WEAK IN THE KNEES

ACUTE FLACCID PARALYSIS IN A YOUNG MALE

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TED GILES CLINICAL VIGNETTES
CSIM ANNUAL MEETING
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CASE

ID: 31 year old male in ER

RFR: Lower extremity weakness

A: Mentating well, able to provide a history – no airway concerns

B: SpO2 99% (room air)

C: HR 120 beats/min, BP 190/110 mmHg

TRIAGE NOTE

PT WOKE THIS AM AT 0730HRS FEELING WEAK. PT TRIED TO AMBULATE OUT OF BED BUT FELL TO THE FLOOR, DENIES HITTING HEAD PT STATES HE HAD A HEADACHE LAST NIGHT. PT DOES FEEL SOME NAUSEA, NO VOMITING. PT HAS LEG WEAKNESS, ARM WEAKNESS,CANNOT MOVE EXTREMITIES FREELY. JOINTS ARE STIFF. PUPILS EQUAL AND REACTIVE TO LIGHT.

HISTORY

- Was eating and drinking with some friends the night before: ate a grilled cheese sandwich x 2, drank 2 – 4 bottles of beer
- Went to sleep afterward ~midnight
- Woke up ~6h later – attempted to walk to the washroom
- Was able to get out of bed, but then collapsed (“my legs gave out”) – called for brother, who brought him to the ED

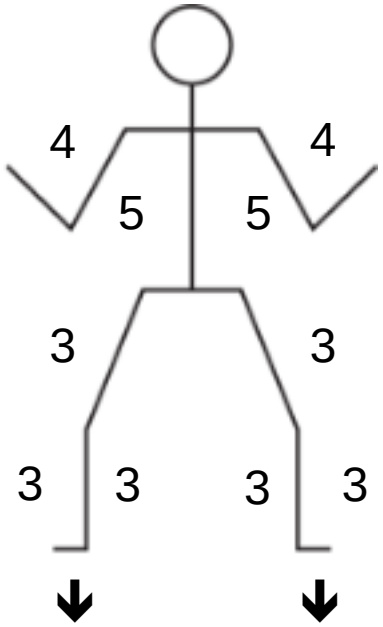
EXAM

- **Vitals:**
  - **BP**: 190/110 mmHg, **HR**: 120 BPM, **SpO_2**: 99%, **T**: 36.9
- **CVS:** Tachycardic, regular – S1/S2, no additional heart sounds, no murmurs
- **Resp:** Normal breath sounds bilaterally. RR 18
- **Abdo:** SNT

