MEDICAL GRAND ROUNDS

PARKLAND MEMORIAL HOSPITAL

December 19, 1968

PERIODIC PARALYSIS

CASE I - [redacted]

This 20 year old [redacted] male was well until approximately 4 1/2 years prior to admission. At that time he began to notice short periods of weakness of his lower extremities, frequently accompanied by increased sweating, and occurring mainly after marked muscular activity. The weakness could always be "walked off". At about the time the weak episodes began he noted increased nervousness and increased appetite which was accompanied by a loss of weight.

His first admission to this hospital was about 30 months prior to this admission and was brought about by an episode of almost complete paralysis of his lower extremities. On admission then, in addition to areflexic paralysis, he was noted to have the signs of hyperthyroidism (PBI 12 μ%). His serum potassium concentration was 1.8 mEq/L. There was no history of vomiting or diarrhea. He was treated with KCl and propylthiouracil and discharged to be followed in clinic. However, he was soon lost to follow-up.

This admission was incident to continuing symptoms and signs of hyperthyroidism. Since his first admission he had had no paralytic episodes. He had taken PTU irregularly. On admission his serum potassium concentration was 3.6 mEq/L; PBI was 11.4 μ%; RAI 62% (24 hrs.).

STUDIES

1. Control

Membrane Potential = -75mV

ECG - Normal

Serum Electrolytes	
pH	7.42
pCO_2	37.5
Na	137
K	3.6
Cl	99
CO_2	24
Ca	9.9
Phosph.	3.6

Muscle Electrolytes

Morphology Normal

K 149.5 mEq/L ICF

Na 44.6 mEq/L ICF

Predicted MP = -90.5 mV

INDUCED PARALYSIS

1. Method: Glucose and Insulin Administration

Membrane Potential = -77 mV

ECG - Small U waves

Serum Electrolytes	
Na	138
K	1.7
Cl	104
CO_2	23

Muscle Electrolytes

K 143.6 mEq/L ICF

Na 38.8 mEq/L ICF

Predicted MP = -102 mV

II. Method: Oral CHO load at night

Membrane Potential (paralyzed) = -85 mV
(recovery) = -85 mV

Serum Electrolytes

	Paralyzed	Recovery
Na	138	139
K	3.4	3.8
Cl	102	102
CO_2	27	28

III. Method: Oral CHO load at night

Membrane Potential = -65 mV (Weakness)

Serum Electrolytes

Na	137
K	3.8
Cl	101
CO_2	24

II. Control - Three days after final CHO load - No weakness.

Membrane Potential = -65 mV

Serum Electrolytes

Na	137
K	3.8
Cl	101
CO_2	24

CASE 2 - [redacted]

The patient was a 48 year old [redacted] female with about a nine month history of increasing nervousness, emotional lability, increased appetite with marked weight loss. She had also noted increasing generalized muscle weakness. For the two months prior to admission she had found that muscle weakness, especially in the legs, was worse after eating. Did not give a history of frank paralysis. Just prior to admission she became extremely short of breath and orthopnic.

She was obviously severely thyrotoxic and had a venous congestive state (VP 20 cm CT 9 sec.). The PBI was 25μ%; RAI 66% in 24 hrs. A Tensiton test was negative.

STUDIES

I. Control (Shortly after admission)
Weakness only
Membrane Potential = -79 mV ECG - Normal

Serum Electrolytes	
Na	141
K	2.5
Cl	98
CO_2	29
Ca	9
Phosp.	4.2

Muscle Electrolytes
Morphology Normal
K 173.5 mEq/L ICF
Na 56.6 mEq/L ICF

Predicted M.P. = -101 mV

II. Control (12 days post admission)
Normal Muscle Strength

Membrane Potential = -86 mV ECG-Normal

Serum Electrolytes	
Na	130
K	4.4
Cl	98
CO_2	23

I. Method:-Large nocturnal CHO load.
Profound paralysis produced.

Membrane Potential = -74 mV

Serum Electrolytes	
Na	135
K	3.9
Cl	100
CO_2	25

II. Method: Same as above.
Marked paralysis

Membrane Potential = -63 mV ECG - Normal

Serum Electrolytes	
Na	135
K	3.9 to 3.3
Cl	99
CO_2	24

CASE 3 - [redacted]

This 26 year old [redacted] male had his first attack of paralysis at the age of 23 years. That attack was quite typical and severe occurring during the early morning hours. The evening before he had ingested 3 beers after the evening meal (not unusual for him) and had noted "hard, achey" thigh muscle before going to bed. He was first admitted to another hospital where a diagnosis of hypokalemic paralysis was made (serum potassium on admission was 2.1 mEq/L; ECG showed U waves). However, attempts to induce another attack with CHO loads, insulin and salt were unrewarding. At that time, thyroid studies were normal. A history of excessive salt tablet ingestion for over a year prior to admission was obtained. There was no family history of periodic paralysis.

Three years after onset, he was admitted to our hospital for study.

