전신성 혈관염에 의한 말초신경병증

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Peripheral neuropathies associated with systemic vasculitis

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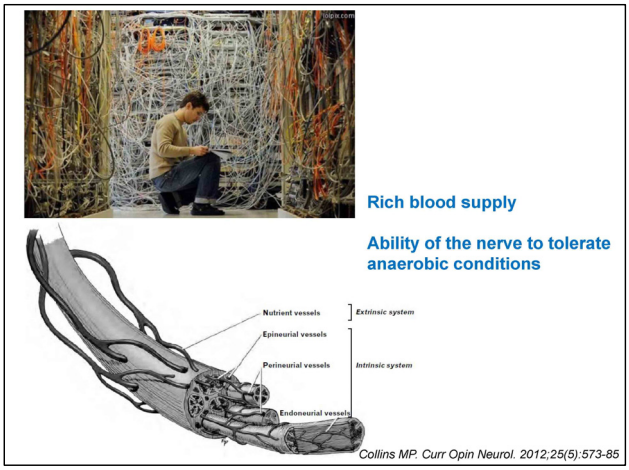
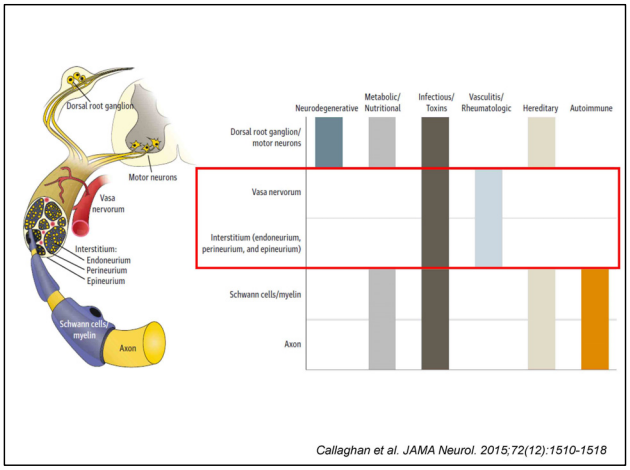
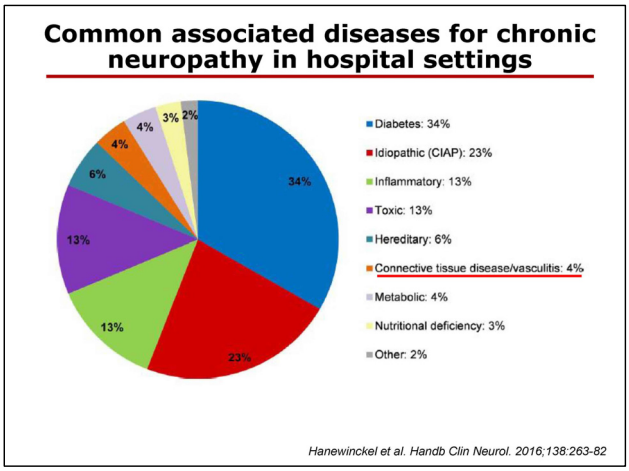
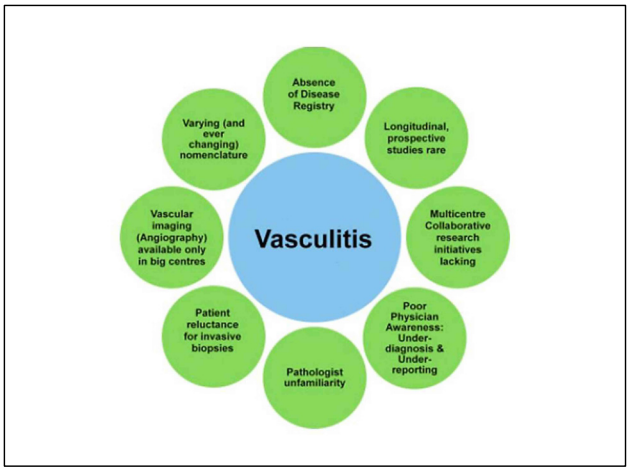








PNS NSVN GUIDELINE

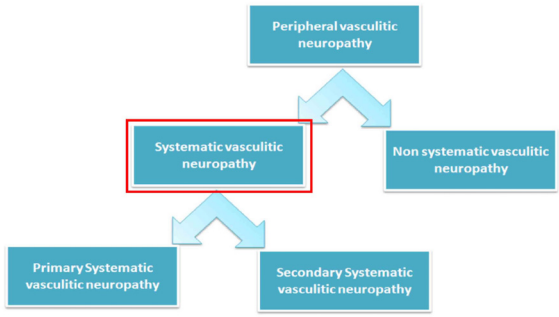
Peripheral Nerve Society Guideline* on the classification, diagnosis, investigation, and immunosuppressive therapy of non-systemic vasculitic neuropathy: executive summary

Michael P. Collins (Chair), USA; P. James B. Dyck, USA; Gary S. Gronseth, USA; Loic Guillevin, France; Robert D. M. Hadden, UK; Dieter Heuss, Germany; Jean-Marc Léger, France; N.C. Notermans, The Netherlands; John D. Pollard, Australia; Gérard Said, France; Gen Sobue, Japan; A.F.J.E. Vrancken, The Netherlands; John T. Kissel (Co-Chair), USA.