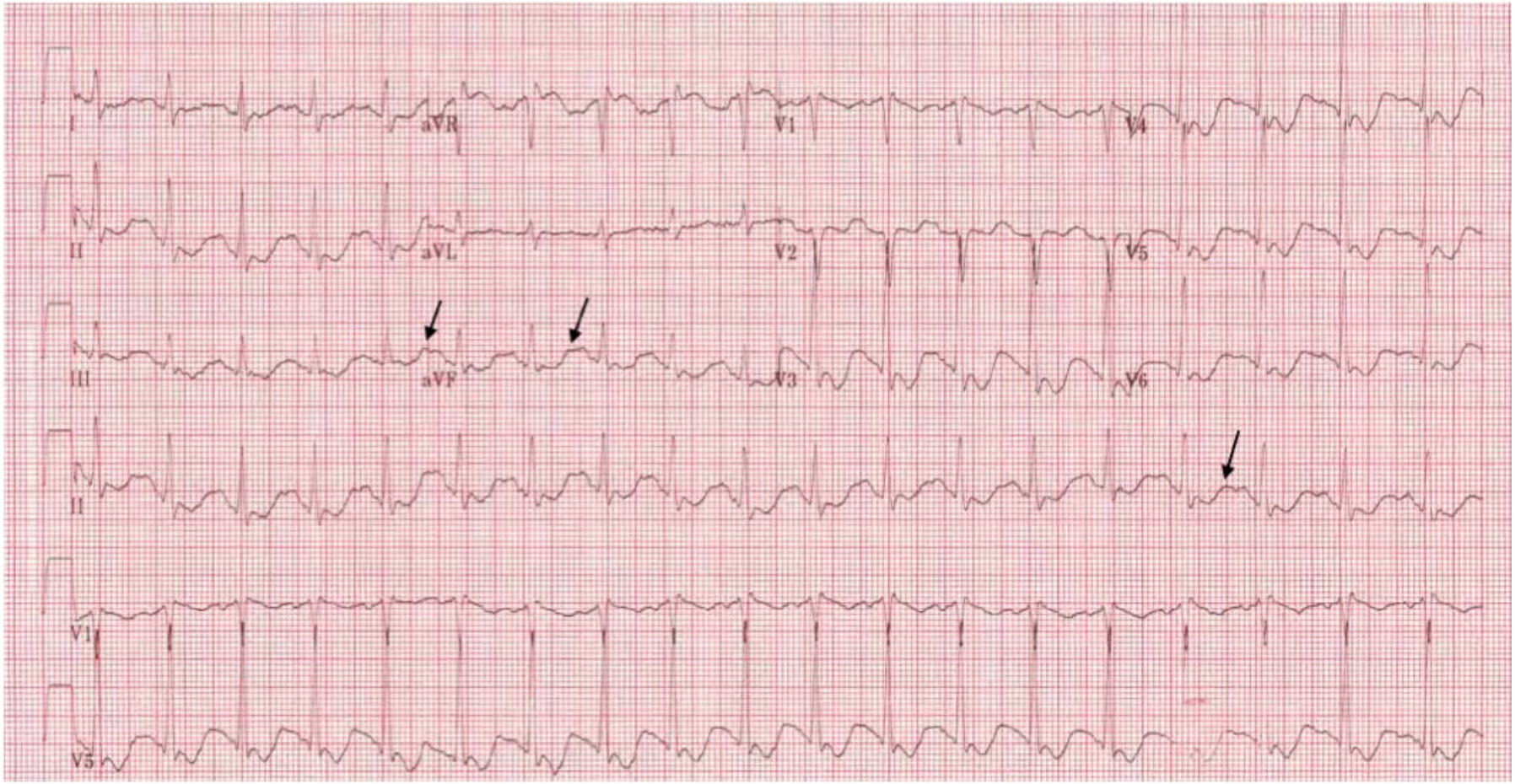
EXAM

Neurologic/MSK exam

- **General:** GCS 15, A/O x 3
- **CNs**: II-XII normal. No oculomotor/bulbar dysfunction
- **Sensory**: fully intact – sharp + dull
- **Motor** : lower extremity muscle groups: 3/5
- **Reflexes:** 2+ at patella
- **Tone:** no spasticity, no rigidity
- **UMN:** downward going toes
- **Gait:** deferred
- **Cerebellar:** normal rapid-alt.motions, unable to perform heel – shin. No dysmetria



ECG



Interpretation: Sinus rhythm, diffuse ST depressions with possible U wave formation

INVESTIGATIONS

Chemistry

- **Na^+**: 139
- **K^+**: **1.9**
- **Cl^-**: 103
- **Cr:** 50
- **Urea:** 1.9
- **CK: 3853**

VBG

- pH 7.37/pCO_2 39/HCO_3 23

CBC

- unremarkable

Severe hypokalemia with elevation in creatinine kinase. No overt acid/base abnormalities

CASE CONTINUED

- **Approach to hypokalemia**
  - **Extrarenal:** intake normal, no GI losses
  - **Renal:** no drugs affecting renal K^+ handling, 24h K^+ collection normal
  - **Shift:** no alkalosis
- **K^+ replenished through IV and PO**
- **Normalized on repeat that evening (3.6)**
- **Improved strength + patient seen ambulating independently that evening**
- **Remained hypertensive and tachycardic**

HYPERTENSION/TACHYCARDIA IN A YOUNG MALE

- **Drugs**
  - Sympathomimetics - cocaine, methamphetamines, amphetamines energy drinks
- **Endocrinopathy**
  - Hyperthyroidism
  - Hyperaldosteronism
  - Pheochromocytoma/paragangliomas
  - Hypercortisolism/Cushing's
- **Structural**
  - Renal artery stenosis
  - Coarctation of the aorta
  - CKD
- **"Appropriate"**
  - Anxiety
  - Pain

THE ANSWER...

Thyroid testing	Value	Normals
TSH	0.01 mIU/L ↓	0.5 – 5.0 mIU/L
Free T4	29 pmol/L ↑	10-20 pmol/L
Free T3	21.0 pmol/L ↑	3.5-6.5 pmol/L
TRAB	405 U/L ↑	negative

- **Further history:** 40 lb unintentional weight loss in the last ~2 months
- **Family history:** “something to do with the thyroid” on his maternal side.

