Cyber & Specialist Operations Command

Phenotypes of Modern Non-Freezing Cold Injury: Implications for Diagnosis and Return to Duty

Surgeon Commander (OF4) J Lowe BMBS FRCEM FFRRHHEd RN

UK Defence Lead for NFCI Research

Thematic Lead (Environmental Medicine), Academic Department of Military Emergency Medicine

Head of Research, British Antarctic Survey Medical Unit, Plymouth, UK

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COLD WEATHER MEDICINE

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This work represents the opinion of the author, produced as part of their working for the UK Ministry of Defence. The abstract was conceived by the author. There are no competing interests to be declared. This work did not receive any funds or grands. Patient consent is not required for its publication. Ethical approval was not required.

Surg Cdr J Lowe BMBS FRCEM RN

Academic Emergency Physician

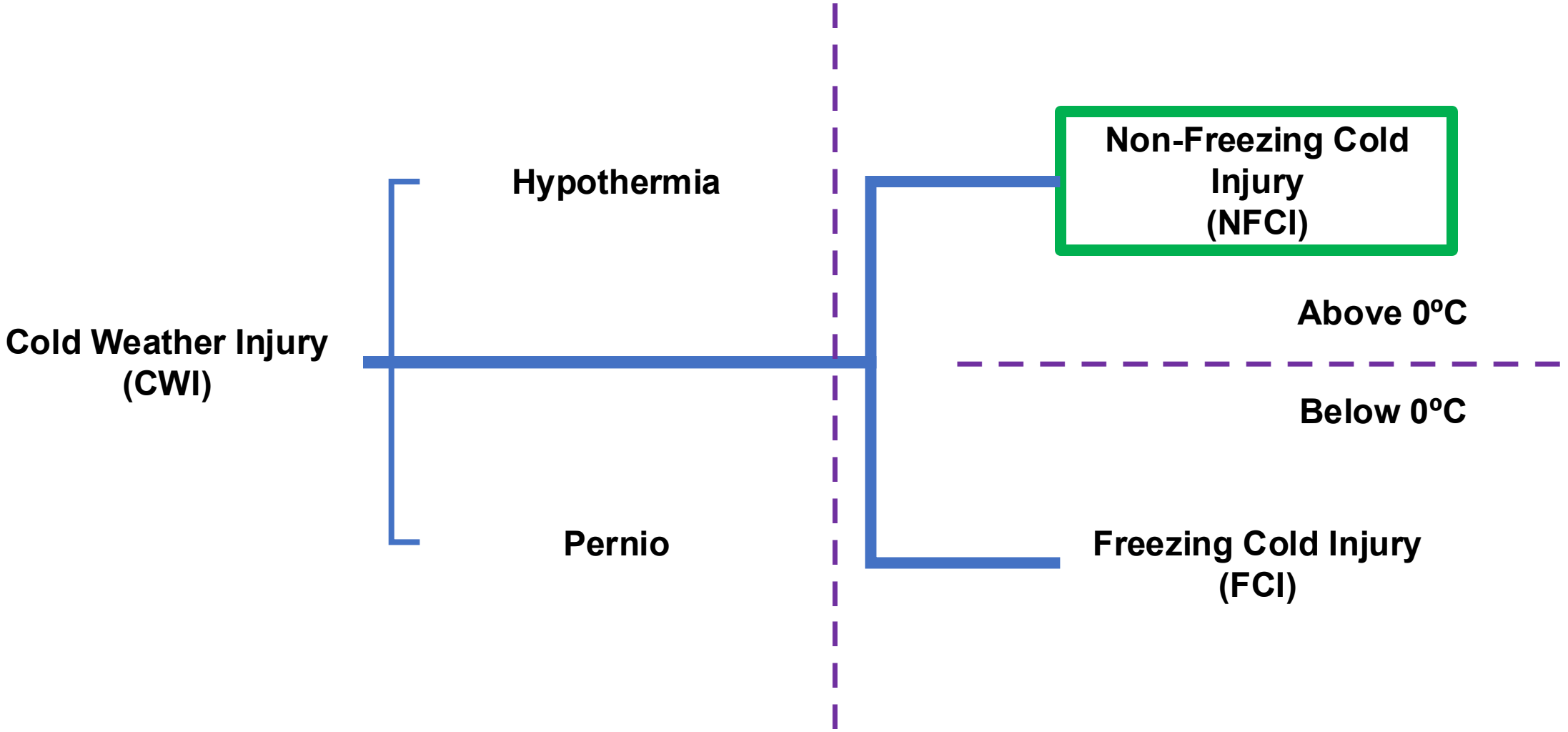
UK Defence Lead, Cold Weather Research

Portfolio Focus:

- Cold Weather Injuries (Mechanism and Management)
- Environmental Adaptation
- Impact on Medical Materiel

Doctoral Fellow, Imperial College London

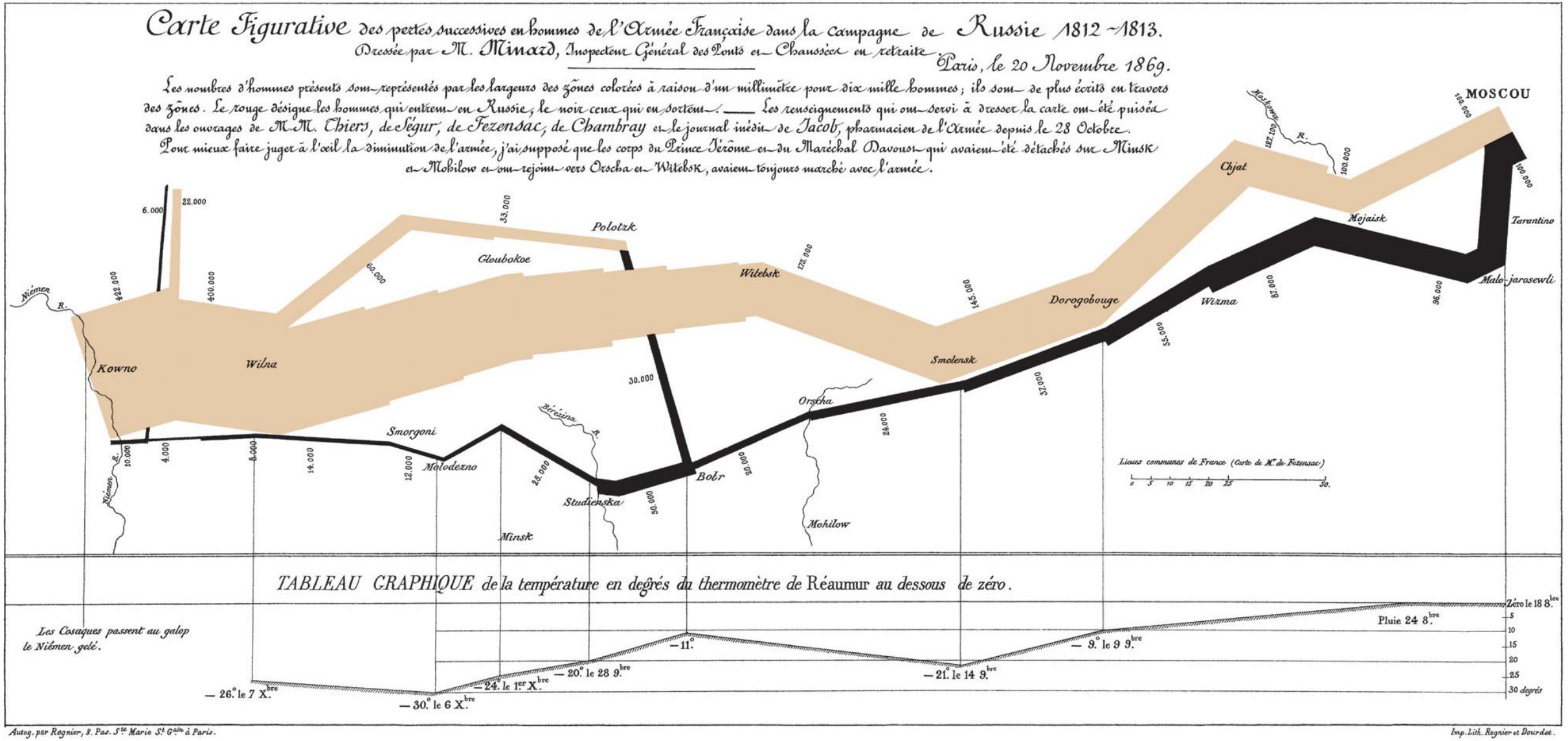
CANREGRO Trial (ISRCTN11180128)