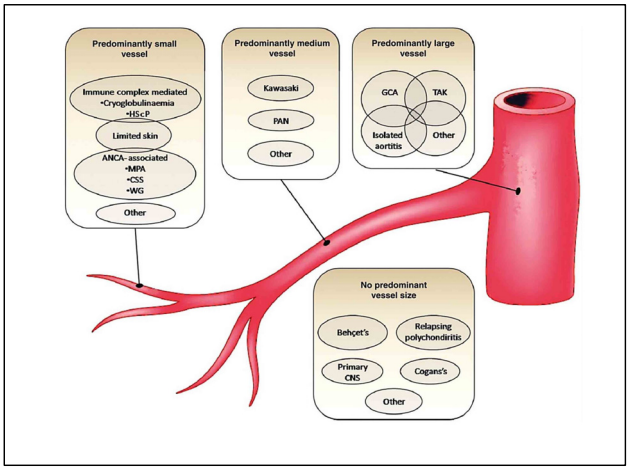
Journal of the Peripheral Nervous System 15:176–184 (2010)

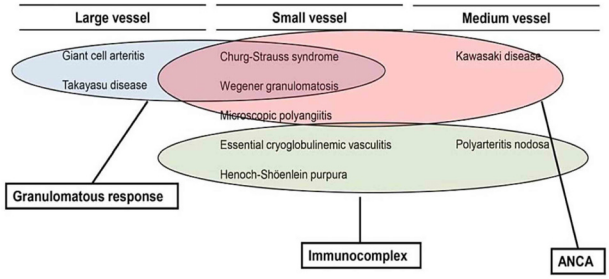
Table 1. Classification of vasculitides associated with neuropathy.

I. Primary systemic vasculitides
  1. Predominantly small vessel vasculitis
    a. Microscopic polyangiitis*
    b. Churg–Strauss syndrome*
    c. Wegener's granulomatosis*
    d. Essential mixed cryoglobulinemia (non-HCV)
    e. Henoch–Schönlein purpura
  2. Predominantly medium vessel vasculitis
    a. Polyarteritis nodosa (PAN)
  3. Predominantly large vessel vasculitis
    a. Giant cell arteritis
II. Secondary systemic vasculitides associated with one of the following
  1. Connective tissue diseases
    a. Rheumatoid arthritis
    b. Systemic lupus erythematosus
    c. Sjögren's syndrome
    d. Systemic sclerosis
    e. Dermatomyositis
    f. Mixed connective tissue disease
  2. Sarcoidosis
  3. Behcet's disease
  4. Infection (such as HBV, HCV, HIV, CMV, leprosy, Lyme disease, HTLV-I)
  5. Drugs
  6. Malignancy
  7. Inflammatory bowel disease
  8. Hypocomplementemic urticarial vasculitis syndrome
III. Non-systemic/localized vasculitis
  1. Non-systemic vasculitic neuropathy (includes non-diabetic radiculoplexus neuropathy and some cases of Wartenberg's migrant sensory neuritis)
  2. Diabetic radiculoplexus neuropathy
  3. Localized cutaneous/neuropathic vasculitis
    a. Cutaneous PAN
    b. Others



Amini et al. Rev Clin Med. 2014;1(1):25-28





Carbone et al. IUBMB Life. 2015;67(1):18–28

Frequency of peripheral nerve involvement in systemic vasculitis

Disorder	FPI	Reference
Systemic vasculitis		
A. Primary		
Giant cell arteritis	Rare	(Pfadenhauer *et al.*, 2007; Fineles and Arnold, 2007)
Classical panarteritis nodosa	35-75%	(Schaublin *et al.*, 2005; Kostina-O'Neil *et al.*, 2007)
Thrombangitis obliterans (Buerger disease)	Rare	(Vincent *et al.*, 1985)
Kawasaki syndrome	1 patient	(Hicks *et al.*, 1982)
Churg-Strauss syndrome	65-80%	(Zwerina *et al.*, 2008; Djukic *et al.*, 2008)
Wegener granulomatosis	14-50%	(Schaublin *et al.*, 2005; Feuerlein *et al.*, 2008)
Cryoglobulinemia	30-70%	(Schaublin *et al.*, 2005; Cacoub *et al.*, 2008)
M. Behcet	20%	(Gulturk *et al.*, 2008)
Microscopic polyangitis	6-70%	(Schaublin *et al.*, 2005)
Schönlien-Henoch purpura	Rare	(Bulun *et al.*, 2001; Ohnuma *et al.*, 2008)
B. Secondary		
1. Mixed connective tissue disease		
Systemic lupus erythematosus	27%	(Servioli *et al.*, 2007; Shoshtary *et al.*, 2005)
Rheumatoid arthritis	50%	(Schaublin *et al.*, 2005; Muramatsu *et al.*, 2008)
Sjögren syndrome	45%	(Terrier *et al.*, 2007; Iopate Lopate *et al.*, 2006)
2. Infection		
Hepatitis C	Unknown	(Said and Lacroix, 2005; Cacaoub *et al.*, 2008)
Streptococcal infection	Unknown	(Traverso *et al.*, 1997)
HIV	< 1%	(Schaublin *et al.*, 2005)
Cytomegaly virus	Rare	(Schaublin *et al.*, 2005)
Histoplasmosis	Rare	(Berry *et al.*, 1999)
Lues	Rare	(Mathew *et al.*, 2007)
3. Sarcoidosis	47%	(Said and Lacroix, 2005; Vital, 2008; Allen *et al.*, 2003)
4. Medication	Rare	(Schapira *et al.*, 2008)
5. Malignancy	32%	(Schaublin *et al.*, 2005; Fain *et al.*, 2007)
6. Radiation	1 patient	(Rubin *et al.*, 2001)
7. Diabetic/non-diabetic plexopathy	Not applicable	(Schaublin *et al.*, 2005; Said and Lacroix, 2005)
Non-systemic vasculitis	Not applicable	(Said and Lacroix, 2005)

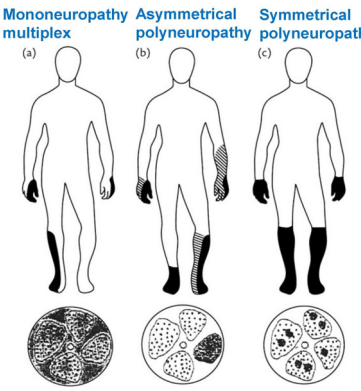
FPI: frequency of PNS involvement.