In the interum, he had had two additional severe paralytic episodes, but took extra KCl orally and did need hospital admission. He had many episodes of weakness and stated he could not "walk them off". Weakness most frequently occurred in the early morning hours and was not obviously related to prior food intake or muscular activity. However, he had developed the habit of taking extra oral KCl when he knew that increased muscular activity would be required.

STUDIES

1. Control (Off KCl 3 days - No weakness)
   Membrane Potential = -87 mV ECG - Normal

   Serum Electrolytes PBI - 6.5 μ%

Na	138
K	3.8
Cl	100
CO_2	24
Ca	9.4
Phosph.	3.7

1. Method - CHO load, Insulin and Isotonic saline IV.
   Profound paralysis induced.

   Membrane Potential = -144 mV ECG - Normal

   Serum Electrolytes

Na	135
K	3.2
Cl	104
CO_2	20

   Muscle Electrolytes
   Morphology - Small vacuoles
   K 135.8 mEq/L ICF
   Na 21.2 mEq/L ICF
   Predicted M.P. = -89 mV

DIFFERENTIAL CHARACTERISTICS OF PARALYSIS

Hypokalemic Type

1. Paralytic episodes start in late childhood or third decade.
2. Paralysis primarily nocturnal.
3. Duration of paralysis hours to days.
4. Some attacks characterized by complete paralysis of arms and legs; may involve respiratory muscles.
5. Paralytic episodes usually widely spaced by days; sometimes by months or years.
6. Paralysis usually follows extreme exercise or large meals.

Hyperkalemic Type

1. Paralytic episodes begin in infancy.
2. Paralysis occurs usually during the waking hours.
3. Paralysis involves small numbers of muscle groups; thus complete paralysis is rare. Attacks "mild".
4. Episodes of weakness and paralysis frequent. May occur many times during a day.
5. Paralytic episodes characteristicly occur after a short rest following exercise.
6. Attacks may occur after fasting.
7. Myotonic features, especially of eyelids, are common.

FACTORS WHICH INDUCE PARALYSIS

Hypokalemic

1. Stresses
   a) Trauma
   b) Surgery
   c) Infection
   d) Anger, fear, anxiety
   e) Exposure to cold
   f) Muscular exertion

2. Carbohydrate Loads
   a) High CHO meal particularly at night
   b) Beer, wine, candy particularly when associated with a stress under 1 above.