- **Other testing:** plasma renin/aldosterone ratios normal, dexamethasone suppression testing initially ordered but then cancelled. CT head + MRI spine initially considered, but cancelled

THYROID EXAMINATION

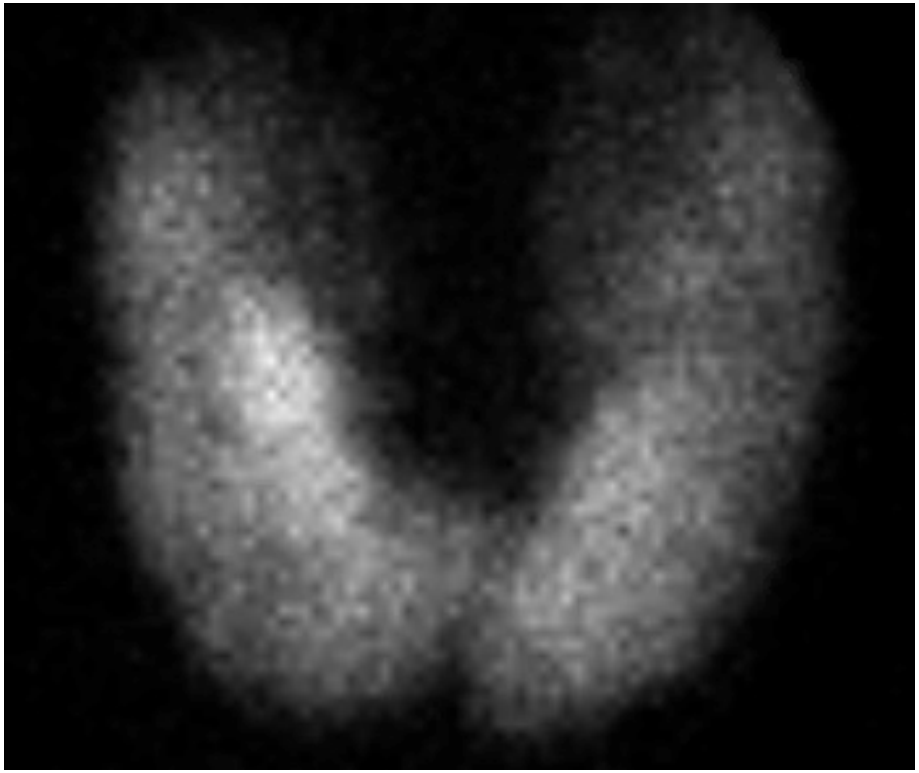
Examination of thyroid: Diffuse enlargement, nontender. No skin changes, no palpable nodules, no lymphadenopathy. No signs of obstructive goiter (SVC obstruction, distention of veins on chest).

Side note: pistol shot sounds heard along femoral arteries (picked up by endocrinology fellow) – indicative of **high cardiac output state**

IMAGING

Thyroid scintigraphy with I-131 administered orally and subsequent administration of Tc-99 (pertechnate). Avid trapping of pertechnate demonstrated within an enlarged thyroid gland, with diffuse nonuniformity consistent with…

GRAVE'S DISEASE



THYROTOXIC PERIODIC PARALYSIS

- **Definition:** a transient state of painless, flaccid paresis/paralysis secondary to hypokalemia mediated by thyrotoxicosis
- **Epidemiology**
  - Well described among East Asian, Japanese populations (1.8-1.9% of thyrotoxic patients)
  - In North American populations: 0.1-0.2% (but increasing)
  - Predominantly seen among **men** (as opposed to hyperthyroidism, which has a greater female preponderance)
  - **Minimal** genetic or epidemiologic features in common with **familial hypokalemic periodic paralysis**
  - Majority of cases associated with **Graves' disease**

