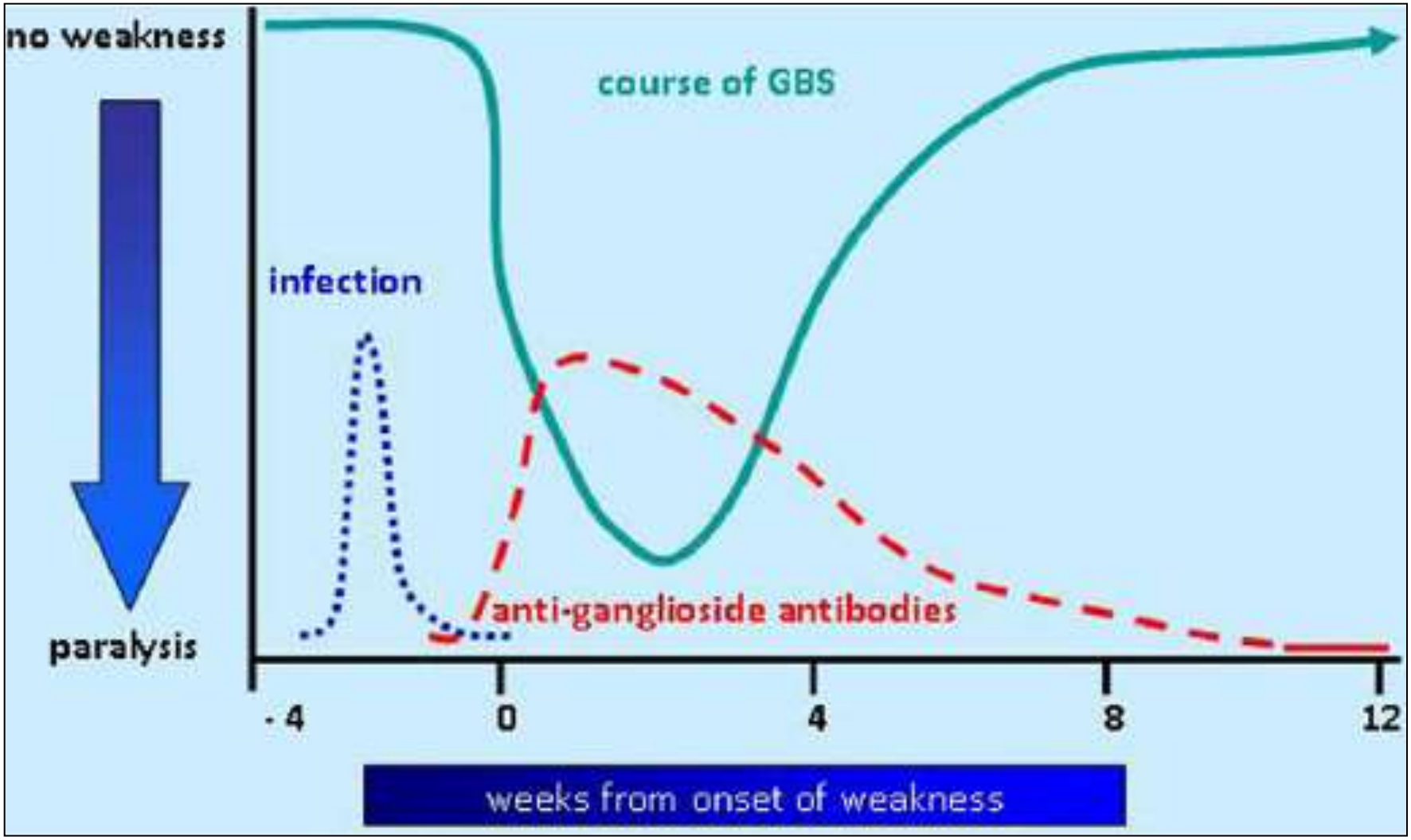
REQUIRED CRITERIA

1. **Progressive weakness > 2 limbs**
2. **Areflexia**
3. **Progression for < 4 weeks**
4. **Other cause of acute neuropathy excluded**

SUPPORTIVE CRITERIA

1. **Mild sensory signs**
2. **Raised CSF protein**
3. **conduction block in EMG**

EVOLUTION



Van Doorn et al – Press Med - 2013