Finsterer J. Acta Neurol Belg. 2009;109(2):100-13

Disease	Frequency	Reference
Primary systemic vasculitis		
Giant cell arteritis	Rare	[Chia *et al.* 1996; Koike *et al.* 2013]
Polyarteritis nodosa	65–85%	[Schaublin *et al.* 2005; Ohyama *et al.* 2013b]
Churg–Strauss syndrome	65–80%	[Hattori *et al.* 1999; Zwerina, 2008]
Granulomatosis with polyangiitis	5–50%	[Schaublin *et al.* 2005; De Souza *et al.* 2010]
Microscopic polyangiitis	6–75%	[Hattori *et al.* 2002; Schaublin *et al.* 2005]
Cryoglobulinemia	30–70%	[Cacoub *et al.* 2008; Collins and Periquet, 2008]
Secondary systemic vasculitis		
1. Connective tissue diseases		
Systemic lupus erythematosus	20–27%	[Vital *et al.* 2006; Servioli *et al.* 2007]
Rheumatoid arthritis	15–70%	[Voskuyl *et al.* 2003; Agarwal *et al.* 2008; Muramatsu *et al.* 2008]
Sjögren's syndrome	30–45%	[Delalande *et al.* 2004; Terrier *et al.* 2007]
Systemic sclerosis (scleroderma)	5–30%	[Dyck *et al.* 1997; Collins and Periquet, 2008]
2. Others		
Infections (hepatitis B virus, hepatitis C virus (HCV), HIV)	5–70%	[Said and Lacroix, 2005; Schaublin *et al.* 2005; Cacoub *et al.* 2008; Collins and Periquet, 2008, Ohyama *et al.* 2013b]
Sarcoidosis	5–10%	[Chen and McLeod, 1989; Allen *et al.* 2003; Vital *et al.* 2008]
Malignancy	Rare*	[Oh *et al.* 1991; Fain *et al.* 2007]
Drugs	Rare	[Schapira *et al.* 2000; Thaisetthawatkul *et al.* 2011]

Blaes F. Ther Adv Musculoskelet Dis. 2015;7(2):45-55

Progression of vasculitic neuropathy



As the process progresses, it becomes more confluent and symmetrical

Oxford Textbook of Vasculitis, 3rd Edition, p161

Neuropathy patterns in vasculitic neuropathy

	1981 Wees et al. SNV	1985 Kissel et al. SNV	1991 Hawks et al. SNV	1986 Bouche et al. SNV	1995 Midroni and Bilbao SNV	2000 Claussen et al. SNV	2002 Collins et al. S/NSNVc	1987 Dyck et al. NSVN	1996 Davies et al. NSVN	2003 Collins et al. NSDN	2005 Karazizou et al. NSVN	Total SNV	Total NSVN	Total
Mononeuropathy multiplex	3	2	16	9	12	10	3[d]	12	10	6	9	55 (29%)	37 (32%)	92 (30%)
Mononeuropathy	(2)[b]					(5)						(7)	(7)	(14)
Asymmetrical polyneuropathy	4	8	10	7	5	4	18[d]	4	7	37	4	56 (30%)	52 (45%)	108 (36%)
Symmetrical polyneuropathy	3	6	8	3	14	21	1	4	8	5	8	56 (30%)	25 (22%)	81 (27%)
Sensory			(1)					(8)	(2)	(1)		(11)	(1)	(13)
Asymptomatic neuropathy	7	0	3	1	9							20 (12%)	0	20 (7%)
Myopathy	(2)					(3)						(5)	0	(5)
Total cases	17	16	34	22	32	44	22	20	25	48	22	187	115	302

Oxford Textbook of Vasculitis, 3rd Edition, p165

	smPNP	MonMP	MoNP	CN	sNP	aNP	Plexopathy
GCA	x						x
PAN	x	x	x	x			
Thrombangitis				x		x	
Kawasaki	x						
CSS	x	x	x	x	x		
Wegener	x	x		x		(x)	
Cryoglobulinaemia	x	x		x	x	x	
Behcet	x	x	x	x	x	x	
Microscopic polyangitis	x	x	x	x			
Schoenlein Henoch	x	x	x				

GCA: giant cell arteritis, PAN: classical panarteritis nodosa, smPNP: sensorimotor polyneuropathy, MonMP: mononeuritis multiplex, MoNP: mononeuropathy, CN: cranial nerve involvement, sNP: sensory neuropathy, aNP: autonomic neuropathy.