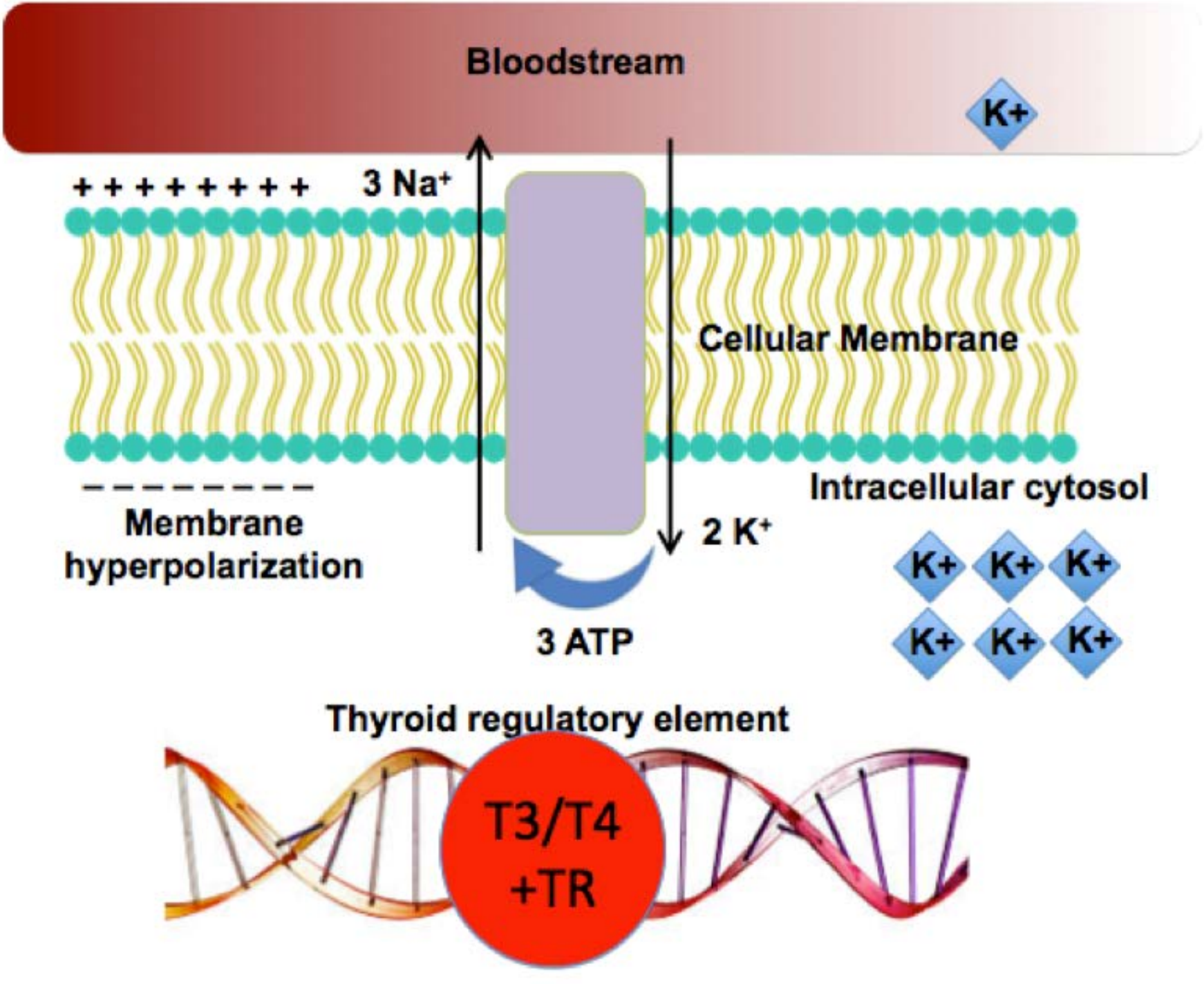
	Feature
✓	Adult young men
	Sporadic
✓	Recurrent acute paralysis with complete recovery
✓	Limb > trunk involvement
✓	Precipitated by heavy carbohydrate load, high-salt diet, alcohol, exertion
✓	Family history of hyperthyroidism
✓	Clinical features of hyperthyroidism
✓	Hypokalemia
✓	Normal acid-base balance
	Low potassium excretion rate
	Low phosphate excretion
	EMG: low-amplitude compound muscle action potential with no change after epinephrine

Kung *et al*. V. Thyrotoxic periodic paralysis: a diagnostic challenge. J Clin Endocrinol Metab 2006;91:2490-5

