



# The role of plasmapheresis in Myasthenia Gravis

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# Myasthenia Gravis

- ◆ S/S:

- 2/3 initial symptoms: Ocular motor disturbances, ptosis or diplopia.

- 1/6: Oropharyngeal muscle weakness

- 1/10: limb weakness

- ◆ severity of the weakness fluctuates

- ◆ orbicularis oculi muscle and jaw muscle weakness



# Diagnosis

- ◆ Tensilon test: AChE inhibitor  
2mg IV and monitored for 60 seconds.  
Subsequent injections are 3 and 5 mg.
- ◆ EMG: decremental response to repetitive motor elective stimulation.
- ◆ AChR: titer not relative severity of MG  
associated with thymoma
- ◆ CXR, CT: soft tissue mass at ant.  
Mediastinum



## Osserman`s classification

- ◆ I, ocular myasthenia.
- ◆ IIa, mild generalised myasthenia.
- ◆ IIb, moderate generalised myasthenia.
- ◆ III, acute severe myasthenia.
- ◆ IV, late severe myasthenia.



# Pathophysiology

- ◆ autoimmune condition: antibodies to the AChR on skeletal muscle
- ◆ 10% to 15%: thymoma
- ◆ 80%: thymic hyperplasia



# Treatment

- ◆ Thymectomy  
benefit in 50% to 80%  
max favorable response : 2 to 5 years  
< 60 y/o poor response for thymectomy
- ◆ Extubation: within hours after surgery
- ◆ Repeat thymectomy: chronic, refractory  
for residual thymic tissue or good response  
to the original surgery.



# Acetylcholinesterase Inhibitors

- ◆ Pyridostigmine bromide (Mestinon)  
neostigmine bromide (Prostigmin)
- ◆ ½ to 1 tablet (60 mg ) every 4 to 8 hours
- ◆ Side effect:  
cholinergic crisis: persistent depolarization  
of the muscle fiber, then muscle weakness
- ◆ GI complication:  
loose stools, nausea, vomiting, abdominal  
cramps, and diarrhea



# Immune Modulation

- ◆ **Corticosteroids**

  - ocular MG, not respond to AChEI.**

  - initial dose 1.5 to 2 mg/kg/day**

  - excellent response in before or after removal  
thymoma**

- ◆ **Azathioprine :initial dose 50 mg/day**

  - leukopenia, GI irritation, AST/ALT ↑2倍**





# Immunosuppression

- ◆ Cyclosporine: initial dose 5 to 6 mg/kg/day  
combined prednisone 10-20 mg qod
- ◆ Cyclophosphamide:  
Alopecia and less common: leukopenia,  
nausea, vomiting, anorexia, and  
discoloration of the nails and skin



# Intravenous Immunoglobulin

- ◆ 2 gm/kg infused over 2 to 5 days
- ◆ down-regulation of antibodies and symptom relief.
- ◆ Side effect: headaches, chills, and fever  
less common: alopecia, aseptic meningitis, leukopenia, and retinal necrosis



# Plasma Exchange

- ◆ short-term intervention for acute exacerbation
- ◆ rapidly improve strength before surgery
- ◆ postoperative deterioration
- ◆ chronic intermittent treatment for refractory disease.



# Plasma Exchange

- ◆ Side effect:

cardiac arrhythmias, nausea, lightheadedness, chills, visual obscurations, and pedal edema, thromboses, thrombophlebitis, and subacute bacterial endocarditis.



# Comparative effects of plasma exchange and pyridostigmine on respiratory muscle strength and breathing pattern in patients with myasthenia gravis

Thorax 1995;50:1080-1086



# Patient list

Patients	Age (yrs)	Sex	Antibodies				Duration of both disease and treatment (yrs)	STD (mg × 10 <sup>3</sup> )	Thymectomy
			AchR		SM				
			C	PE	C	PE			
1	68	M	20	8	1:160	<1:80	6	21.6	Yes*
2	63	M	54	42	1:160	<1:80	8	28.8	Yes*
3	65	F	85	52	-	-	4	21.6	No
4	57	M	44	25	1:160	<1:80	1	10.8	Yes*
5	22	F	35	15	-	-	1	10.8	Yes
6	30	F	18	7	-	-	2	14.4	Yes
7	33	F	15	10	-	-	4	21.6	Yes
8	38	F	28	13	-	-	1	10.8	Yes
9	30	F	64	29	-	-	5	27.0	Yes

AchR = acetylcholine receptor; SM = skeletal muscle; C = control; PE = plasma exchange; STD = steroid total dose (daily dose × 180 days × years).