3. Forced inactivity - particularly after marked exertion or CHO loads.

4. Drugs
   a) Insulin
   b) Epinephrine
   c) Thyroid
   d) Sodium Chloride loads
   e) Mineral corticoids

Hyperkalemic

1. Stresses

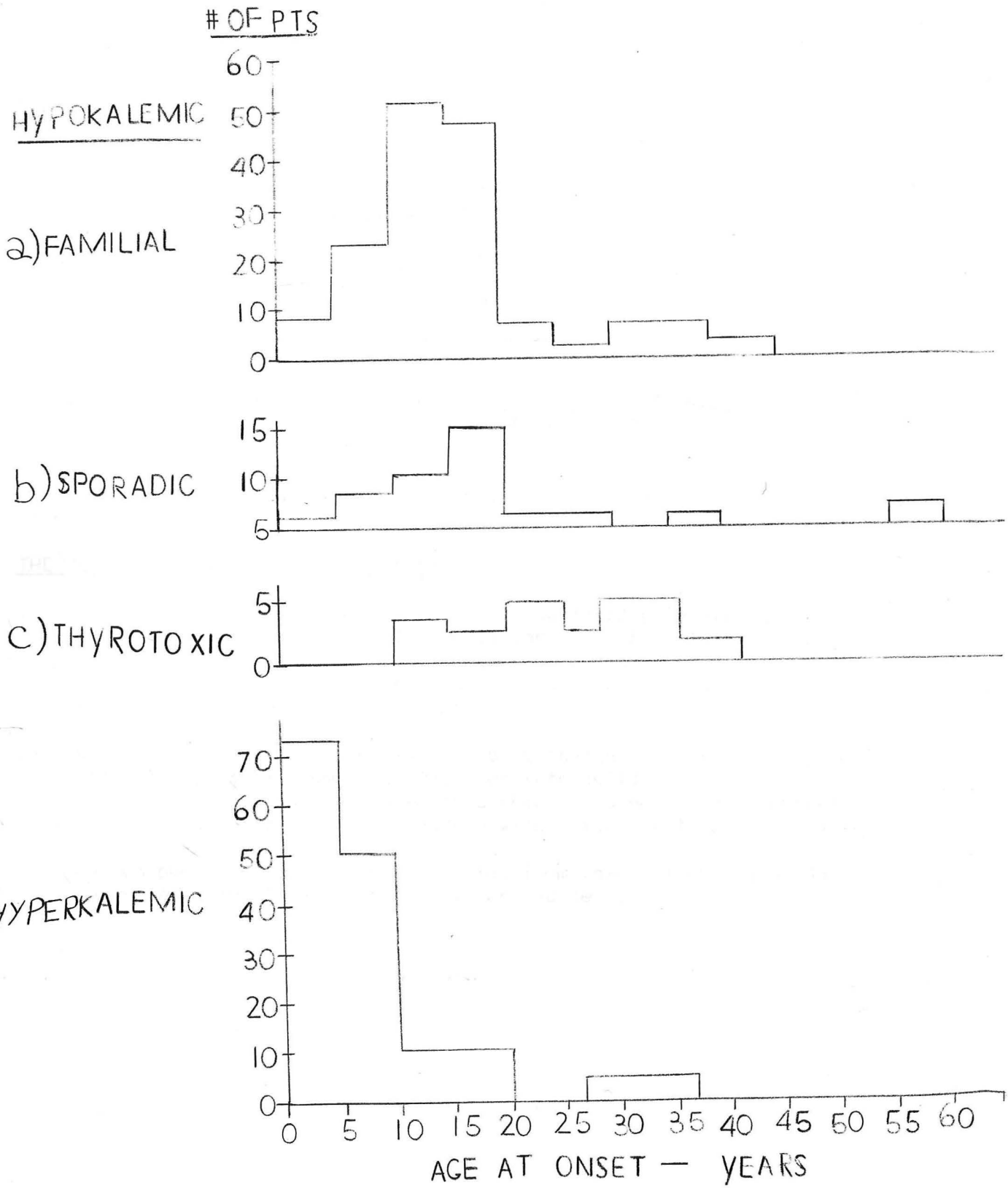
2. Carbohydrate loads

3. Forced inactivity

4. Drugs
   a) Insulin
   b) Potassium Chloride

5. Fasting

AGE INCIDENCE OF PERIODIC PARALYSIS *



*AFTER CONN AND STREETEN

MEMBRANE POTENTIAL (Em)

NERNST EQUATION:

$$Em = -61.5 \log \frac{[K]i}{[K]o}$$

GOLDMAN EQUATION:

$$Em = -61.5 \log \frac{Pk\ [K]i + PNa\ [Na]i + PCl\ Cl\ o}{Pk\ [K]o + PNa\ [Na]o + PCl\ Cl\ i}$$

$$Em = -61.5 \log \frac{[K]i}{[K]o + (0.01)\,[Na]o}$$

$$-90 = -61.5 \log \frac{28.1}{1} \longrightarrow \log \frac{150}{3.8 + (0.01)\,(140)}$$

$$-66 = -61.5 \log 111.8 \longrightarrow \log \frac{150}{3.8 + (0.06)\,(140)}$$

$$-144 = -61.5 \log 219.6 \longrightarrow \log \frac{150}{3.8 + ?}$$

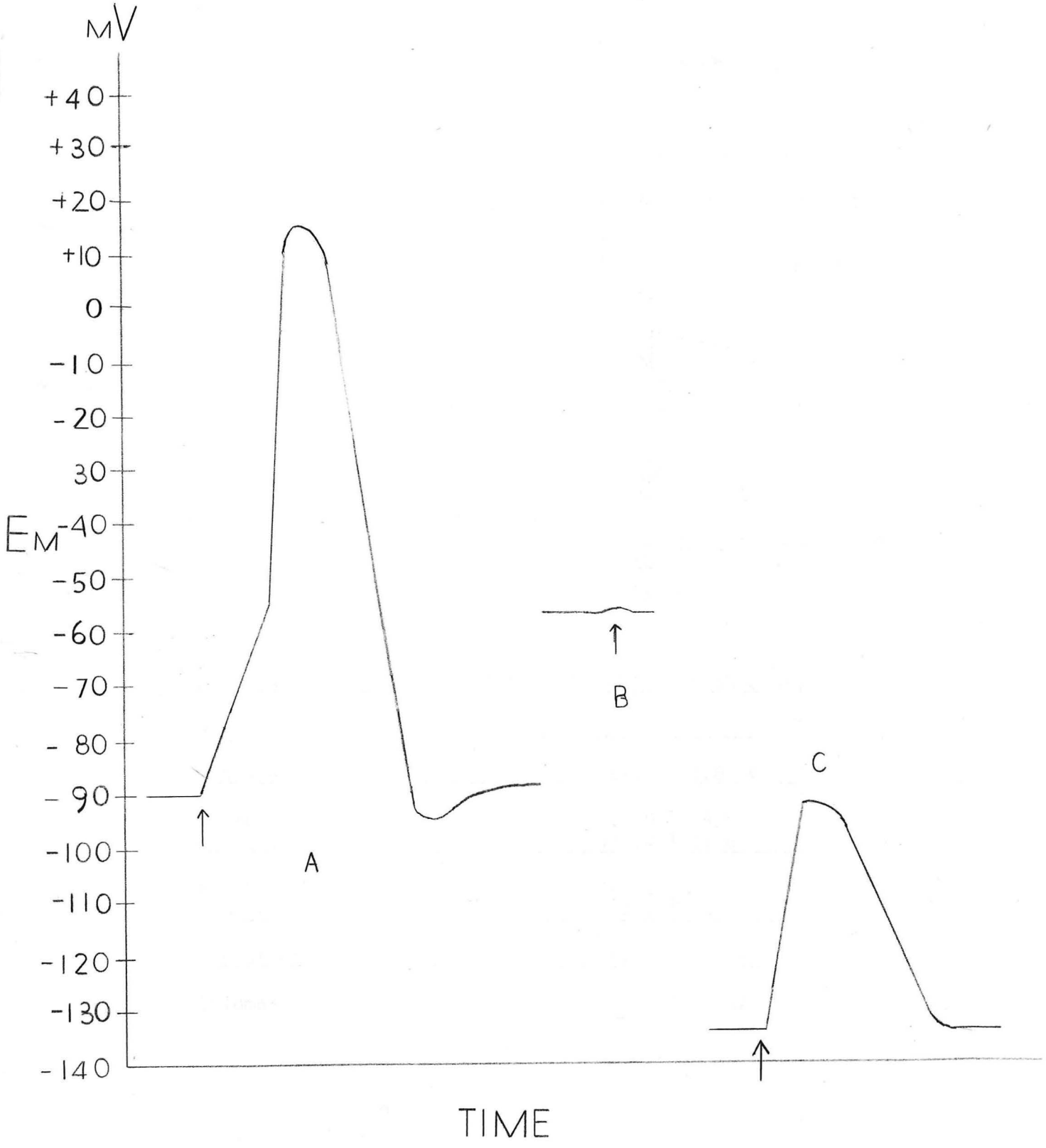
THE MEMBRANE POTENTIAL RESULTS FROM:

