DECODING

LEMS

DECIPHER THE MYSTERY

CONTENTS

MISSION DEBRIEFING

LEMS Counterintelligence →

The Dossier on LEMS →

Known Associates →

LEMS SURVEILLANCE

Recognizing the Signs →

What to Look For →

ALIASES AND DOUBLE AGENTS

Myasthenia Gravis (MG) →

Small Cell Lung Cancer (SCLC) →

CONFIRMATION AND NEUTRALIZATION

LEMS Diagnostic Methods →

Treatment of LEMS →

MISSION DEBRIEFING

LEMS COUNTERINTELLIGENCE

Congratulations on securing this codebook—it is an essential asset in the fight against Lambert-Eaton myasthenic syndrome, aka LEMS. Never let it out of your sight!

LET'S BEGIN

Named for the 2 investigators who first identified the syndrome in the late 1950s[1], LEMS is an insidious disorder that steals muscle, decimates health, and yet continues to evade the eyes and attention of even our most seasoned agents.[1-3]

Your mission is to uncover the signs of LEMS, decipher its mysterious codes, confirm its identity, and finally bring this menace out into the light of day where its effects can be dealt with.

Decryption is the key to unlocking the mystery of LEMS

DECRYPTION KEY

MISSION DEBRIEFING

THE DOSSIER ON LEMS

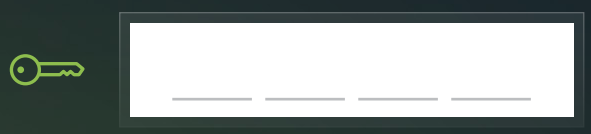
- A rare, immune-mediated disorder of the neuromuscular junction[2]
- Causes debilitating and progressive muscle weakness and fatigue[1,2]
- Associated with small cell lung cancer (SCLC) in about 50% of cases[3]
- Characterized by several distinguishing signs and symptoms that will be described on the following pages
- Left unchecked, it leads to diminished physical functioning, quality of life, and independence[1]

LEMS IS A MASTER OF DISGUISE

In one study of 241 LEMS patients, more than half were initially diagnosed with another condition[3]

BREAK THIS CODE

LEMS is estimated to affect at least



people in the US[4]

DECRYPTION KEY

A	B	C
D	E	F
G	H	I
J	K	L
M	N	O
P	Q	R
S	T	U
V	W	X
Y	Z	1
2	3	4
5	6	7
8	9	0

MISSION DEBRIEFING

LEMS KNOWN ASSOCIATES

WHERE TO LOOK

LEMS can be difficult to identify but is often associated with two particular groups.

AUTOIMMUNE DISEASE[3,5,6]

In LEMS not associated with cancer, pre-existing autoimmune conditions are frequently observed.[3] Examples include hypo- and hyperthyroidism, celiac disease, type 1 diabetes, ulcerative colitis, Addison's disease, and rheumatoid arthritis. Like many other autoimmune disorders, a genetic susceptibility may be present in LEMS not associated with cancer.[5,6]

SMALL CELL LUNG CANCER

~50%-60% of LEMS cases are paraneoplastic syndromes—most frequently associated with SCLC—but LEMS can also occur with other cancers.[5,7,8]

WHEN TO LOOK

LEMS has 2 peak ages of onset:

~35 YEARS
for patients without SCLC[2]

~60 YEARS
for patients with SCLC[2]

BREAK THIS CODE

LEMS is estimated to affect at least

of patients with lung cancer—frequently SCLC—develop a paraneoplastic syndrome.[3]

LEMS is the most common antibody-mediated neurologic paraneoplastic syndrome **associated with SCLC**[3]

DECRYPTION KEY

A	B	C
D	E	F
G	H	I
J	K	L
M	N	O
P	Q	R
S	T	U
V	W	X
Y	Z	1
2	3	4
5	6	7
8	9	0

LEMS SURVEILLANCE

RECOGNIZING THE SIGNS

LEMS IS CHARACTERIZED BY A CLINICAL TRIAD OF SYMPTOMS[3]