THYROTOXIC PERIODIC PARALYSIS

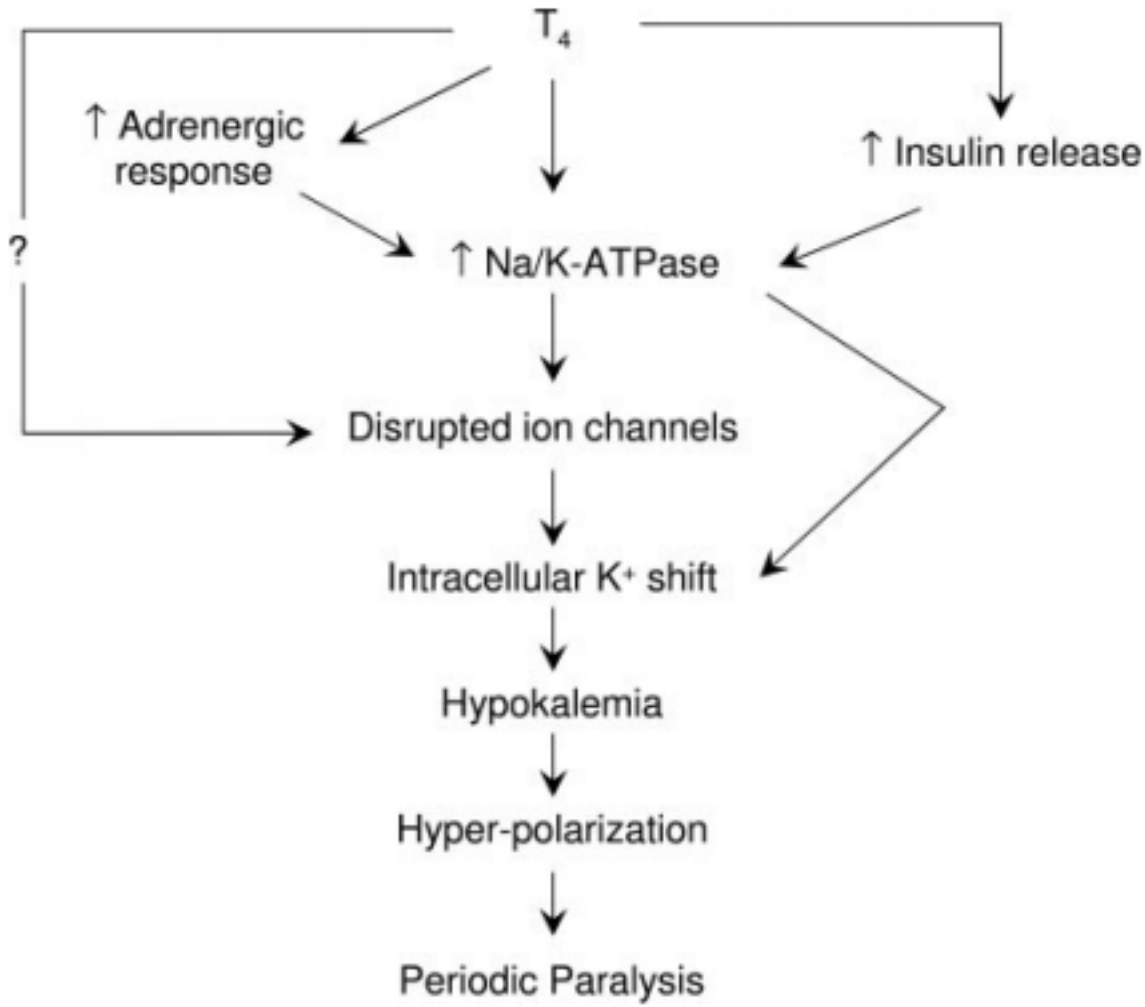
Pathophysiology: hypermetabolic state leading to increased transcription and activity of the **Na^+/K^+ ATPase pump**

- Pump causes influx of 2 K^+ ions and efflux of 3 Na^+
- Leads to membrane **hyperpolarization**
- Failure of skeletal/striated muscle cells to depolarize and initiate action potentials
  - Action potentials in neurons seem to be unaffected
- Dysfunction in **somatic** control of large, proximal muscle groups


Bloodstream
K+
+ + + + + + + + +
3 Na+
Cellular Membrane
– – – – – – – –
Membrane
hyperpolarization
2 K+
Intracellular cytosol
K+ K+ K+
K+ K+ K+
3 ATP
Thyroid regulatory element
T3/T4
+TR

TRIGGER?