Cold Weather Injury
(CWI)
Hypothermia
Pernio
Non-Freezing Cold
Injury
(NFCI)
Above 0ºC
Below 0ºC
Freezing Cold Injury
(FCI)

The National WWI Museum and Memorial. Trench Warfare. https://www.theworldwar.org/learn/about-wwi/trench-warfare [Accessed 01 July 26]

Fig. 2.—Distribution of sensory loss and of anhidrosis in another moderately severe case, in the hyperæmic stage. Dotted line and crosses mark the upper levels for sensory loss to light touch of cotton-wool and to moderate pin-prick respectively. Black areas indicate heavy sweating, dotted areas moderate sweating, and unshaded areas absence of sweating (sweat test by chinizarin method, Guttmann 1940). In the right great toe the black area indicates the site of superficial gangrene.

Ungley, C.C. Peripheral Vasoneuropathy After Chilling "Immersion Foot and Immersion Hand". The Lancet, 1942. 10.1016/s0140-6736(00)58135-5 [Accessed 01 July 26]



Age of Revolution. Waterloo Association. https://ageofrevolution.waterlooassociation.org.uk/200-object/flow-map-of-napoleons-invasion-of-russia/ [Accessed 01 July 26]

Background

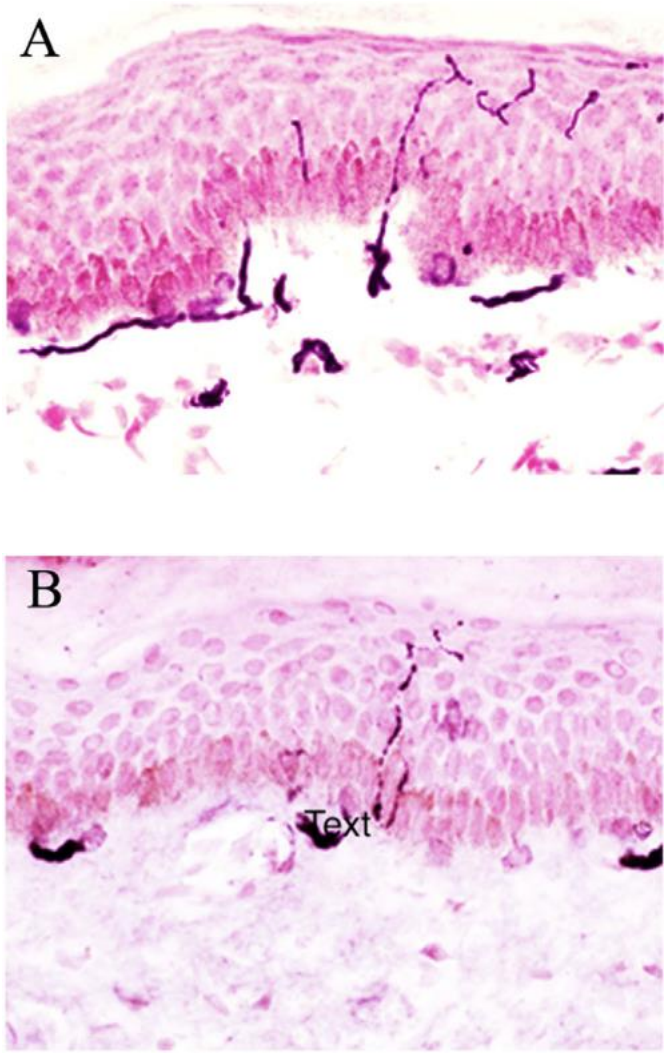
- 2015 – 2019:
  - 118 patients seen in a 3º peripheral neuropathy service.
  - 104 complete records used in analysis.
  - All patients had a history of ***cold*** exposure ***and*** ongoing symptoms.