\* Thymoma.



- ◆ Medication: menstinon 1# tid or qid  
prednisone 20-60 mg/day
- ◆ Plasma exchange:
  - (a) 750-1000 ml saline.
  - (b) 500 ml 10 percent colloidal solution of low molecular weight dextran in saline
  - (c) three Baxter electrolytic rehydrating Solution (300 ml) plus 5000 IU heparin
  - (d) four 50 ml vials of 20 percent human albumin



# PROTOCOL

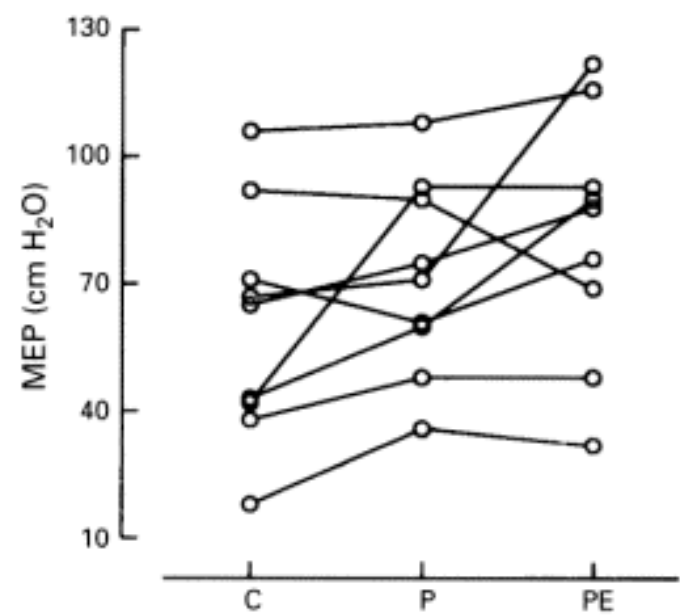
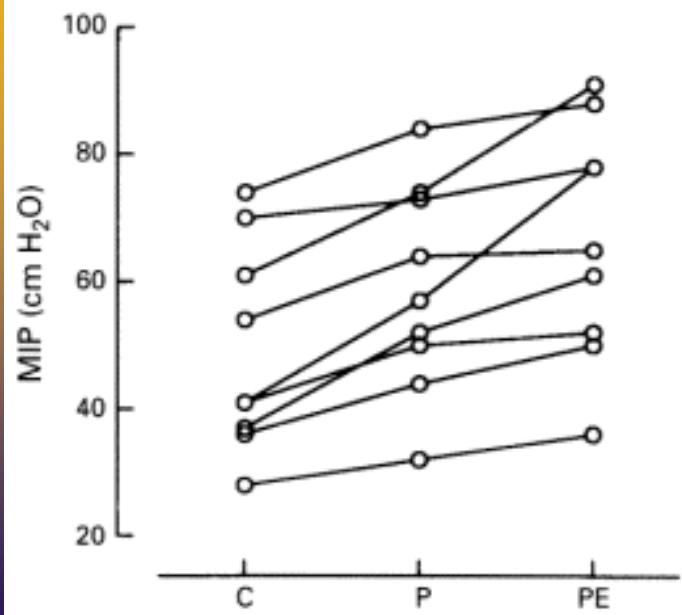
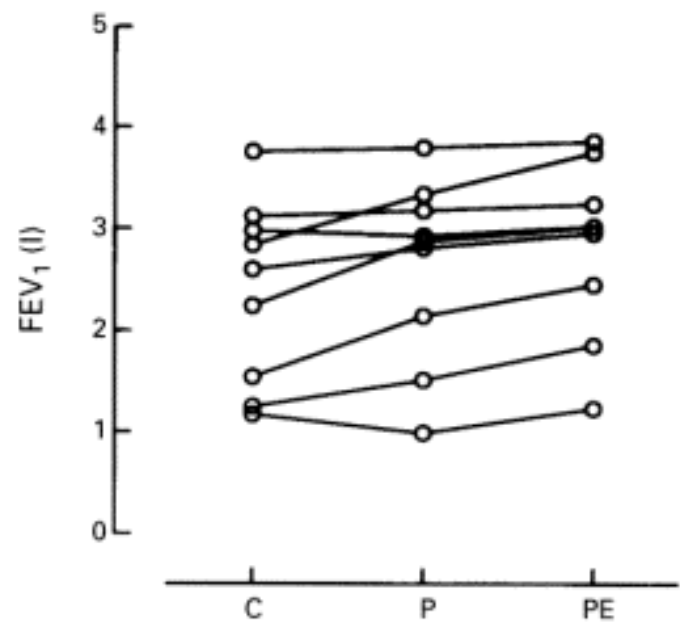
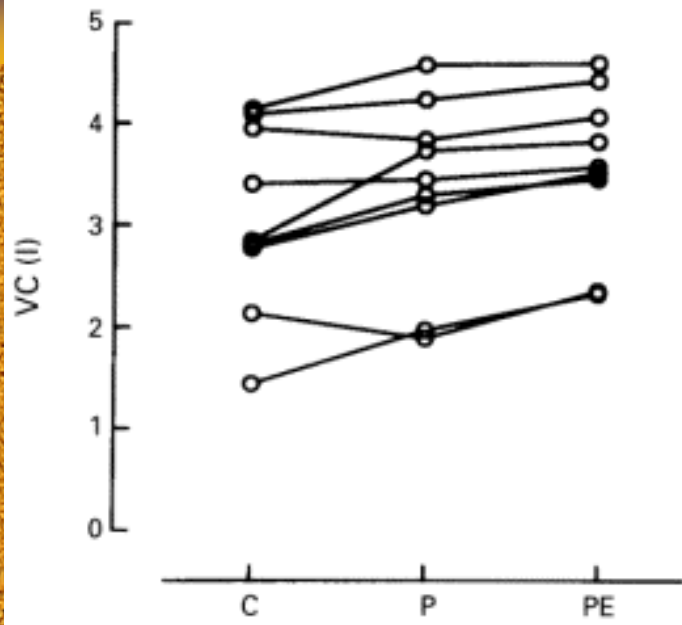
- ◆ Study I: fasted and a single dose (120 mg) of mestinon, Functional evaluation after 30 min.
- ◆ Study II: underwent the first of 5-9 courses of plasma exchange, re-evaluated at the same time in the morning
- ◆ Study III: on-steroid or off-steroid day 30 minutes and two hours after a dose of 120 mg pyridostigmine.