- **Precipitants: trauma, cold exposure, alcohol, infections, carbohydrate-heavy meals**
- **Patient's meal prior to admission:**



Maciel RM *et. al*. Novel etiopathophysiological aspects of thyrotoxic periodic paralysis. Nat Rev Endocrinol 2011;7:657-67

Insulin resistance in subjects with a history of thyrotoxic periodic paralysis (TPP)

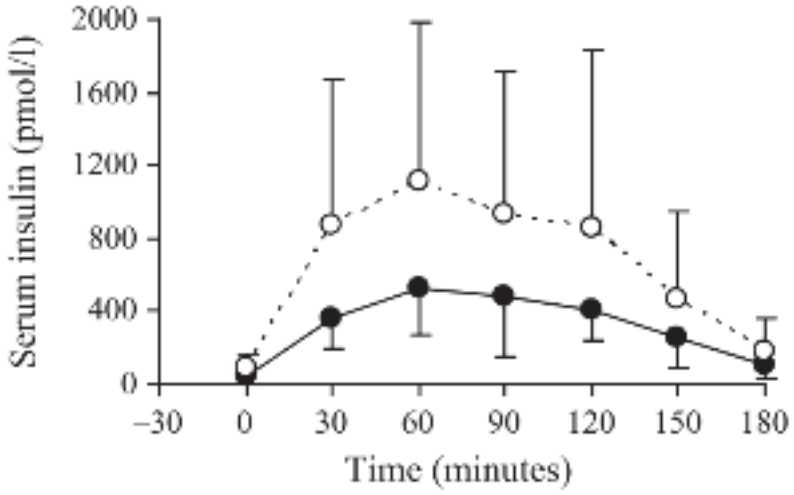
Supamai Soonthornpun, Worawong Setasuban and Atchara Thamprasit

Division of Endocrinology and Metabolism, Department of Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand

- Enrolled 20 Thai patients with a history of thyrotoxicosis and split them into two groups
  - History of TPP
  - No history of TPP
- 75g oral glucose tolerance test and euglycemic hyperinsulinemic clamp administered to both groups

Table 1. Characteristics at time of study

	TPP group ($n = 10$)	Control group ($n = 10$)	P
Age (year)	38 ± 9	42 ± 7	0·348
Duration after diagnosis (year)	4·4 ± 4·1	5·6 ± 2·6	0·470
BMI (kg/m^2)	26·56 ± 5·28	21·98 ± 2·27	0·021
Waist circumference (cm)	88·7 ± 11·1	77·2 ± 8·2	0·022
Hip circumference (cm)	97·5 ± 10·1	90·1 ± 5·5	0·066
Waist : hip ratio	0·91 ± 0·05	0·86 ± 0·06	0·046
Systolic blood pressure (mmHg)	127 ± 17	127 ± 9	0·911
Diastolic blood pressure (mmHg)	78 ± 13	75 ± 5	0·508
FT4 (pmol/l)†	16·60 ± 3·39	16·94 ± 3·08	0·820
TSH (mIU/l)†	3·32 ± 3·24	3·31 ± 2·45	0·994



Serum insulin levels of hyperthyroid patients during administration of 20% dextrose solution (euglycemic clamp).

- White: TPP
- Black: no TPP

…Role for compensatory hyperinsulinemia in TPP?

OUTCOME

- **Patient was initiated on nadolol and methimazole while hospitalized – became clinically euthyroid and was discharged**
- **Followed up with endocrinology as an outpatient**
- **Chose radioiodine ablation of his thyroid 2-3 months after his initial admission for TPP**
- **Biochemically and clinically euthyroid at follow up 6 months after discharge**
- **No further attacks of periodic paralysis**

TAKE HOME POINTS

- **Thyrotoxic periodic paralysis (TPP) is an uncommon presentation of a common illness (hyperthyroidism)**
- **Predominantly seen in Asian populations, but prevalence in North American populations is increasing**
- **Metabolic causes of paralysis/paresis are not often high on the differential**
- **Thyrotoxicosis should be considered as a cause of acute flaccid paralysis, particularly in patients with a high pre-test probability**

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DISCLOSURES

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QUESTIONS?

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McMaster University
MEDICINE

ACUTE APPENDICULAR PARALYSIS

- **Infectious**
  - Poliomyelitis
  - West Nile virus
  - Epidural abscess
  - Botulism
- **Inflammatory**
  - Multiple sclerosis
  - Guillain – Barre syndrome
  - Transverse myelitis
- **Structural**
  - Spinal cord infarct
  - Spinal cord injury