Finsterer J. Acta Neurol Belg. 2009;109(2):100-13

Nerve involvement in vasculitic neuropathy

		Frequency of nerve involvement by clinical neurological evaluation*								
Study	N	Peroneal	Sural	Tibial	Femoral	Median	Ulnar	Radial	Other nerves	Cranial (n)
Della Rossa et al., 2002	19	73% Based on 11 patients with neuropathy	27%	36%	–	9%	18%	–	–	2nd (1), 7th (2)
Guillevin et al., 1999a	96	84% Based on 75 patients with mononeuropathy multiplex	–	41%	–	–	55%	29%	–	3rd (1), 6th (1), 7th (2)
Guillevin et al., 1999b	85	77% Based on 49 patients with mononeuropathy multiplex	–	–	–	–	37%	20%	–	unspecified (6)
Guillevin et al., 2003	65	70% Based on 37 patients with mononeuropathy multiplex	–	–	–	–	41%	19%	–	none
Guillevin et al., 2005	115	85% Based on all 96 patients with mononeuropathy multiplex	–	–	–	–	26%	13%	–	–
Nishino et al., 1993	324	95% Based on 22/42 patients with mononeuropathy multiplex	–	55%	9%	36%	45%	14%	–	2nd (10), 3rd (2), 4th (2), 5th (5), 6th (8), 7th (8), 8th (2), 9th (1), 10th (1), 12th (2)
Wolf et al., 2010	14	63%* Based on 8 patients with mononeuropathy multiplex	69%*	50%*	6%*	50%*	31%*	35%*	–	2nd (1), 5th (1), 7th (1), 8th (1)

Vrancken et al. Handb Clin Neurol. 2013;115:463-83

		Frequency of nerve involvement by clinical neurological evaluation*							
Study	N	Peroneal	Sural	Tibial	Femoral	Median	Ulnar	Radial	Other nerves	Cranial (n)
Biopsy-supported vasculitic neuropathy										
Bennett et al., 2008	53	86% 76%* Based on 44 patients with motor deficits	–	51% 40%*	32% 26%*	58% 52%*	63% 55%*	35% 30%*	9%, 9%* Musculocutaneous	3rd (1), 5th (2), 6th (1)
Chang et al., 1984	19	89% Based on all 19 patients with mononeuropathy multiplex	84%	68%	–	26%	42%	16%	–	
Collins et al., 2000#	36	79%	72%	61%	–	54%	68%	50%	–	3rd (1), 6th (1), 7th (8), 10th (1)
Collins et al., 2003#	48	90% 82%* Based on motor nerve involvement	–	81% 73%*	63% 59%*	48% 45%*	65% 58%*	44% 42%*	52%, 49%* Superior gluteal 40%, 39%* Musculocutaneous 40%, 38%* Axillary 13% Thoracic	7th (4)
Dyck et al., 1987	65	58% Based on 12 patients with mononeuropathy multiplex	8%	17%	8%	50%	75%	33%	8% Lateral femoral cutaneous 17% Ischiadic/lumbar plexus 8% Thoracic 8% Obturator 8% Axillary 17% Digital hands	5th (1), 10th (1)
Hattori et al., 1999	28	96% Based on sensory impairment	57%	57%	–	46%	57%	–	–	7th (2)
Oka et al., 2011	22	91%	77%	86%	–	27%	45%	18%	–	–
Puechal et al., 1995##	32	91% Based on 18 patients with mononeuropathy multiplex	–	52%	–	13%	35%	4%	–	3rd (1), 5th (1)
Said et al., 1988##	100	76% Based on 94 patients with neuropathy	–	11%	9%	9%	28%	9%	–	–
Said, 1997##	200	96%	–	33%	6%	25%	34%	10%	2% Ischiadic	5th (1), 7th (1)
Said and Lacroix, 2005##	425	57%	–	33%	–	–	25%	–	–	–
Clinical vasculitis-associated neuropathy										
Cattaneo et al., 2007	64	52% 43%* Based on 27 patients with neuropathy	–	37% 30%*	–	19% 9%*	15% 7%*	11% 6%*	7%, 4%* Ischiadic	3rd (1), 4th (1), 7th (1), 12th (1)
de Groot et al., 2001	128	92% Based on 25 patients with mononeuropathy multiplex	8%	24%	–	12%	24%	8%	–	2nd (4), 3rd (2), 5th (1), 7th (1)

Vrancken et al. Handb Clin Neurol. 2013;115:463-83

TABLE 2. Individual Nerves and Their Frequency of Involvement by Vasculitis

Nerve	Frequency of Involvement
Peroneal	90%
Sural	84%
Tibial	11–81%
Ulnar	28–65%
Median	9–48%
Radial	12–44%
Femoral	6–63%
Sciatic	3%

Lacomis et al. J Clin Neuromuscul Dis. 2007;9(1):265-76

Definition of vasculitic neuropathy

Table 5. Case definition of clinically probable vasculitic neuropathy.

I. Nerve/muscle biopsy evidence of probable or possible vasculitic neuropathy (see Table 3) OR established diagnosis of systemic vasculitis (clinical or pathological in other tissues).
II. Clinical presentation typical for vasculitic neuropathy:*
1. Sensory-motor or sensory;
2. Asymmetric/multifocal (non-length-dependent);
3. Lower limb-predominant;
4. Distal-predominant;
5. Painful;
6. Course characterized by one or more acute attacks.
III. Electrodiagnostic evidence of an axonal, sensory-motor or sensory neuropathy.
IV. None of the following:
1. Purely motor signs and symptoms;
2. Entirely proximal signs and symptoms;
3. Perfectly symmetric by history, examination, and EMG;
4. CSF pleocytosis (NSVN);
5. CSF protein >110 mg/dl (NSVN).
V. For *systemic* vasculitic neuropathy, should also have:
1. At least one of the following abnormal laboratory markers: ↑ ESR, ↑ CRP, ↑ RF, MPO- or PR3-ANCAs, ↑ β2-microglobulin, ↑ VEGF, ↓ complement (some of these can also be found in NSVN: See classification criteria for NSVN); AND
2. At least one of the following:
a. Concurrent condition known or suspected to predispose to vasculitis (connective tissue disease, sarcoidosis, certain infections, active cancers, mixed cryoglobulins);
b. Clinical evidence or laboratory surrogates of multiorgan involvement;
c. Definite vasculitis in other tissues.