1) The escaping tendency of the high intracellular potassium and can be predicted by the ration of intracellular to extracellular potassium concentration if an allowance is made for a small but significant sodium permeability of the muscle membrane. Low intracellular sodium is maintained by a nonionic outward pump.

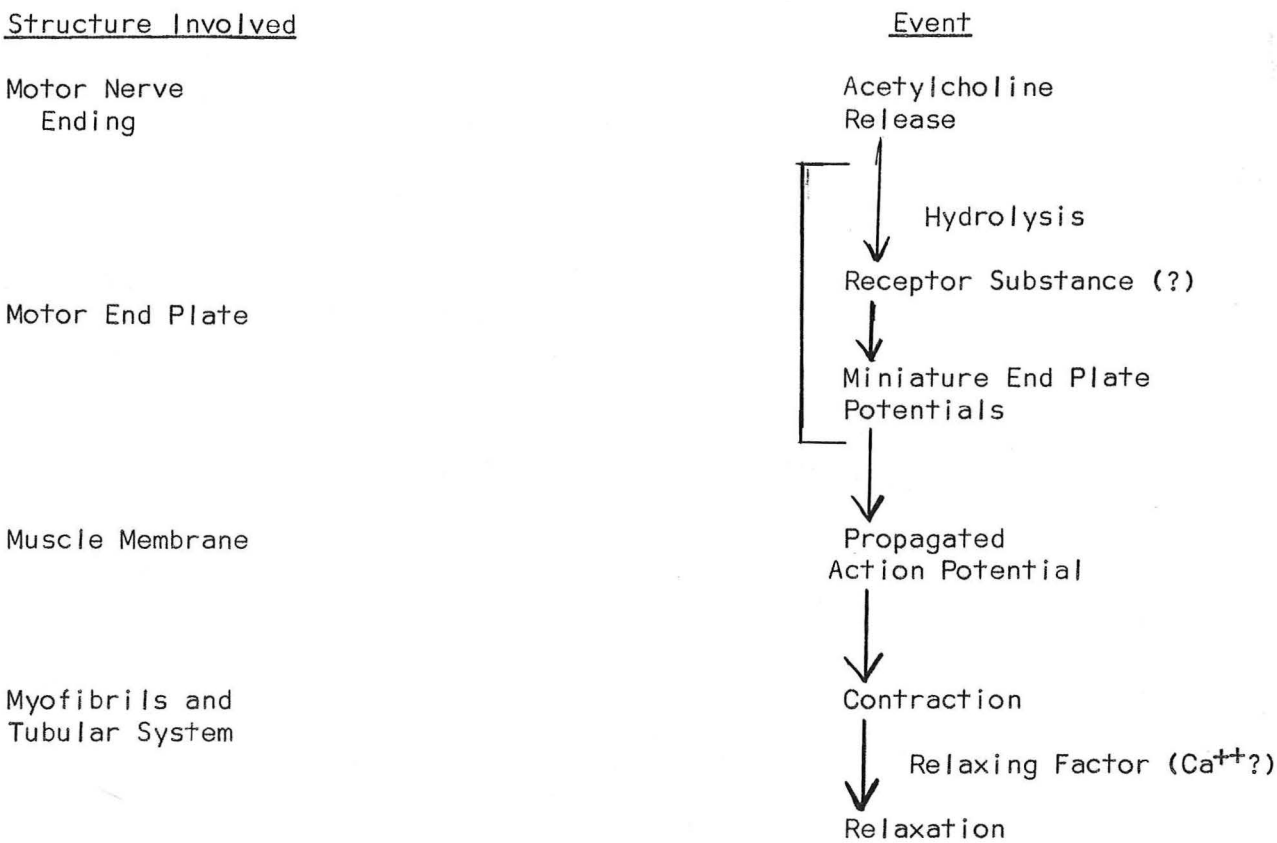
2) Within the cell there are fixed anionic charges that show the greatest affinity for potassium, thus the high intracellular concentration. In the vicinity of these fixed anionic charges, a negative potential (the membrane potential) can be measured with reference to extracellular fluid.

