



# The ICON 2022 Diagnostic Criteria for Optic Neuritis

SLCTRIMS 21-JAN-2024, 7:00-7:30, Symposium 4









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# Disclosures

NIHR UK, UCSF Stichting MS Research NL Novartis, Heidelberg Academy









# The ICON 2022 story

### THE LANCET Neurology



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### Optic Neuropathies

Published: September 22, 2022

#### **Executive Summary**

Optic neuropathies can reflect a wide range of pathophysiologies, both acquired and inherited. This Series provides an update on the clinical, imaging, and laboratory findings that differentiate these disorders, allowing clinicians to focus their diagnostic studies and optimise treatments. Multimodality optic nerve imaging-including fundus photography, optical coherence tomography, and MRI-has greatly advanced the diagnosis and follow-up of patients with optic neuropathies. Also reviewed in this Series, new evidence shows that optic neuritis can frequently indicate autoimmune neurological disorders, including multiple sclerosis and the recently recognised disease categories of aquaporin-4 antibody-associated neuromyelitis optica spectrum disorder and myelin-oligodendrocyte glycoproteir antibody-associated disease. Early clinical recognition of optic neuritis is, therefore, important for prognosis and treatment. Also reviewed in the Series, a unifying feature in the pathophysiology of hereditary disorders of the optic nerve is mitochondrial dysfunction. Treatments are emerging for chic neuropathies, including immunotherapies and genetic therapies.



#### Imaging of the optic nerve: technological advances and future prospects

Valérie Biousse, Helen V Danesh-Meyer, Amit M Saindane, Cédric Lamirel, Nancy J Newman

The Lancet Neurology Published: September 22, 2022

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### Optic neuritis and autoimmune optic neuropathies: advances in diagnosis and treatment

The Lancet Neurology

Published: September 22, 2022

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#### Understanding the molecular basis and pathogenesis of hereditary optic neuropathies: towards improved diagnosis and management

The Lancet Neurology Published: September 22, 2022

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#### Relat content

### POSITION PAPER Diagnosis and classification of optic

The Lancet Neurology

Published: September 27, 2022

### Myelin-oligodendrocyte glycoprotein antibody-associated disease

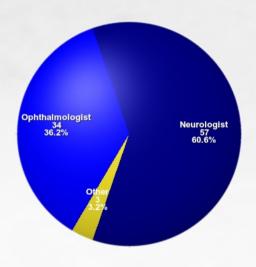
The Lancet Neurology, Vol. 20, No. 9 Published: September, 2021 Full-Text HTML | PDF