AUTONOMIC SYMPTOMS

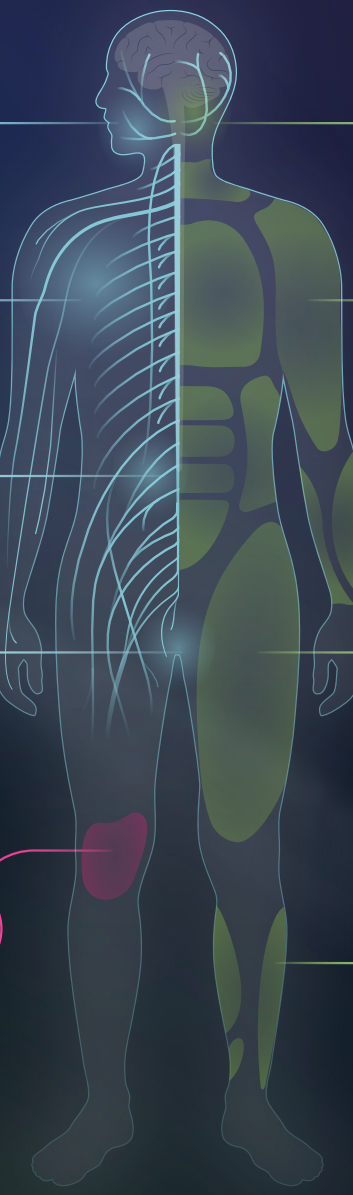
- Dry mouth — 83%
- Orthostatic hypotension — 29%
- Constipation — 34%
- Impotence — 65%

NEUROMUSCULAR SYMPTOMS

- Oculobulbar involvement — 50%
- Proximal arm muscle weakness — 78%
- Proximal leg muscle weakness — 97%
- Distal leg muscle weakness — 31%

TENDON REFLEX SYMPTOMS

- Areflexia/Hyporeflexia — 90%



DECRYPTION KEY

A	B	C
D	E	F
G	H	I
J	K	L
M	N	O
P	Q	R
S	T	U
V	W	X
Y	Z	1
2	3	4
5	6	7
8	9	0

LEMS SURVEILLANCE

WHAT TO LOOK FOR

LEARNING THESE HALLMARK LEMS SIGNS MAY FACILITATE A MORE TIMELY DIAGNOSIS

PROXIMAL MUSCLE WEAKNESS

In up to 97% of LEMS cases, muscle weakness begins in the upper legs and hips, including the pelvic girdle.[3,9] As this weakness progresses, it can lead to an unsteady gait.[1,2] LEMS weakness typically spreads upward affecting arm muscles[9] but may also spread downward impacting the distal leg muscles.[3]

AUTONOMIC DYSFUNCTION

Signs or symptoms of autonomic dysfunction have been found in 80%-96% of LEMS patients.[3,9]

The autonomic signs most frequently seen in LEMS patients include dry mouth, impotence, constipation, and orthostatic hypotension.[3]

HYPOREFLEXIA OR AREFLEXIA

Patients with LEMS will often present with decreased or even absent tendon reflexes (>90%).[3,9]

A characteristic phenomenon of LEMS is a short-term return of tendon reflexes and muscle strength following muscle contraction, with fatigue returning afterward.[3,9]

OCULOBULBAR SYMPTOMS

Although oculobulbar symptoms typically develop later in the course of the disorder, up to 80% of LEMS patients will experience them.[1,3]

These symptoms may include diplopia, ptosis, disconjugate gaze, involuntary lid closure, prolonged upgaze, dilated pupils, and poorly reactive pupils.[10,11]

BREAK THIS CODE

Ptosis is 1 of the 2 most common oculobulbar signs of LEMS; the other is

_ _ _ _ _ _ _ _

otherwise known as double vision.[10,12]

DECRYPTION KEY

ALIASES AND DOUBLE AGENTS

MYASTHENIA GRAVIS (MG)

LEMS IS OFTEN MISTAKEN FOR MG OR OTHER NEUROMUSCULAR DISORDERS[3]

The clinical presentation of LEMS can resemble several other neuromuscular and neurologic disorders, but MG is the condition most often mistaken for LEMS.[3,9]

INITIAL DIAGNOSIS PRIOR TO CONFIRMATION OF LEMS[3]

MORE THAN 1/3 OF LEMS PATIENTS

were previously diagnosed as having MG[3]

DISTINGUISHING LEMS FROM MG[3]

Only LEMS is strongly associated with **autonomic dysfunction and hyporeflexia/areflexia**