3) An ion pump continuously pumps sodium from the cell and by so doing generates a negative potential within the cell.

ACTION POTENTIAL



MUSCLE CONTRACTION



MEMBRANE POTENTIAL AND MUSCLE DATA IN NORMAL SUBJECTS

# Subjects	7
Measured Em	-89.7 ± 1.8 mV
Na mEq/L ICF	30.9 ± 4.5
K mEq/L ICF	141.4 ± 11.8
Na mEq/L ECF	142.2 ± 5.8
K mEq/L ECF	4.1 ± 0.4
Nernst Prediction	-96.4 ± 2 mV
Goldman Prediction	-88.4 ± 2 mV

General Reviews

1. McArdle, Brian. Metabolic and Endocrine Myopathies in Disorders of Voluntary Muscle. Ed. Walton, J.N. pp. 389-95. Little, Brown and Co. Boston 1964.

A short well written summary of periodic paralysis with adequate references.

2. Adams, R.P., Denny-Brown, D. and Pearson, C.M. Diseases of Muscle 2nd Ed. pp. 641-650, 664-666, 599-600. Harper & Row, New York 1965.

These authors regard all cases of hereditary hyperkalemic periodic paralysis as Paramyotonia. Hypokalemic periodic paralysis and thyrotoxic periodic paralysis are briefly reviewed.

3. Kloepfer, H.W. Genetic Aspects of Neuromuscular Disease in Disorders of Voluntary Muscle. Ed. Walton, J.N. pp. 451-452. Little, Brown and Co. Boston 1964.

Both hypo and hyperkalemic periodic paralysis show transmission by an autosomal dominant gene with complete penetrance for males and variable penetrance for females. This short discussion sights all the pertinent references.

Origin of Muscle Membrane Potential

4. Cirillo, V.P. Symposium on bioelectro-chemistry of microorganisms. I. Membrane potentials and permeability. Bacteriological Reviews 30:68, 1966.

A well presented discussion of the possible origins of membrane potentials.

5. Mullins, L.J. and Awad, M.Z. The control of the membrane potential of muscle fibers by the sodium pump. J. Gen. Phys. 48:761, 1965.

Original work suggesting that an electrogenic sodium pump is responsible for the membrane potential in skeletal muscle.

6. Johns, R.J. Potential Changes in the Normal and Diseased Muscle Cell in Disorders of Voluntary Muscle. Ed. Walton, J.N. pp. 579-603. Little, Brown and Co. Boston 1964.

A good, practical presentation describing methods and results in human muscle.

Hypokalemic Periodic Paralysis

7. Talbott, John H. Periodic paralysis. Medicine, 20:85, 1941.

The author made several important points:
1. Periodic paralysis is a syndrome which may be hereditary, but shows both dominant and recessive traits. (Incorrect: confused recessive with penetrance.)
2. Sporadic cases occur in susceptible individuals in association with thyroid disease.
3. Strenuous exercise and high carbohydrate diets invite attacks. Both may be associated with increased adrenalin production.

He recognized only the hypokalemic form of the syndrome.

8. Gass, H., Cherhasky, M., Savitsky, N. Potassium and periodic paralysis. Medicine. 27:105, 1948.

This is one of the longest case reports in history and of interest describes ECG changes (bigeminal rhythm) during an induced attack of periodic paralysis. It is further emphasized that serum levels of potassium do not absolutely dictate the onset of paralysis. (The patient reported was of the hypokalemic type.)

9. Danowski, T.S., Elkinton, J.R., Burrows, B.A. and Winkler, A.W. Exchanges of sodium and potassium in familial periodic paralysis. J. Clin. Invest. 27:65, 1948.

From balance studies concluded that there was an intracellular uptake of K during attacks not accompanied by changes in the intracellular and extracellular volume.

10. Conn, J.W. and Streeten, D.H.P. Periodic Paralysis in The Metabolic Basis of Inherited Disease. 1st Edt. pp. 867-918. Ed. Stanbury, J.B. Wyngaarden, J.B. and Fredrickson, D.S. McGraw-Hill Book Co. New York 1960.

11. Streeten, D.H.P. Periodic Paralysis in The Metabolic Basis of Inherited Disease 2nd Edition pp. 905-938. Ed. Stanbury, J.B., Wyngaarden, J.B. and Fredrickson, D.S. McGraw-Hill Book Co. New York 1966.