#### Mitochondrial disease in adults: recen advances and future promise

The Lancet Neurology, Vol. 20, No. 7 Published: July, 2021







Definition of consensus >80% expert agreement



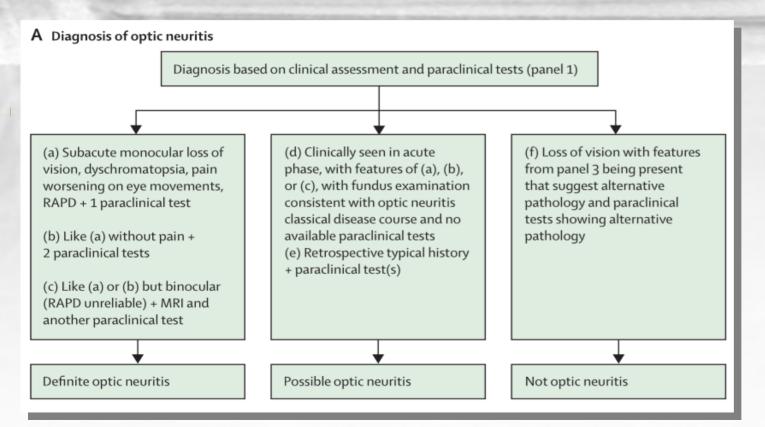








# ICON 2022 Diagnostic Criteria





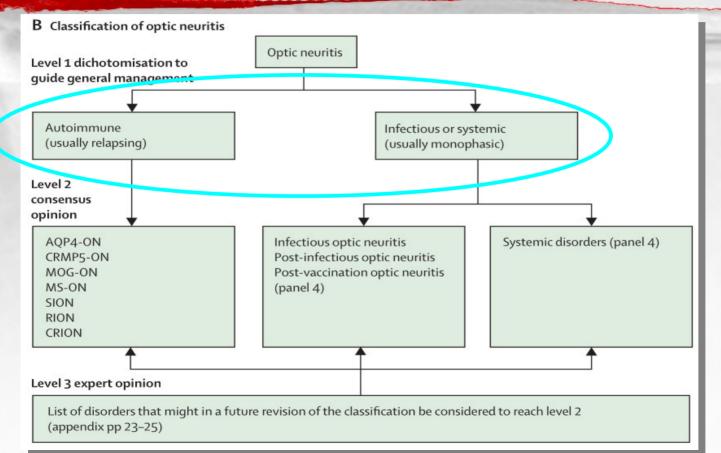






UCL

# ICON 2022 Classification













### 1st Case

- 34 year old Caucasian female patient
- 7 day history of pain in the right eye which worsens on eye movements
- Reduced colour vision
- VA RE: 6/9, left eye LE: 6/5
- Right RAPD
- Reports: fatigue, cognitive problems, urinary incontinence, depression
- PmHx: right sided numbness lasting 1m, 3y ago







### 1st Case

- Bloods all normal except for low Vitamin D at 22 nmol/L (normal 50-200 nmol/L)
- MRI: DIS & DIT three Gd+ non-symptomatic lesions
- CSF not done

What is the most likely diagnosis?









### 2<sup>nd</sup> Case

- 28 year old, Afrocaribbean male
- Painless loss of vision LE (6/38)
- Dyschromatopsia
- L RAPD
- Several steroid responsive episodes over ~20 y fup
- OCT: pRNFL atrophy LE (IEPD >5%)
- MRI a swollen, Gd+, left optic nerve. No lesions elsewhere
- AQP4 seropositive



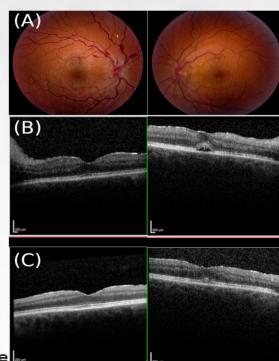






### 3<sup>rd</sup> Case

- 72 year old male develops febrile illness in Vietnam
- 2-3 weeks later bilateral, sequential, painless loss of vision (PL)
- no RAPD (but both pupils constrict with accomodation)
- Fundus (next slide):
  - Bilateral disc edema
  - RE hemorrhages
  - LE macular scar, CMO
- No recovery @ 6m fup
   (IVMP given ~6w after onset)







# 3 clinical scenarios of increasing complexity

- Case 1: is this MS?
   Scenario A: painful, monocular, subacute LOV, dyschromatopsia, RAPD
- Case 2: is this NMO?
   <u>Scenario B</u>: no pain, monocular, subacute LOV, dyschromatopsia, RAPD
- Case 3: what is this?
   Scenario C: binocular, subacute LOV, dyschromatopsia, no pain, no RAPD







### Panel 1: Diagnostic criteria for optic neuritis

### Clinical criteria

- A: Monocular, subacute loss of vision associated with orbital pain worsening on eye movements, reduced contrast and colour vision, and relative afferent pupillary deficit
- B: Painless with all other features of (A).
- C: Binocular loss of vision with all features of (A) or (B).

### Paraclinical criteria

- OCT: Corresponding optic disc swelling acutely or an inter-eye difference in the mGCIPL of >4% or >4  $\mu$ m or in the pRNFL of >5% or >5  $\mu$ m within 3 months after onset.
- MRI: Contrast enhancement of the symptomatic optic nerve and sheaths acutely or an intrinsic signal (looking brighter) increase within 3 months.
- Biomarker: AQP4, MOG, or CRMP5 antibody seropositive, or intrathecal CSF IgG (oligoclonal bands).