Collins et al. J Peripher Nerv Syst. 2010;15(3):176-84

Systemic vasculitic neuropathy

Criteria to distinguish nonsystemic vasculitic neuropathy (NSVN) from systemic vasculitis in a patient meeting case definition (level 1, 2 or 3) for vasculitic peripheral neuropathy. If none of the following is present, then diagnosis is NSVN.[a]

1. Biopsy evidence of vasculitis in tissue other than peripheral nerve, or (by convention) muscle;
2. Signs, symptoms, or laboratory evidence of involvement of organ(s) other than peripheral nerve (or, by convention, muscle) likely due to vasculitis[b];
3. Meets Brighton case definition for any form of vasculitis other than nerve or muscle;
4. Laboratory markers of systemic inflammatory state:
   a. PR3- or MPO-ANCAs;
   b. Mixed cryoglobulins (>trace);
   c. ESR ≥ 100 mm/h;
5. Specific infection associated with vasculitis (such as Hepatitis B and C, HIV, CMV, leprosy, Lyme disease, HTLV-1, parvovirus B19);
6. Predisposing conditions or factors:
   a. Connective tissue disease;
   b. Sarcoidosis;
   c. Inflammatory bowel disease;
   d. Active malignancy;
   e. Drug likely to be causing vasculitis.

Hadden et al. Vaccine. 2017;35(11):1567-1578

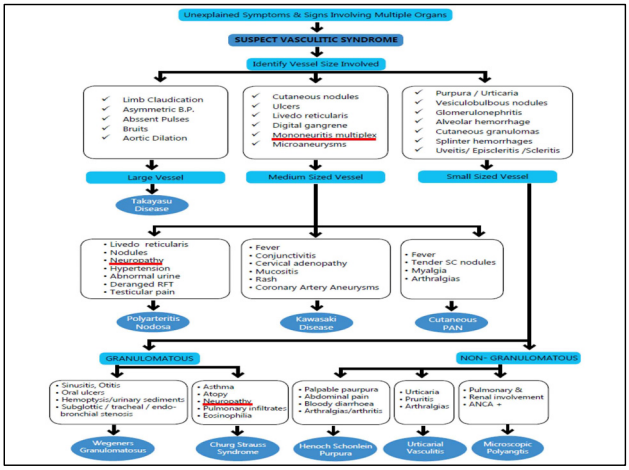
SVN vs NSNV

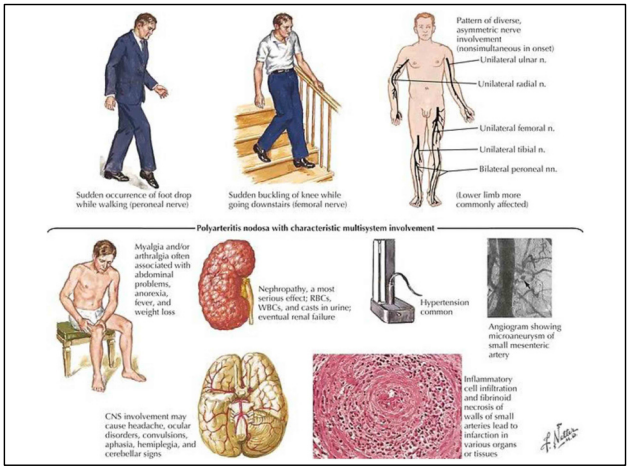
	SNV	NSNV
Pathological differences[a]		
Commonly involved	Epineurial arteriole	Perineurial smaller arteriole
Types	More often definite	More common probable
Severity	More severe	Less severe
Axonal degeneration	No difference	No difference
Ischaemic change	No difference	No difference
Clinical features[a]	Essentially the same	Essentially the same
Laboratory features		
High ESR	Common	Rare
High ANA	Common	Extremely rare
High RF	Common	Extremely rare
Hepatitis B antigen	20%	None
ANCA	47%*	None
Prognosis	Serious	Benign
Diagnosis	Can be diagnosed from Other tissue	Nerve biopsy: sine qua non
Duration of disease	Weeks to months	Months to years
Treatment	Cyclophosphamide	Steroid alone?