These two reviews are notable primarily for their extensive bibliographies. In both, the authors attempt to show that at least hypokalemic periodic paralysis is the result of intermittent aldosterone hypersecretion. From observations by others since 1958 this appears unlikely, at least in most cases.

12. Jones, R.V., McSwiney, R.R. and Brooks, R.V. Periodic paralysis. Lancet 1:177, 1959.

It is shown that sodium retention and increased excretion of aldosterone do not necessarily precede attacks of periodic paralysis.

13. Rowley, P.T. and Klisman, B. The effect of sodium loading and depletion on muscular strength and aldosterone excretion in familial periodic paralysis. Am. J. Med. 28:376, 1960.

In 2 patients, sodium loading generally decreased and sodium depletion generally increased muscle strength. Aldosterone excretion was normal in spontaneous attacks.

14. McArdle, B. Familial periodic paralysis. Brit. Med. Bull. 12:226,1956.

Emphasizes that dietary potassium restriction, ACTH or DOCA administration are capable of inducing attacks. However, body exchangeable K^{42} in an untreated patient was normal.

15. Zierler, K.L. and Andres, R. Movement of potassium into skeletal muscle during spontaneous attack in family periodic paralysis. J. clin. Invest. 36:730, 1957.

The best study showing a large net uptake of potassium by muscle in spontaneous and induced paralysis and the release of potassium during spontaneous recovery or recovery induced by KCl administration.

The inward nocturnal course of K seemed to be an exaggeration of that seen in normal individuals. (See J. clin. Invest. 36:723, 1957.)

16. Grob, D., Liljestrand, A. and Johns, R.J. Potassium movement in normal subjects. Effect on muscle function. Am. J. Med. 23:340, 1957.

17. Grob, D. Johns, R.J. and Liljestrand, A. Potassium movement in patients with familial periodic paralysis. Am. J. Med. 23:356,1957.

Normal

1. Contraction - K out
2. Glucose and perhaps epinephrine $\longrightarrow$ K in
3. Insulin $\longrightarrow$ K out (when hypokalemic)
4. Hyperkalemia $\longrightarrow$ K in

Periodic Paralysis

1. Glucose induced uptake greater than normal.
2. Epinephrine effect greater than normal.
3. Even when hypokalemic Insulin increased uptake of K.
4. During attacks, uptake of K increased.

Concluded that abnormal muscle uptake of potassium could lead to a hyperpolarization block.

18. Owen, E.E. and Verner, J.V. Renal tubular disease with muscle paralysis and hypokalemia. Am. J. Med. 28:8, 1960.

A presentation of nine cases with hypokalemia without primary muscle disease. During paralysis serum K was very low (range 1.5 to 2.8) unlike periodic paralysis where usually during paralysis serum K is only modestly reduced.

19. Shy, G.M., Wanko, T., Rowely, P.T. and Engel, A.G. Studies in familial periodic paralysis. Experimental Neurology 3:53, 1961.

This excellent paper describes the results of numerous studies in a family with periodic paralysis. Important observations and conclusions are:

1. Muscle K and Na not elevated during attacks.
2. Em of single fibers not changed from normal. (However, normal values were low; -70 -75 mV).
3. During paralysis membrane is silent - not stimulated.
4. Paralysis can occur without hypokalemia.
5. Aldosterone secretion not increased.
6. Both glucagon and epinephrine produce weakness.
7. Metabolic defect probably related to CHO metabolism in muscle.

(See also references 26 and 45)

20. Biemond, A. and Daniels, A.P. Familial periodic paralysis and its transition into spinal muscular atrophy. Brain 57:91, 1934.

This was apparently the first recognition of permanent muscle damage. However, the authors thought it was spinal nerve degeneration. In any event, the significance of permanent proximal weakness and paralysis was long overlooked.

21. Pearson, C.M. The periodic paralysis: Differential features and pathological observation in permanent myopathic weakness. Brain 87:341, 1963.

There are 3 or more types of periodic paralysis. Stresses the occurrance of permanent proximal myopathic weakness in long standing cases that resembles adult muscular dystrophy. In any one patient, the serum K at paralysis may be normal, high or low, although usually the K change is consistent.

22. Odor, D.L., Patel, A.N. and Pearce, L.A. Familial hypokalemic periodic paralysis with permanent myopathy. J. Neuropath. and Expr. Neurol. 26:98, 1967.

Another example of permanent weakness and proximal muscle atrophy. Interestingly, this was associated with myotonic lid-lag.

23. Engel, A.G. et al. Clinical and electromyographic studies in a patient with primary hypokalemic periodic paralysis. Am. J. Med. 38:626, 1965.

Intra-arterial epinephrine into the forearm produced weakness without inducing systemic changes in glucose or potassium concentrations.

24. de Graeff, J. and Lameijer, L.D.F. Periodic Paralysis. Am.J.Med. 39:70, 1965.

In some patients with hypokalemic form, cortisone therapy greatly decreased the frequency of attacks, especially when salt restriction and K supplements were of little therapeutic value.