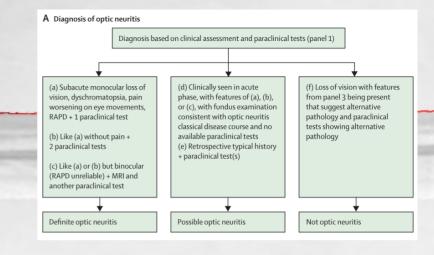
### Application of the clinical and paraclinical criteria

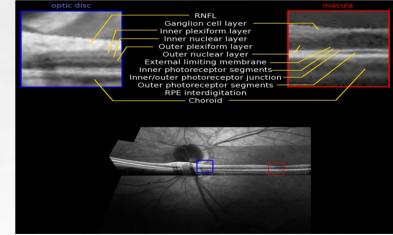
### Definite optic neuritis

- (A) and one paraclinical test
- (B) and two paraclinical tests of different modality
- (C) and two different paraclinical tests of which one is MRI

### Possible optic neuritis

- (A), (B), or (C) if seen acutely but in absence of paraclinical tests, with fundus examination typical for optic neuritis and consistent with the natural history during follow-up
- Positive paraclinical test or tests, with a medical history suggestive of optic neuritis









### OCT in MS-ON

	Device	MSON Control			Weight (%)		Mean difference* (µm; 95% CI)	
		Mean (µm; SD)	Total eyes	Mean (µm; SD)	Total eyes			(µm, 93% CI)
Peripapillary RNFL								-15·30 (-17·54 to -13·06)
Balk et al (2014)2	н	76-4 (11-6)	144	91-7(6-8)	126	7.3		-10-00 (-15-53 to -4-47)
Behbehani et al (2015)22	T	101-3 (14-4)	32	111-3 (8-7)	51	5.8		-12-90 (-21-83 to -3-97)
Behbehani et al (2016)23	Z	82 (14-1)	10	94-9(6)	40	41		
Esen et al (2016) <sup>25</sup>	Z	82-2 (11-8)	40	96-7(8-2)	60	6.5	-	-14-50 (-18-70 to -10-30)
Feng et al (2013) <sup>26</sup>	Z	71-8 (19-2)	12	102-1 (8-1)	28	3.2	<b>←</b>	-30-30 (-41-57 to -19-03)
Gelfand et al (2012)30	н	80-2 (17-8)	262	101-3 (10-1)	106	7.1	-	-21·10 (-23·99 to -18·21)
Gonzalez-Lopez et al (2014)31	Z	79-6 (13-6)	36	99-3 (8-7)	140	6.2		-19-70 (-24-37 to -15-03)
Huang-Link et al (2015)34	Z	67-7 (7-91)	15	93-6(8-9)	68	6.3		-25-90 (-30-43 to -21-37)
Khalil et al (2016)36	0	84-1 (13-5)	30	117-8 (26-2)	23	3.1	<b>←</b>	-33-70 (-45-45 to -21-95)
Lange et al (2013) <sup>40</sup>	н	73-9 (15-2)	13	98-4(8-8)	100	4.3		-2450 (-32-94 to -16-06)
Oberwahrenbrock et al (2012) <sup>43</sup>	H	77-8 (14-6)	183	100-6 (8-8)	183	7.2	+	-22-80 (-25-27 to -20-33)
Oberwahrenbrock et al (2013)6	н	82-1 (18)	16	101-4 (7-4)	90	4.1		-19-30 (-28-25 to -10-35)
Park et al (2014) <sup>64</sup>	H	70-1 (6)	15	100-1 (9-3)	24	6.2	-	-30-00 (-34-80 to -25-20)
Rebolleda et al (2011) <sup>46</sup>	Z	81(0)	18	93-5(0)	18	**		Not estimable
Schneider et al (2013)49	H	85-3 (13-3)	20	100-1 (10-8)	34	5.1		-14-80 (-21-67 to -7-93)
Soufi et al (2015) <sup>51</sup>	T	77 (11)	7	104(8.7)	58	4.3	<del></del>	-27-00 (-35-45 to -18-55)
Syc et al (2012)54	Z	78-7(11-7)	73	93-4 (10-4)	100	6.9		-14·70 (-18·07 to -11·33)
Walter et al (2012)55	н	78-4(13-6)	87	92-9 (9-9)	61	6.7		
Xuet al (2016) <sup>56</sup>	Z	73-6(14-8)	35	97-1 (11-5)	41	5.5		-14-50 (-18-29 to -10-71)
Total(N)			1030		1333	100-0		
Heterogeneity: $\tau^2$ =23-83; $\chi^2$ =97-3	5. df=17 (p-	<0-0001): P=83%			4333	100-0	•	-20-10 (-22-76 to -17-44)
Test for overall effect: Z=14-82 (p	<0.0001)	, , , , , ,						
Test for overall effect: Z=14-82 (p	<0.0001)						-20 -10 0 10 20	
Heterogeneity: r <sup>2</sup> =23-83; $\chi^2$ =97-3	2' math (b						-20 -10 0 10 20	
Total(N)	r 46-17 (p.	-0.0001): P=83%	200200					
Xuet al (2016)"	7	12.0(******)	1030		1333		Man difference (95% CI)	