TABLE 2. Distinguishing features between TPP and FHPP

	TPP	FHPP
Age (yr)	20–40	<20
Sex distribution	Predominantly male	Equal
Heredity	Sporadic	Autosomal dominant
Ethnicity	Asian, American Indian/Hispanic, Caucasian	Caucasian, Asian
Family history	History of thyrotoxicosis	History with hypokalemic paralysis
Clinical features of hyperthyroidism	Yes	No
Genetic predisposition	Associated with SNPs of $Ca_v1.1$ (−476A→G, intron 2 nt 57G→A, intron 26 nt 67A→G)	Mutations of $Ca_v1.1$ (R5258H, R1239H, R1239G), $Na_v1.4$ (R669H, R672G, R672H), $K_v3.4$ (R83H)

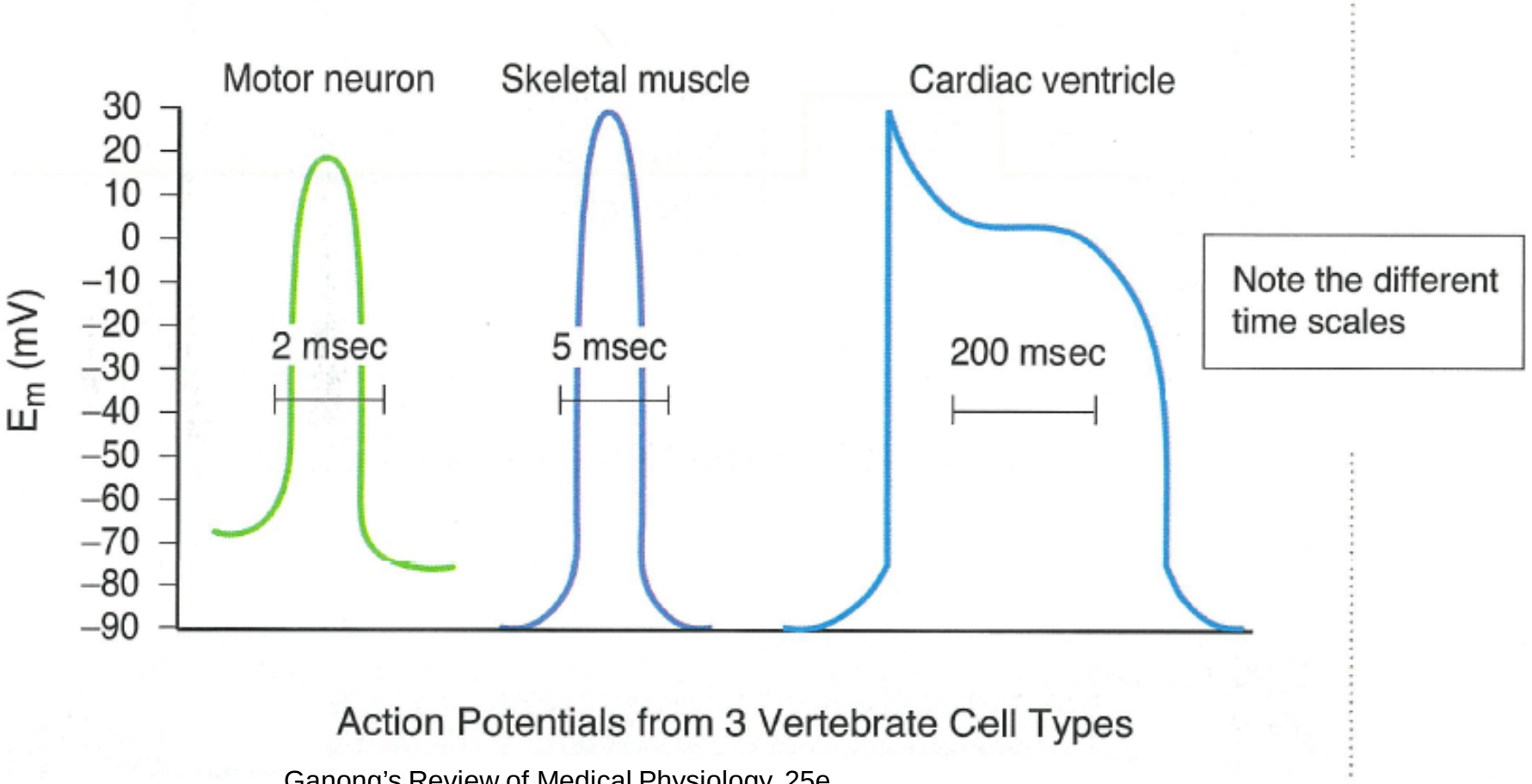
Patients with TPP usually experience the attack a few hours after a heavy meal or in the early morning upon waking: more than two thirds of patients present to the emergency department between 2100 and 0900 h. Such timing of presentation led the condition to be initially described as nocturnal paralysis or night palsy (16). Patients may give a history of similar but milder attacks before presentation.