25. Resnick, J.S. and Engel, W.K. Myotonic lid lag in hypokalemic periodic paralysis. J. Neurol. Neurosurg. Psychiat. 30:47, 1967.

Three patients with hypokalemic periodic paralysis are described that have prominent eyelid myotonia. Myotonia is not then the exclusive provance of the hyperkalemic form.

26. Riecher, G. and Bolte, H.D. Membrane potentials of single muscle cells in hypokalemic periodic muscular paralysis. Klin. Wschr. 44:804, 1966.

In a patient with a serum potassium of 2.0 mEq/L during paralysis, the Em was 49.1 mV. Normal range by these workers was 87.2 ± 5.2 mV. Ascribed the low Em to decrease K permeability and/or increased Na permeability of the muscle membrane.

(See also references 19 and 45)

27. Buchem Van, F.S.P. The electrocardiogram and potassium metabolism. Am. J. Med. 23:376, 1957.

In a single patient, with normal or near normal serum potassium between and during paralysis, the ECG had U waves. The author concludes that skeletal muscle drains K from cardiac muscle, a doubtful conclusion.

(See also references 28 and 37.)

28. Onat, A., Ozdamas, E. and Berkol, S. Sodium and potassium metabolism in a case of familial meriodic paralysis. J. clin. Endo. & Metab. 21:1079, 1961.

An interesting case study showing that attacks were usually preceeded by Na retention, but not always. In addition, in this patient, between attacks, with normal serum potassium, the ECG occasionally showed narrow, peaked T-waves suggestive of hyperkalemia. (See above reference.)

29. Engel, A.G., Potter, C.S. and Rosenear, J.W. Studies on carbohydrate metabolism and mitochondrial respiratory activities in primary hypokalemic periodic paralysis. Neurol. 17:329, 1967.

Biochemical studies carried out in one patient with hypokalemic periodic paralysis.

1. No defect in the pathway of glycogen synthesis could be found.
2. No accumulation of any anionic, phosphorylated intermediate of glycolysis was found.
3. No abnormality in ATP or ADP concentrations were found. Phosphocreatine was reduced.
4. The in-vitro respiratory activities of mitochondria were normal.

Normokalemic Periodic Paralysis

30. Poshanzer, D.C. and Kerr, D.N.S. A third type of periodic paralysis, with normokalemia and favorable response to sodium chloride. Am. J. Med. 31:328, 1961.

Basically a description of a family of 45, 21 of whom had periodic paralysis. Serum potassium remained normal during paralysis. Potassium loads brought on paralysis with little change in serum potassium concentration. Paralysis severe, as in hypokalemic paralysis. Muscle pathology same as hyper and hypokalemic types. Treated patients with 1) NaCl, 2) 9-alpha-fluorohydrocortisone and 3) Diamox plus 9-alpha-fluorohydrocortisone.

Hyperkalemic Periodic Paralysis

31. Tyler, F.H., Stephens, F.E., Gunn, F.D. and Perkoff, G.T. Studies in disorders of muscle. VII. Clinical manifestations and inheritance of a type of periodic paralysis without hypopotassemia. J. clin. Invest. 30:492, 1951.

This is the first description of what later was to be called hyperkalemic periodic paralysis. However, in the patients studied, the serum potassium was not significantly elevated during paralysis. From other findings, these patients do not appear to fall into the normokalemic group, however.

32. Gamstorp, I. Adynemia Episodica Hereditaria. Acta Pediatrica 45: Suppl 108, 5, 1956.

This author is responsible for medical Latin name for hyperkalemic periodic paralysis. At the time of this paper there were 138 patients; 68 of these were examined by the author. There were no deaths due to paralysis, but she did note occasional cranial nerve involvement (myotonia?). In only 2 older patients was permanent muscle weakness observed. Potassium excretion did not change during an attack of paralysis. Paralysis could usually be corrected by IV calcium. The heredity was apparently correctly described.

33. Conn, J.W. and Streeten, D.H.P. Adynamia Episodica Hereditaria in The Metabolic Basis of Inherited Disease. 1st Edition pp 919-926. Ed. Stanbury, J.B., Wyngaarden, J.B. and Fredrickson, D.S. McGraw-Hill Book Co. New York 1960.

The authors note four reports, in addition to Gamstorp's 13 reports, from the older literature that were apparently cases of hyperkalemic periodic paralysis rather than the more usual hypokalemic type.

34. McArdle, B. Adynamia episodica hereditaria and its treatment. Brain 85:121, 1962.

An excellent review.

35. Samaha, F.J. Hyperkalemic periodic paralysis. Arch. Neurol. 12:145 1965.

First suggested use of chlorthiazides to effectively reduce the number and severity of paralytic attacks.

36. Hudson, A.J. et al. Serum enzyme studies in familial hyperkalemic periodic paralysis. Clin. Chim. Acta 17:331, 1967.

Interestingly serum CPK and SGOT rose 48 hours after and induced attack and peaked between 72 - 96 hours following the attack.