Oxford Textbook of Vasculitis, 3rd Edition, p171

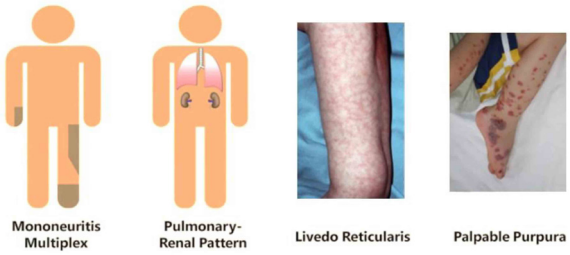
	Histopathology	Vessels affected	Other organs clinically involved (%)	Laboratory studies (%)	PNS, CNS changes
Polyarteritis nodosa	Necrotising vasculitis; mixed infiltrate; sparse immune deposits	Small and medium arteries	Skin (55–60%), joints (~50%), kidneys (40–50%), GI (~30%), testes (2–29%), heart (10–15%), ENT (rare), lungs (rare)	↑ESR (~85%), ↑WBC (~70%), ↓haemoglobin (~60%), ↑platelets (~60%), RF (~30%), Hep B (20–30%), ↓comp (~25%), ANA (~15%), Hep C (5–10%), ANCA (<10%), angio (angiogram abnormal in 70%, evidence of aneurysm)	PNS (65–67%), CrN (<5%), CNS (~5%)
Microscopic polyangiitis	Necrotising vasculitis; mixed infiltrate; sparse immune deposits; LCV in skin	Arterioles, capillaries, venules, veins affected more than small and medium arteries	Kidney (75–90%), joints (40–60%), skin (30–60%), lungs (35–50%), GI (30–40%), ENT (20–30%), heart (10–20%), testes (rare)	↑ESR (>90%), ANCA (75–85%; MPO>PR3), RF (25–50%), ANA 20–30%), ↓comp (rare), Hep B/C negative, angio (rare)	PNS (40–50%), CNS (10–15%)
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome)	Necrotising vasculitis; mixed infiltrate with eosinophils; granulomas; sparse immune deposits; LCV in skin	Small and medium arteries, arterioles, capillaries, venules, veins	Lungs (100%, asthma; 40–75%, infiltrates); ENT (sinusitis, rhinitis; 60–80%), skin (50–70%), GI (35–50%), joints (30–50%), heart (30–50%; 60% by MRI), kidney (15–30%)	↑Eosinophils (100%), ↑ESR (~85%), ↑IgE (~75%), ANCA (30–40%; MPO>PR3), RF (40–50%), ANA (~10%), ↓comp (rare), Hep B/C negative, angio (angiogram abnormal in 30%)	PNS (65%), CrN (<5%), CNS (10–15%)
Granulomatosis with polyangiitis (Wegener's granulomatosis)	Necrotising vasculitis; granulomas; collagen necrosis; sparse immune deposits; LCV in skin	Small and medium arteries, arterioles, capillaries, venules, veins	ENT (90–95%), lungs (65–85%), kidney (60–75%), eyes (50–60%), skin (25–50%), joints (65–75%), heart (5–20%), GI (5–10%)	ANCA (80–90%, PR3>MPO), ↑ESR (~85%), ↓haemoglobin (~75%), ↑platelets (55%), RF (50–60%), ↑WBC (~35%), ANA (~25%)	PNS (20–25%), CNS (5–10%), CrN (15%)
IgA vasculitis (Henoch-Schönlein purpura)	LCV in skin; IgA vascular deposits	Arterioles, capillaries, venules	Skin (100%), joints (65–70%), GI (~60%), GN (~40% children; ~70% adults), testes (~15%), lungs (rare)	↑ESR (50–60%), ↑IgA (~50%), ↑WBC (~50%), ↑ASO (20–50%), cryoglobulins (20–25%), ↓comp (10–20%), ↓haemoglobin (5–15%), RF (~5%), ANA (~5%), ANCA (<5%)	PNS (rare), CNS (rare)
Cryoglobulinaemic vasculitis	Necrotising vasculitis; microangiopathy; non-IgA immune deposits; LCV in skin	Small arteries, arterioles, capillaries, venules	Skin (~95%), joints (70–90%), GN (~30%), salivary glands (sicca; ~30%), Raynaud's (25–50%), GI (pain; 10–20%)	Hep C (80–90%), ↓comp (70–90%), RF (70–90%), ↑ESR (~70%), ↓haemoglobin (~70%), ANA (~55%), Hep B (~5%), ANCA (<5%), angio (infrequent)	PNS (~65%), CNS (rare)
Giant cell arteritis	Necrotising vasculitis; mononuclear infiltrate; granulomas and giant cells (~50%)	Medium–large arteries	PMR (~50%), liver (~30%; abnormal LFTs), subclavian-axillary-brachial (6–8%), aorta (15–20%), superficial femoral-popliteal (2–7%), kidney (GN) (~10%)	↑CRP (98–100%), ↑ESR (85–100%), ↓haemoglobin (55–60%), ↑WBC (20–30%), ANCA (rare), RF negative, ANA negative, angio (infrequent)	Otological (60–90%), optic nerve (15–20%), PNS (~5%), CNS (~5%)
Non-systemic vasculitic neuropathy	Necrotising and non-necrotising vasculitis in epineurium and perineurium much more than endoneurium; mononuclear infiltrate; immune deposits	Small arteries, arterioles, capillaries, venules	Muscle (25%)	↑ESR (~50%), ANA (~25%), ↓haemoglobin (~20%), ↑WBC (~15%), RF (~10%), ↓comp (~5%)	PNS (100%), CNS (0%)

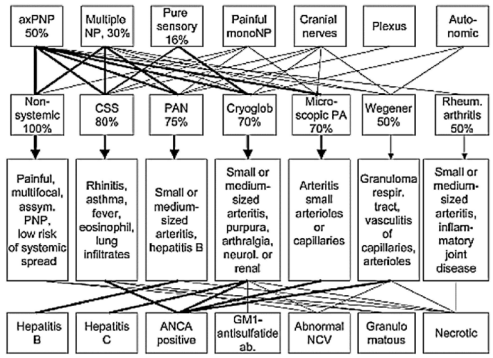
Gwathmey et al. Lancet Neurol. 2014;13(1):67-82



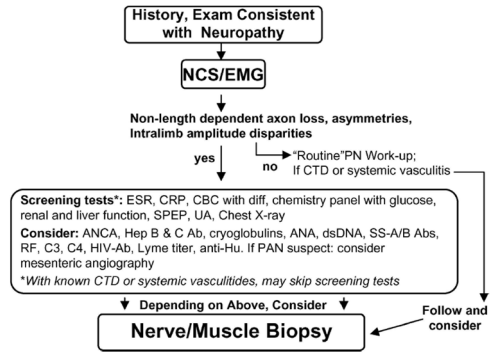


Clinical features highly suggestive vasculitis





Finsterer J. Acta Neurol Belg. 2009;109(2):100-13



Lacomis et al. J Clin Neuromuscul Dis. 2007;9(1):265-76

Panel 2: Consensus recommendations for laboratory investigation of suspected vasculitic neuropathy

1 Routinely indicated studies: Complete blood count, eosinophil count, chemistry panel (electrolytes, renal function, and liver function), urinalysis, glycated haemoglobin, and/or 2-h glucose tolerance test, erythrocyte sedimentation rate, C-reactive protein, antinuclear antibodies, rheumatoid factor, antineutrophil cytoplasmic antibodies, serum protein immunofixation electrophoresis, complement (C3, C4, total), cryoglobulins, hepatitis B surface antigen, hepatitis C antibodies, and chest x-ray.