Whall et al (2015)\*\*

Lange et al (2013)\*\*

Oberwalvenbrock et al (2

Oberwalvenbrock et al (2

Oberwalvenbrock et al (2

Park et al (2014)\*\*

Eboblieda et al (2011)\*\*

Schneider et al (2013)\*\*

Schneider et al (2013)\*\*

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Walter et al (2012)\*\*

Walter et al (2012)\*\*

Biotherian et al. (2015)\*
Biotherian et al. (2016)\*
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Fong et al. (2016)\*
Gografie et al. (2013)\*
Huang-line et al. (2013)\*
Huang-line et al. (2013)\*
Lange et al. (2013)\*\*
Dhewaltrenbrock et al. (2012)\*
Oberwaltrenbrock et al. (2013)\*

12.77	8) 35	Control		Weight	Mean difference (95	leterice (35
	MsoN Mean (SD) To	otal Mean (SD)	Total			-28·93 (-40·41 to -17·45
Albrecht (2007) <sup>4</sup> Bock (2010) <sup>9</sup> Burkholder (2009) <sup>12</sup> Fisher (2006) <sup>10</sup> Frohman (2009) <sup>13</sup> Klistoner (2008) <sup>15</sup> Merie (2008) <sup>16</sup> Pulicker (2009) <sup>16</sup> Pulicker (2009) <sup>16</sup> Siger (2008) <sup>18</sup> Sepulcre (2007) <sup>18</sup> Sepulcre (2007) <sup>18</sup> Tip (2005) <sup>18</sup> Zaver (2008) <sup>18</sup> Total Test for heterogeneity Test for overall effect	74-47 (22-15) 86-2 (16-2) 85-7 (19) 35 (17) 70-3 (13-4) 84-5 (15-1) 83-85 (24-12) 84-46 (-) 84-2 (14-7) 88-3 (16-5) -(-) 88-9 (18-8) 81-8 (19-3)	21 103-4 (10-5 73 105-2 (9-4) 28 104-5 (10-7 63 105 (12-1) 12 101-9 (8-9) 32 104 (9-2) 30 106-24 (12-1) 82 102-7 (11-5 57 102-9 (11-5) 40 100-3 (12-1) 50 100-3 (12-1) 51 100-9 (14-6) 63 104-6 (10-5) 64 (11-1)	406 ) 219 72 8 25 46) 46 25 ) 94 77 ) 58 ) 24 6) 15 85	3.6% 11.6% 13.8% 9.7% 4.6% 7.8% 4.9% 11.4% 12.1% 6.7% 4.2% 9.6% 100.0%		-19.00 (-22.83 to -15.17) -18.80 (-21.30 to -16.30 -20.00 (-25.03 to -14.97 -31.60 (-41.37 to -21.83) -19.50 (-25.85 to -13.15) -22.39 (-31.74 to -13.04) Not estimable -18.50 (-22.44 to -14.56 -14.10 (-17.66 to -10.54) Not estimable -16.38 (-23.68 to -9.08) -34.20 (-44.64 to -23.76 -22.80 (-22.86 to -17.9)