# Results

	<i>VC</i> ( <i>SR</i> )	<i>RFC</i> ( <i>SR</i> )	<i>RV</i> ( <i>SR</i> )	<i>TLC</i> ( <i>SR</i> )	<i>FEV<sub>1</sub></i> ( <i>SR</i> )	<i>FEV<sub>1</sub>/VC</i> (%)	<i>MIP</i> (% <i>pred</i> )	<i>MEP</i> (% <i>pred</i> )
C	-1.46 (1.88)	1.21 (1.26)	1.74 (1.96)	-0.14 (1.17)	-1.52 (1.65)	77.7 (16.3)	56.2 (19.5)	38.2 (18.8)
P	-0.80 (1.72)	1.23 (1.46)	1.14 (2.03)	-0.25 (1.18)	-0.96 (1.54)	76.8 (12.7)	68.5 (21.2)	45.2 (16.2)
PE	-0.35 (1.56)	0.775 (1.26)	0.77 (1.79)	0.10 (1.22)	-0.47 (1.43)	78.4 (13.6)	75.8 (21.3)	50.6 (16.5)
Analysis of variance								
F	12.71	6.99	4.79	2.21	10.43	0.28	30.35	4.013
p	0.0005	0.01	0.025	NS	0.002	0.76	0.0001	0.05
Bonferroni test ( <i>p</i> values)								
P v C	<0.05	NS	NS	NS	NS	NS	<0.05	NS
PE v C	<0.05	<0.05	<0.05	NS	<0.05	NS	<0.05	<0.05
PE v P	NS	<0.05	NS	NS	NS	NS	<0.05	NS