2 Occasionally indicated studies: SSA or SSB antibodies, other antibodies against extractable nuclear antigens, double-stranded DNA antibodies, cyclic citrullinated peptide antibodies, angiotensin converting enzyme, lysozyme, vascular endothelial growth factor, β2-microglobulin, HIV antibodies, Lyme antibodies, hepatitis C RNA, cytomegalovirus antigen or DNA, paraneoplastic autoantibodies, lactate dehydrogenase, HDL cholesterol, porphyria screen, DNA for PMP22 deletion associated with hereditary neuropathy with liability to pressure palsies, DNA for transthyretin gene, chest CT, gallium-67 scan, visceral angiography, salivary gland biopsy, lumbar puncture, and other body imaging for malignancy.

Gwathmey et al. Lancet Neurol. 2014;13(1):67-82

Diagnostic sensitivity

Authors	Patients	No. cases	Nerve biopsy	Muscle biopsy	Comments
Dyck et al. (1987)	SNV, Biopsy proven VN	45	58% (26/45)	25% (3/12)	Sural/gastrocnemius
Said et al. (1988)	SNV, Biopsy proven VN	83	51%	75%	Superficial fibular (peroneal)/peroneus brevis
Said (1995)	SNV, Biopsy proven VN	?	62%	54%	Same as above?
Claussen et al. (2000)	SNV, suspected[c]	115	39%	17%	Sural in all/anterior tibialis in 2/3 of cases
	SNV, biopsy proven VN	45	100%	42%	
Collins et al. (2000)	SNV[d], suspected	70	27%	16%	Superficial fibular (peroneal)/peroneus brevis
	SNV, biopsy proven VN	22	90%	50%	
Said (2005)	SNV, biopsy proven VN	425	76.5%	59.5%	Superficial fibular (peroneal)/peroneus brevis
Maxeiner et al. (1952)	SNV, suspected	136[a]		13%	
	SNV, biopsy proven	26		35%	
Dahlberg et al. (1989)	SNV, suspected	26[b]	1	9%	
Rapport (1993)	SNV, suspected	29	20%		Sural nerve biopsy
Cruz Martinez et al. (1988)	SNV, biopsy proven VN	14	86%	79%	
Dyck et al. (1987)	NSV, biopsy proven VN	20	100%		All by the sural nerve biopsy
Davies et al. (1996)	NSV, biopsy proven VN	25	100%		All by the sural nerve biopsy
Collins et al. (2003)	NSV, biopsy proven VN	48	100%		Sural in 30; SP/PB in 19; Sup radial in 2
Karanizou (2004)	NSV, biopsy proven VN	22	100%		All by the sural nerve biopsy
Vital (2006)	CV, suspected	178[e]	62%		Superficial fibular (peroneal)/peroneus brevis
	Biopsy proven VN[f]	85	73%	59%	

Oxford Textbook of Vasculitis, 3rd Edition, p163

Ultrasound of the peripheral nerves in systemic vasculitic neuropathies

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Journal of the Neurological Sciences 347 (2014) 44–49

Ultrasonic measurements.

Mean CSA in mm²	Vasculitic neuropathies	Control	ANOVA
Median nerve, proximal	**11.0 ± 2.5**	**9.0 ± 1.6**	**$p = 0.028$**
Median nerve, middle	**11.6 ± 2.5**	**9.6 ± 2.1**	**$p = 0.044$**
Median nerve, distal	8.4 ± 1.4	7.5 ± 1.7	$p = 0.165$
Ulnar nerve, proximal	**8.5 ± 2.1**	**6.9 ± 2.2**	**$p = 0.039$**
Ulnar nerve, distal	7.1 ± 1.8	6.3 ± 1.5	$p = 0.152$
Fibular nerve	**10.7 ± 2.4**	**8.0 ± 1.8**	**$p = 0.006$**
Tibial nerve, proximal	**31.9 ± 5.7**	**21.0 ± 3.9**	**$p < 0.001$**
Tibial nerve, distal	**11.9 ± 2.6**	**8.8 ± 2.3**	**$p = 0.008$**
Sural nerve	**3.3 ± 1.4**	**2.1 ± 0.7**	**$p = 0.043$**
Vagal nerve	2.0 ± 0.4	2.2 ± 0.7	$p = 0.785$
C6 in mm	3.1 ± 0.6	3.1 ± 0.4	$p = 0.989$

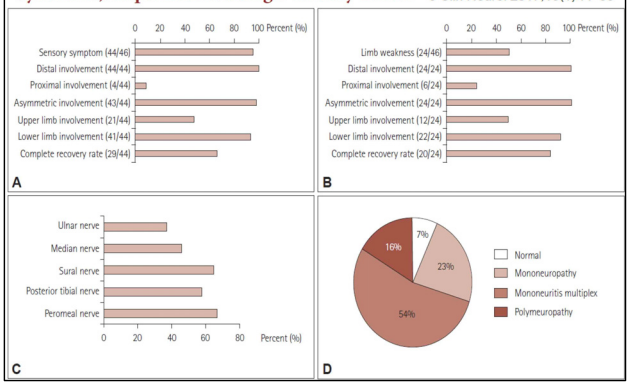
Ultrasonic measurements in comparison to demyelinating and axonal neuropathies.