Total Number (M:F %)		104 (M:F 94.2:5.8)
Age (years)		29 ± 6.05
Time to CIC (weeks)		17.5 (IQR 10-80.8)
Time to ICL (weeks)		40.5 (IQR 24-101)
Ethnicity (%)	White	44 (42.3)
	Black African	41 (39.4)
	Black Caribbean	10 (9.6)
	Asian	2 (1.9)
	Other	4 (3.8)
	Unknown	3 (2.9)

Table 1: Key Demographics

Method

- Full Assessment:
  - Neurological examination.
  - Quantitative sensory testing (QST).
  - 3mm calf skin punch biopsy for intraepidermal nerve fibre assessment (IENF).
  - *Nerve conduction studies.*



Images from: Trench foot or Non-Freezing Cold Injury As a Painful Vaso-Neuropathy: Clinical and Skin Biopsy Assessments. Anand, P *et al*. Frontiers in Neurology. 10.3389/fneur.2017.00514 [Accessed 01 July 26]

Method

- Assessment results were reviewed and scored based upon findings.
  - Neurological examination:
    - Normal, score = 0
    - Abnormal, score = 2
  - QST:
    - Normal, score = 0
    - Abnormal in at least one domain, score = 2
  - Biopsy and IENF:
    - Normal, score = 0
    - Borderline (normal PGP 9.5 but other histology abnormal), score = 1
    - Abnormal (abnormal PGP 9.5 value), score = 2
- Scores were then combined and categorised using a 3-letter description:
  - 2 + 2 + 2 = AAA

Results

Neurological Exam (%)	Normal	28 (26.9)
	Abnormal	76 (73.1)
Conduction Studies (%)	Normal	84 (80.8)
	Abnormal	20 (19.2)
QST (%)	**Monofilament**	
	Normal	45 (43.3)
	Abnormal	59 (56.7)
	Vibration	
	Normal	59 (56.7)
	Abnormal	45 (43.3)
	Thermal Thresholds	
	Normal	14 (13.5)
	Abnormal	90 (86.5)

Table 2: Examination Findings

PGP9.5 Calf 15 (n)	2.49 ± 1.73	*(6.5 ± 1.4)*
PGP9.5 Calf 50 (n)	4.50 ± 2.48	*(8.3 ± 0.3)*
TRPV1 (n)	3.04 ± 1.92	*(5.7 ± 1.4)*
SNSR Calf (n)	1.25 ± 1.54	*(3.6 ± 0.64)*
GAP43 Calf (n)	0.70 ± 1.15	*(0.06 ± 0.2)*
vWF (n)	3.49 ± 1.28	*(2.53 ± 0.16)*
eNOS (n)	2.03 ± 0.72	*(0.93 ± 0.09)*