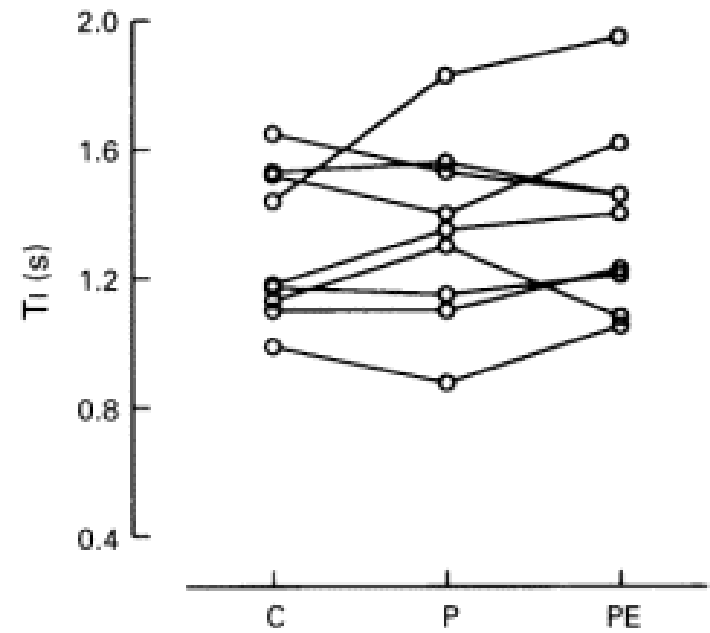
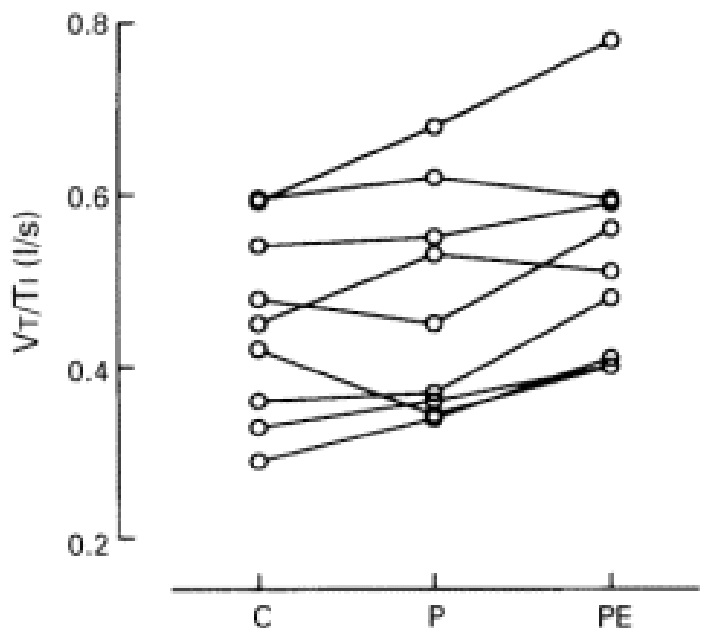
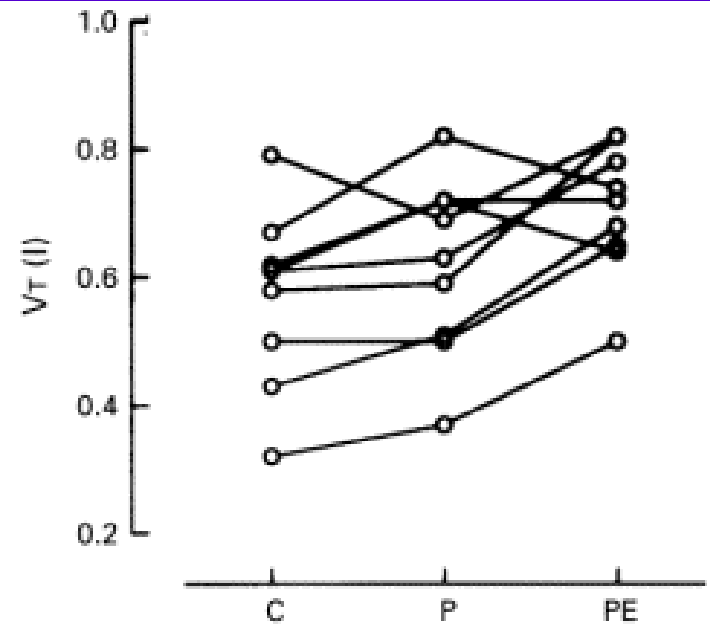
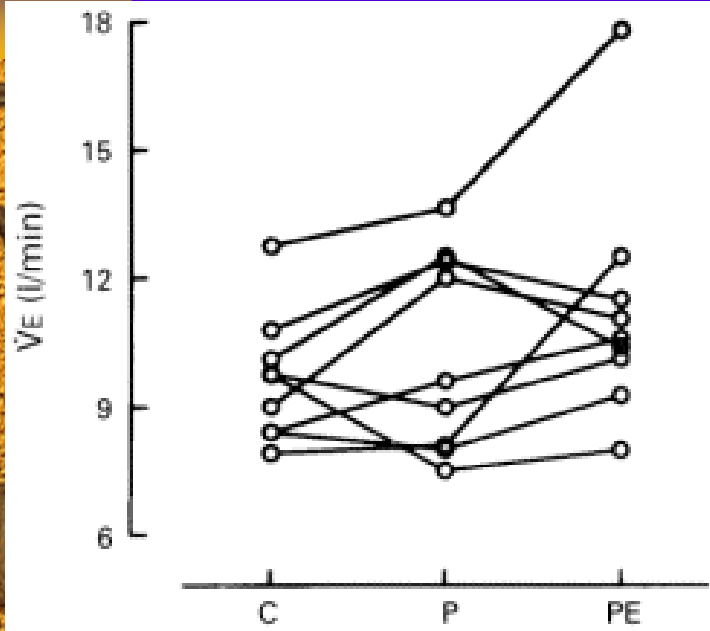
SR = standardised residuals; VC = vital capacity; RFC = functional residual capacity; RV = residual volume; TLC = total lung capacity; FEV<sub>1</sub> = forced expiratory volume in one second; MIP = maximal inspiratory pressure; MEP = maximal expiratory pressure.