In LEMS, **muscle weakness is symmetrical and typically spreads upward**. In MG, symptoms are asymmetrical and generally spread downward

Oculobulbar involvement in LEMS is typically **milder and occurs later**; in MG, onset is early and more prominent

DECRYPTION KEY

A	B	C
D	E	F
G	H	I
J	K	L
M	N	O
P	Q	R
S	T	U
V	W	X
Y	Z	1
2	3	4
5	6	7
8	9	0

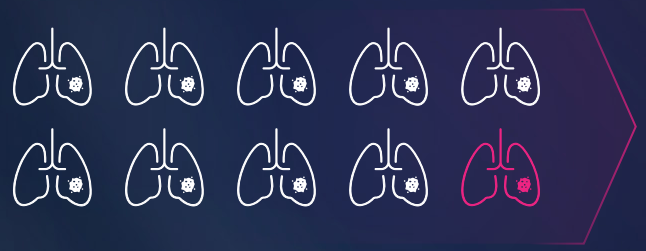
ALIASES AND DOUBLE AGENTS

SMALL CELL LUNG CANCER (SCLC)

LEMS SOMETIMES HIDES BEHIND SCLC OR OTHER CANCERS[3]

Because the effects of tumor burden and/or cancer therapy can negatively impact muscle strength, LEMS muscle weakness may be missed in patients with a co-occurring cancer.[8,13]

ESTIMATED PREVALENCE OF PATIENTS WITH SCLC-ASSOCIATED LEMS[14]



An analysis of claims data suggests that

>90% OF LEMS CASES

associated with SCLC may be undiagnosed[14]

DISTINGUISHING LEMS FROM SCLC[3]

Autonomic symptoms in a patient with SCLC may indicate the presence of a paraneoplastic neurologic syndrome, specifically LEMS.[15] A retrospective observational study of US healthcare claims revealed:

The percentage of patients with SCLC and LEMS who had autonomic symptoms was

9x HIGHER

than in those without autonomic symptoms[14]

BREAK THIS CODE

The onset of LEMS symptoms can occur

≥ ⋈ YEARS

≥ __ YEARS

before, after, or at the time of a cancer diagnosis.[5]

DECRYPTION KEY

A	B	C
D	E	F
G	H	I
J	K	L
M	N	O
P	Q	R
S	T	U
V	W	X
Y	Z	1
2	3	4
5	6	7
8	9	0

CONFIRMATION AND NEUTRALIZATION

LEMS DIAGNOSTIC METHODS

Once you've uncovered a suspicion of LEMS, there are 2 ways to establish the bona fides for a diagnosis: the easy way (a serum antibody test) or the hard way (electrodiagnostic testing).

ANTI-VGCC ANTIBODY TESTING

Antibodies against voltage-gated calcium channels (VGCC) are found in 85%-90% of patients with LEMS and in virtually all patients with SCLC-associated LEMS—so an antibody test can be an effective tool to help confirm a diagnosis of LEMS.[3]

Click for intel on a free test

ELECTRODIAGNOSTIC TESTING

In some cases, increment on high-frequency repetitive nerve stimulation or post-exercise facilitation is also used in confirming a diagnosis of LEMS.[3]

BREAK THIC CODE

Anti-VGCC antibodies are present in virtually

[illegible]%

___ ___ ___ %

of SCLC patients with LEMS.[3]

DECRYPTION KEY

A	B	C
D	E	F
G	H	I
J	K	L
M	N	O
P	Q	R
S	T	U
V	W	X
Y	Z	1
2	3	4
5	6	7
8	9	0

CONFIRMATION AND NEUTRALIZATION

TREATMENT OF LEMS

You've decoded the signs, identified the suspect, and verified its identity—well done! You're now ready for the final phase of the operation: neutralization of the threat. Let's review your objectives…

GOALS FOR LEMS TREATMENT[1,2,16,17]

- Maintenance/improvement in muscle strength and functional mobility
- Screening/assessment for co-occurring cancer, particularly SCLC
- Maintenance/improvement in patient independence and quality of life

UNCOVER A PROVEN TREATMENT OPTION

The current standard of care for LEMS treatment is an agent that works at the site of neuromuscular dysfunction to restore communication between the nerves and muscles.