Table 3: Skin Biopsy Findings

Results

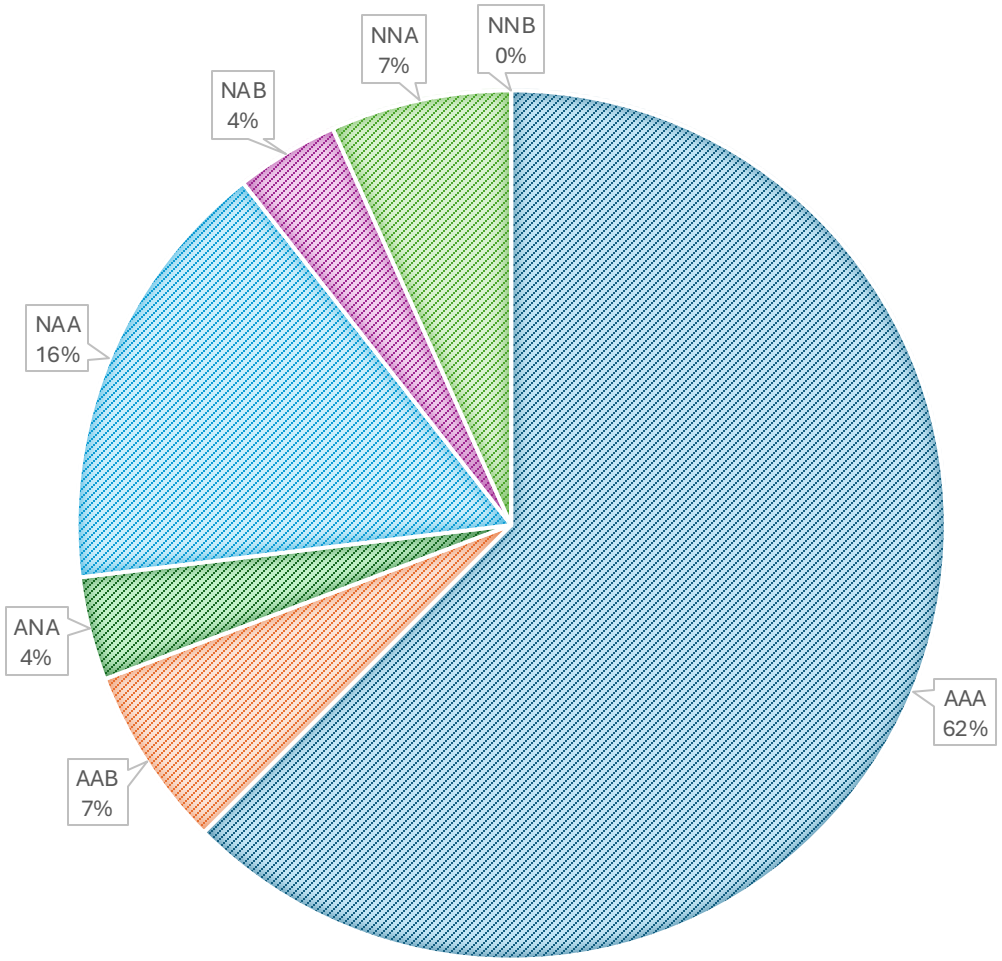


Figure 1: Phenotype Breakdown

Abnormal Neuro	Abnormal QST	Abnormal Biopsy	**AAA**	1A	65.00	**62.50**
Abnormal Neuro	Abnormal QST	Borderline Biopsy	**AAB**	1B	7.00	**6.73**
Abnormal Neuro	Normal QST	Abnormal Biopsy	**ANA**	2A	4.00	**3.85**
Normal Neuro	Abnormal QST	Abnormal Biopsy	**NAA**	2B	17.00	**16.35**
Normal Neuro	Abnormal QST	Borderline Biopsy	**NAB**	3A	4.00	**3.85**
Normal Neuro	Normal QST	Abnormal Biopsy	**NNA**	3B	7.00	**6.73**
Normal Neuro	Normal QST	Borderline Biopsy	**NNB**	3C	0.00	**0.00**
Normal Neuro	Normal QST	Normal Biopsy	**NNN**	N	0.00	**0.00**

Table 4: Phenotype Description

Discussion

- No patient had entirely normal findings across all three modalities, and no patient had a wholly normal IENF analysis.
- Multimodal assessment appears to identify clinically relevant variation in disease phenotype.
- Further analysis ongoing based upon relationship of PGP9.5 (50µ), TRPV1 and specific sensory deficits from QST.
- Further prospective work is needed to determine the significance of these phenotypes, occupational risk stratification and return-to-duty decisions.

Implications for LSCO

- Greatest risk is in sub-threshold environments, with risk of immersion.
- Compounded by prolonged evacuation timelines. Poor understanding of temporal relationship between disease severity and duration of exposure.
- Increasing challenges of rehabilitation with severe disease, impacting fighting force.
- Increasing component of DNBI (estimate 1% all injuries).

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Surgeon Commander (OF4) J Lowe BMBS FRCEM FFRRHHEd RN

Email: Jonathon.lowe100@mod.gov.uk

Email: j.lowe24@imperial.ac.uk

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