	$\dot{V}_E$ (l/min)	$V_T$ (l)	$T_I$ (s)	$R_f$ (breaths/min)	$V_T/T_I$ (l/s)	$T_I/T_{TOT}$
C	9.65 (1.5)	0.57 (0.1)	1.3 (0.2)	17.63 (4.2)	0.45 (0.1)	0.37 (0.06)
P	9.94 (2.2)	0.62 (0.14)	1.34 (0.3)	16.7 (4.6)	0.47 (0.12)	0.36 (0.06)
PE	11.2 (2.7)	0.7 (0.1)	1.4 (0.3)	16.1 (3.8)	0.52 (0.1)	0.37 (0.05)
Analysis of variance						
F	3.16	10.14	1.05	1.99	8.61	0.14
p	NS	0.002	NS	NS	0.005	NS
Bonferroni test (p values)						
P v C	NS	NS	NS	NS	NS	NS
PE v C	NS	<0.05	NS	NS	<0.05	NS
PE v P	NS	<0.05	NS	NS	<0.05	NS

$\dot{V}_E$  = minute ventilation;  $V_T$  = tidal volume;  $T_I$  = inspiratory time;  $R_f$  = respiratory frequency;  $V_T/T_I$  = mean inspiratory flow;  $T_I/T_{TOT}$  = timing.





◆ Plasmapheresis:

FRC↑, RV↓, FEV1↑

MIP↑, MEP↑

VT↑, VT/TI↑

◆ Mestinon:

FRC↑

MIP↑



## Discussion

- ◆ increases in static and dynamic lung volumes and respiratory muscle strength in both.
- ◆ FRC is determined by the balance between lung and chest wall forces  
decrease in plasma exchange, injection AChEI, not at oral AChEI.
- ◆ FRC~~MIP: no relation



- ◆ Post-mestinon 30min and 2-hours
- ◆ Low MIP, MEP---MG, corticosteroid myopathy.
- ◆ Corticosteroid on and off.
- ◆ Animal and human mode, II b fiber atrophy
- ◆ On change in TI.