Kung AW. Clinical review: Thyrotoxic periodic paralysis: a diagnostic challenge. J Clin Endocrinol Metab 2006;91:2490-5.

Electromyogram (EMG) performed during spontaneous weakness typically reveals myopathic changes with reduced amplitude of compound muscle action potentials (34). There is no notable change in the amplitude on epinephrine stimulation. Nerve conduction studies are normal with no peripheral nerve involvement. Similar to FHPP, exercise can

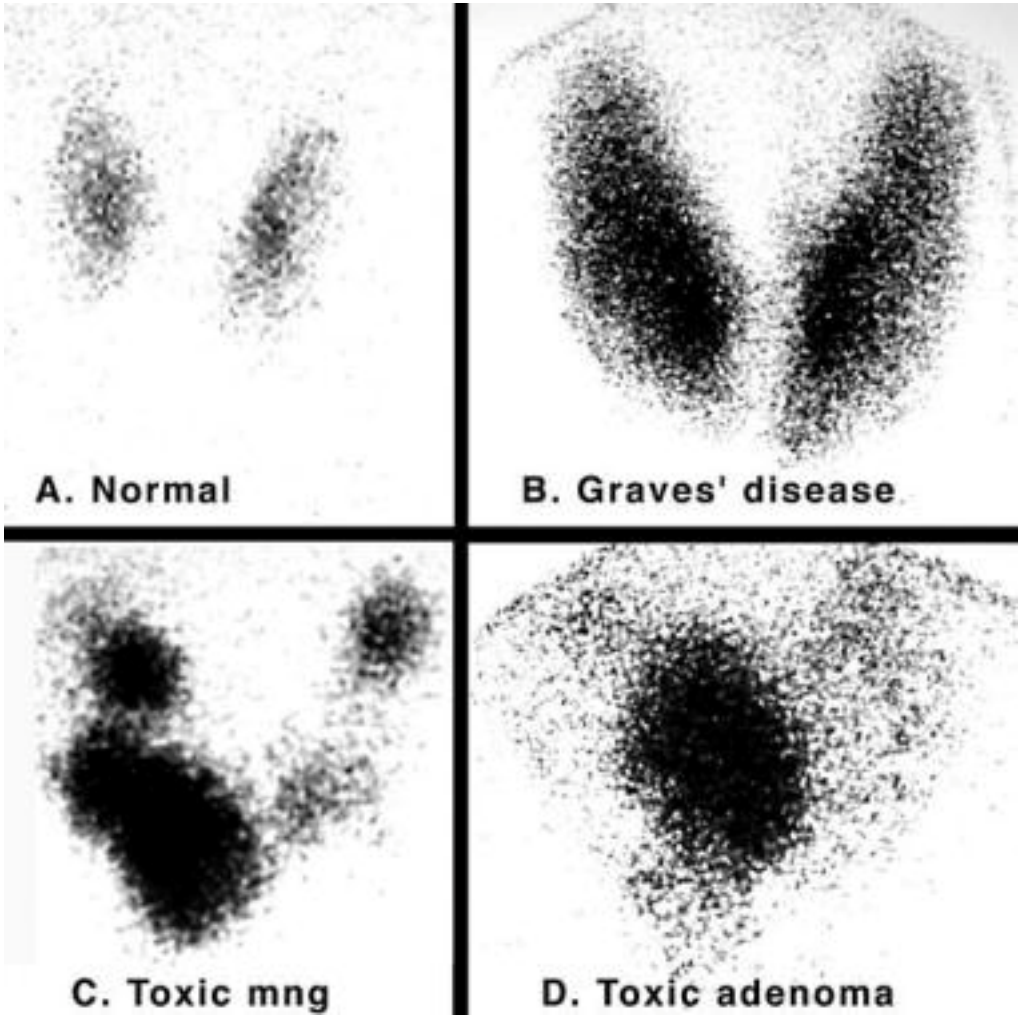
Kung AW. Clinical review: Thyrotoxic periodic paralysis: a diagnostic challenge. J Clin Endocrinol Metab 2006;91:2490-5.

COMPARISON OF CELLULAR ACTION POTENTIALS



Action Potentials from 3 Vertebrate Cell Types

Ganong's Review of Medical Physiology, 25e.



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