Mean CSA in mm²	Vasculitic neuropathies	Demyelinating neuropathies (CIDP, MMN, MADSAM)	Axonal neuropathies (diabetes, alcohol, critical illness)	ANOVA
N	14	22	26	
Mean age in years ± SD	62.0 ± 15.0	56.1 ± 12.2	63.8 ± 13.2	$p = 0.128$
Disease duration in month +-SD	28.2 ± 25.2	21.1 ± 23.0	14.7 ± 20.7	$p = 0.231$
Gender m:w	**5:9**	**20:2**	**17:9**	**$p = 0.002$**
Mean Height in cm	168.8 ± 3.6	175.9 ± 8.6	175.2 ± 8.9	$p = 0.057$
Mean Weight in kg	64.1 ± 10.6	71.0 ± 8.3	73.5 ± 15.5	$p = 0.163$
Enlargement in motor nerves of arms and legs	2.9 ± 1.9	5.4 ± 2.3	1.9 ± 2.0	**$p < 0.001$**
Median nerve, proximal	11.0 ± 2.5	20.0 ± 11.3	10.5 ± 0.3	**$p = 0.013$**
Median nerve, middle	11.6 ± 2.5	19.6 ± 2.1	10.6 ± 0.3	**$p = 0.048$**
Median nerve, distal	8.4 ± 0.4	15.5 ± 1.7	8.2 ± 0.01	**$p = 0.038$**
Ulnar nerve, proximal	8.5 ± 2.1	14.9 ± 2.2	8.4 ± 0.2	**$p = 0.012$**
Ulnar nerve, distal	7.1 ± 1.8	10.3 ± 1.5	6.7 ± 0.1	**$p = 0.001$**
Fibular nerve	10.7 ± 2.4	12.0 ± 1.8	9.2 ± 0.4	**$p = 0.031$**
Tibial nerve, proximal	31.9 ± 5.7	38.3 ± 13.9	28.3 ± 6.9	**$p = 0.033$**
Tibial nerve, distal	11.9 ± 2.6	15.4 ± 5.3	9.5 ± 0.3	**$p < 0.001$**
Sural nerve	3.3 ± 1.4	3.6 ± 0.7	2.0 ± 0.9	**$p = 0.015$**
Vagal nerve	2.0 ± 0.4	4.7 ± 1.7	2.7 ± 0.7	**$p < 0.001$**
C6 in mm	3.1 ± 0.6	4.4 ± 0.4	3.8 ± 0.9	**$p = 0.021$**

Clinical Characteristics and Treatment Response of Peripheral Neuropathy in the Presence of Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss Syndrome): Experience at a Single Tertiary Center

Hye-Jin Cho[a]

J Clin Neurol 2017;13(1):77-83



Treatment

Steroids
1-2 mg/kg/d prednisone (mild cases) or 1 g/d methyl-prednisolone iv for 5 d (severe cases) followed by 1-2 mg/kg/d prednisone until effect (6-8 w), afterwards every second day (same dosage or half dosage)

Cyclophosphamide
If steroids are ineffective or multi-system involvement either 2 mg/kg during 3-12 m or pulse therapy intravenously with 500 mg/m² once every 4-6 w during 1a

Methotrexate
Indicated if cyclophosphamide is ineffective or as long-term therapy after remission under steroids plus cyclophosphamide, start with 0.3 mg/kg (maximally 15 mg) once a week and increase to 15-25 mg/week thereafter

Azathioprine
Indicated if cyclophosphamide is ineffective or as long-term therapy after remission under steroids plus cyclophosphamide, at the beginning 1 mg/kg/d later on 2-2.5 mg/kg/d

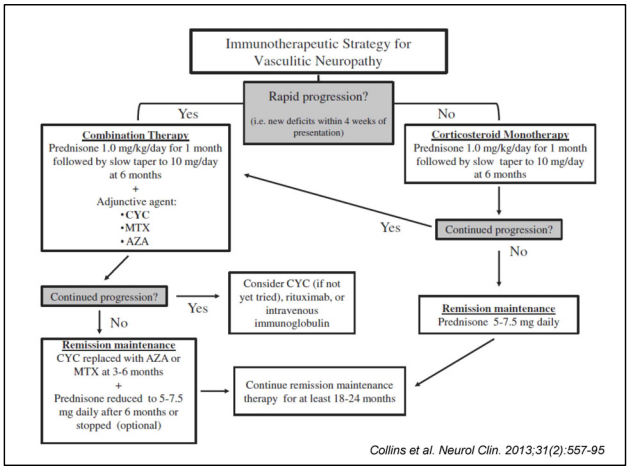
Mycophenolate mofetil
Only pilot studies available, possibly effective in Wegener's granulomatosis

Leflunomide
Only pilot studies available, possibly effective in Wegener's granulomatosis

Rituximab
Only pilot studies available, particularly effective in ANCA-positive vasculitis

Immunoglobulines
Open-label studies suggest clinical benefit and reduction of inflammatory markers

Finsterer J. Acta Neurol Belg. 2009;109(2):100-13



Collins et al. Neurol Clin. 2013;31(2):557-95

Conclusion

- A high index of suspicion is required to identify this relatively rare condition, which is often highly responsive to immunosuppressant therapy
- Vasculitic neuropathy is typically painful
- Although the most suggestive pattern of involvement is mononeuritis multiplex, whether multifocal, asymmetric, or symmetrical patterns of nerve involvement may occur
- Sensory-only neuropathy may occur, but motor-only presentation is distinctly rare
- Steroids are first-line therapy, but combination immunosuppressive therapy, most commonly with cyclophosphamide, is often necessary to induce remission, particularly in aggressive or systemic disease

Thank you for your attention