We've set up a rendezvous point where you can meet this agent and learn more about its specific mode of operation.

Click to access this treatment intel

DECRYPTION KEY

THE MISSION CONTINUES

CONNECT WITH MORE SOURCES OF LEMS INTELLIGENCE

DECODING LEMS

WWW.DECODINGLEMS.COM

LEMS aware

WWW.LEMSAWAREHCP.COM

References:

1. Harms L, Sieb J-P, Williams AE, et al. Long-term disease history, clinical symptoms, health status, and healthcare utilization in patients suffering from Lambert Eaton myasthenic syndrome: results of a patient interview survey in Germany. *J Med Econ*. 2012;15(3):521-530.
2. National Organization for Rare Disorders (NORD) website. Rare disease database: Lambert-Eaton myasthenic syndrome. Accessed August 18, 2022. https://rarediseases.org/rare-diseases/lambert-eaton-myasthenic-syndrome/.
3. Titulaer MJ, Lang B, Verschuuren JJ. Lambert-Eaton myasthenic syndrome: from clinical characteristics to therapeutic strategies. *Lancet Neurol*. 2011;10(12):1098-1107.
4. Data on file, Catalyst Pharmaceuticals.
5. Wirtz PW, Smallegange TM, Wintzen AR, Verschuuren JJ. Differences in clinical features between the Lambert-Eaton myasthenic syndrome with and without cancer: an analysis of 227 published cases. *Clin Neurol Neurosurg*. 2002;104(4):359-363.
6. Gilhus NE. Lambert-Eaton myasthenic syndrome; pathogenesis, diagnosis, and therapy. *Autoimmune Dis*. 2011;2011:973808.
7. Titulaer MJ, Maddison P, Sont JK, et al. Clinical Dutch-English Lambert-Eaton myasthenic syndrome (LEMS) tumor association prediction score accurately predicts small-cell lung cancer in the LEMS. *J Clin Oncol*. 2011;29(7):902-908.
8. Kesner VG, Shin JO, Dimachkie MM, Barohn RJ. Lambert-Eaton myasthenic syndrome. *Neurol Clin*. 2018;36(2):379-394.
9. Merino-Ramírez MÁ, Bolton CF. Review of the diagnostic challenges of Lambert-Eaton syndrome revealed through three case reports. *Can J Neurol Sci*. 2016;43(5):635-647.
10. Young JD, Leavitt JA. Lambert-Eaton myasthenic syndrome: ocular signs and symptoms. *J Neuroophthalmol*. 2016;36(1):20-22.
11. Gordon LK. Paraneoplastic syndromes in neuro-ophthalmology. *J Neuroophthalmol*. 2015;35(3):306-314.
12. Titulaer JM, Wirtz PW, Wintzen AR, et al. Lambert-Eaton myasthenic syndrome with pure ocular weakness. *Neurology*. 2008;70(1):86-87.
13. Huot Jr, Pin F, Bonetto A. Muscle weakness caused by cancer and chemotherapy is associated with loss of motor unit connectivity. *Am J Cancer Res*. 2021;11(6):2990-3001.
14. Morrell D, Drapkin B, Schecter G, Grebla R. Lambert-Eaton myasthenic syndrome is underrecognized in small cell lung cancer: an analysis of real-world data. Presented as a poster at the International Association for the Study of Lung Cancer (IASLC) – WCLC Annual Meeting 2023. September 9-12, 2023; Singapore.
15. Shechter G, Morrell D, Grebla R, Vernino S. Autonomic symptoms may suggest paraneoplastic neurological syndromes in small-cell lung cancer: results from a US database analysis. Abstract presented at: National Comprehensive Cancer Network Annual Conference. April 5-7, 2024; Orlando, FL.
16. Ivanovski T, Miralles F. Lambert-Eaton myasthenic syndrome: early diagnosis is key. *Degener Neurol Neuromuscul Dis*. 2019;9:27-37.
17. Quartel A, Turbeville S, Lounsbury D. Current therapy for Lambert-Eaton myasthenic syndrome: development of 3,4-diaminopyridine phosphate salt as first-line symptomatic treatment. *Curr Med Res Opin*. 2010;26(6):1363-1375.

Catalyst pharmaceuticals

Printed in USA. LEM-0390-1 September 2024