Favours experimental

Favours control

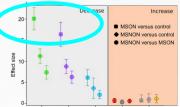
pRNFL atrophy

TLN 2010

20.10 (17.44-22.76) μm

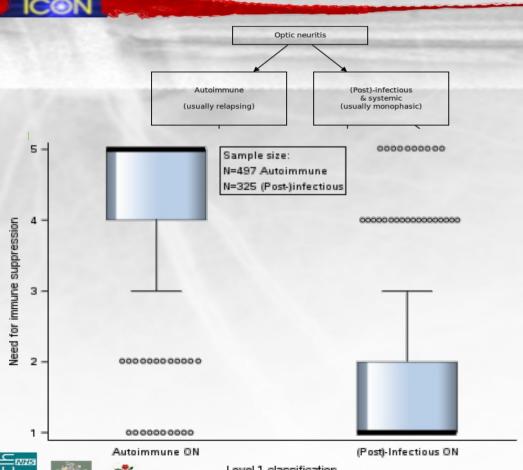
TLN 2017

20.38 (17.91-22.86) μm



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# How did we get there?



Level 1: 95% agreement

Based on iterative assessments from Delphi rounds 2-21

Relevant for patient management

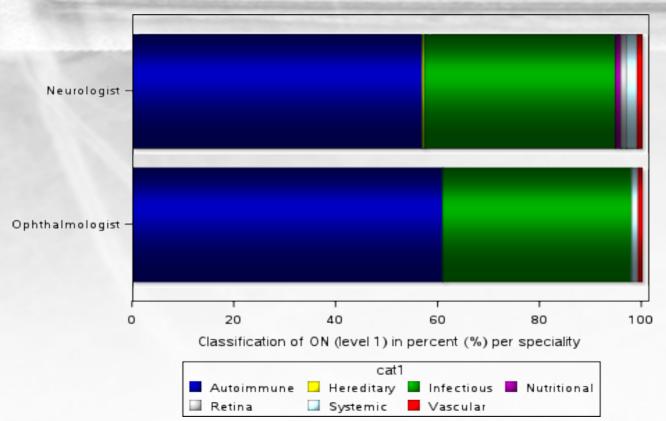








# Agreement: Speciality







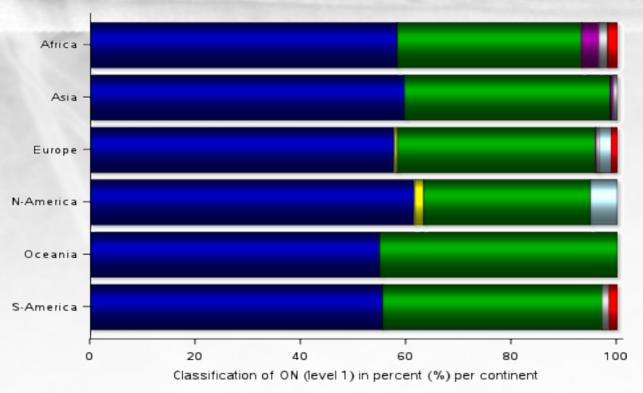








# Agreement: Continent















## Cases summary

- Case 1: MS-ON
   Scenario A: painful, monocular, subacute LOV, dyschromatopsia, RAPD
- Case 2: NMO-ON
   Scenario B: no pain, monocular, subacute LOV, dyschromatopsia, RAPD
- Case 3: post-infectious ON (Dengue)
   Scenario C: binocular, subacute LOV, dyschromatopsia, no pain, no RAPD









# Overall summary

- Optic Neuritis: Clinical approach
- ICON 2022 Diagnostic criteria
- ICON 2022 Classification
- Future revisions planned to optimise diagnostic sensitivity and specificity











# Thank you - Q&A