37. Armstrong, F.S. Hyperkalemic familial periodic paralysis. Ann. Int. Med. 57:455, 1962.

A good case report giving data on serum K is induced attacks and clearly showing time course. After exercise, paralysis started in one hour. K 4 to 6. After KCl, paralysis again started in about 1 hour. K 4.4 to 6.3. ECG showed tall, peaked T waves in both cases during paralysis.

(See also references 27 and 28.)

38. Drager, G.A., Hamill, J.F. and Shy, G.M. Paramyotonia congenita. Arch. Neurol. & Psychiat. 80:1, 1958.

First pointed out the prominent occurrance of myotonia in hyperkalemic periodic paralysis.

39. van der Meulen, J.P. et al. Familial hyperkalemic paralysis with myotonia. New Eng. J. Med. 264:1, 1961.

Cases presented that tend strongly to link hyperkalemic paralysis with paramyotonia.

40. Van't Hoff, W. Familial myotonic periodic paralysis. Quart. J. Med. 31:385, 1962.

In a family, a clear relationship is shown between the induction of paralysis by potassium administration and myotonia in the eye lids and extremities.

41. Gamstorp, I. Adynamia episodica hereditaria and myotonia. Acta Neuro Scand. 39:1, 1963.

The first mention by this author of myotonia in her patients. The author believes that true hyperkalemic periodic paralysis does exist without myotonic findings, but that the paralysis and myotonia may represent a spectrum with myotonia without paralysis at one end and paralysis without myotonia at the other.

42. Carson, M.J. and Pearson, C.M. Familial hyperkalemic periodic paralysis with myotonic features. J. Pediat. 64:853, 1964.

A study of a family yielding many important observations. Several are:

1. Low Em between paralytic attacks.
2. Improvement of paralysis by epinephrine and by Aramine.
3. Drugs which increase potassium excretion reduce the attacks of paralysis.
4. During attacks, IV calcium had little or no effect. See Gamstorp and McArdle references.

43. Krull, G.H. et al. Myotonia produced by an unknown humoral substance. Lancet 2:668, 1966.

Perhaps an usual case of paramyotonia with probably attacks of normokalemic paralysis. Serum injected into rabbits and rats (IV) produced transient myotonia in these animals.

44. Layzer, R.B., Lovelace, R.E. and Rowland, L.P. Hyperkalemic periodic paralysis. Arch. Neurol. 16:455, 1967.

An excellent discussion of the occurrence of myotonia in this illness. The authors suggest a membrane defect to explain the paralysis and the myotonia.

45. Creutzeldt, O.D., et al. Muscle membrane potentials in episodic adynamia. Electroenceph. and Clin. Neurophysiol. 15:508, 1963.

Membrane Potentials: Open Method

1. Normal Subject --- -87.4 ± 8.9 mV'
2. Hypokalemic Periodic Paralysis
   Normal K = 4.25 Paralyzed K = 3.17
   -85.6 ± 6.1 mV -77.1 ± 8.2 mV
3. Hyperkalemic Periodic Paralysis
   Normal K = 3.75 Induced Paralysis K = 6.9
   -68.5 ± 5.9 mV -46.3 ± 6.6 mV

(See also references 19 and 26.)

Thyrotoxic Hypokalemic Periodic Paralysis

46. Okinaha, S. et al. The association of periodic paralysis and hyperthyroidism in Japan. J. Clin. Endocrin. 17:1454, 1957.

1. In Japan, the incidence of periodic paralysis in hyperthyroidism is 1.9%.
2. Male incidence 8.2%. Female incidence 0.4%.
3. Out of 119 cases, only one had a family history of periodic paralysis.
4. Attacks usually disappear after effective treatment of hyperthyroidism.

47. Engel, A.G. Thyroid function and periodic paralysis. Am. J. Med. 30:327, 1961.

Interesting study in which a patient with hypokalemic periodic paralysis was given thyroid. There was no effect on his disease as metabolic rate increased, however, when thyroid was withdrawn paralytic episodes (mostly normokalemic) became more frequent. Concludes that thyrotoxic paralysis has different underlying cause than familial periodic paralysis.

48. Okihiro, M.M. and Nordyke, R.A. Hypokalemic periodic paralysis. Experimental precipitation with sodium liothyronine. J. Am. Med. Ass. 198:949, 1966.

In a 44 year old man, free of paralysis 7 years following treatment of thyrotoxicosis, cytomel administration resulted in the return of typical hypokalemic periodic paralysis.

49. Shizume, K. et al. Studies on electrolyte metabolism in idiopathic and thyrotoxic periodic paralysis. I. A-V differences of electrolytes during induced paralysis. Metabolism.

As in familial periodic paralysis, there appears to be un uptake of potassium by muscle in thyrotoxic periodic paralysis.

50. Engel, A.G. Electron microscopic observations in primary hypokalemic and thyrotoxic periodic paralyses. Mayo Clin. Proc. 41:797, 1966.

The electron microscopic changes in both diseases are similar and are characterized primarily by dilation of the sarcoplasmic reticulum.