Schmerzhafte Diabetische Neuropathie

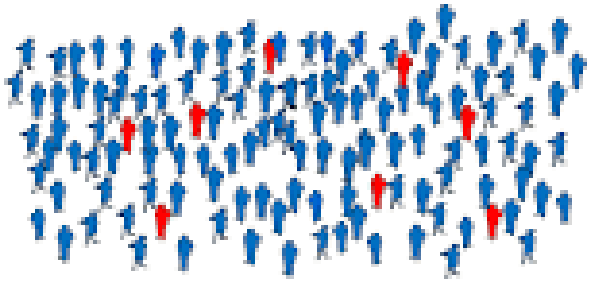
SDN

Einar PV Wilder-Smith

Leitender Arzt, Neurologie
Luzerner Kantonsspital
Dr med, DTM&H, FMH, FAMS
Professor, Neurologie, Universität Bern, Schweiz

luzerner kantonsspital

Epidemiologie



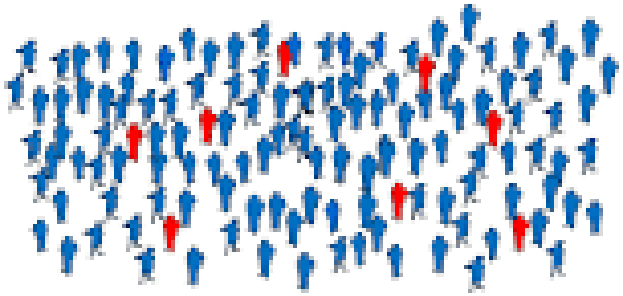
- Schweiz 500'000 **Diabetiker**
- 30% aller Diabetiker schmerzhafte Neuropathie
- Je länger erkrankt, je mehr Neuropathie

Ziegler D et al. Diabetische Neuropathie Diabetologie 2017; 12 (Suppl 2): S101–S114

d i a b e t e s r e s e a r c h a n d c l i n i c a l p r a c t i c e 1 4 4 (2 0 1 8) 1 7 7 –1 9 1

Epidemiologie

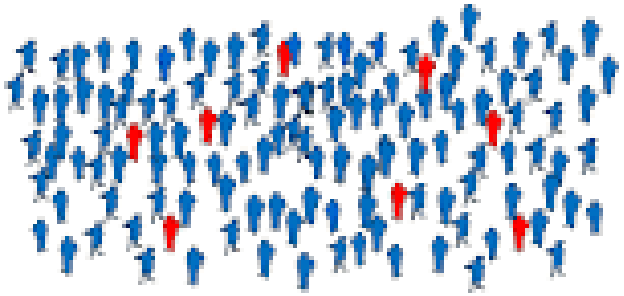
n = 15,692 ambulante diabetische Population in UK



- ***Prävalenz SDN*** ***(Schmerzhafte Diabetische Neuropathie)***
- **20% Type 2 Diabetes**
- **5% Type 1**
- **5% prä-Diabetikern (Erst-Symptom)**

Diabetes Care. 2011 Oct;34(10):2220-4.

Epidemiologie



- SDN mehr prävalent bei
  - Typ 2 Diabetes
  - Frauen
  - Personen aus Süd-Ost-Asien

Diabetes Care. 2011 Oct;34(10):2220-4.

Warum Schmerzen?

- **Abhängig von befallenen Nerven Fasern**
  - **Myelinisierte Fasern**
    - Vibration
    - Berührung
    - Druck
    - Motorisch
  - **Klein unmyelinisiert**
    - Schmerz
    - Temperatur

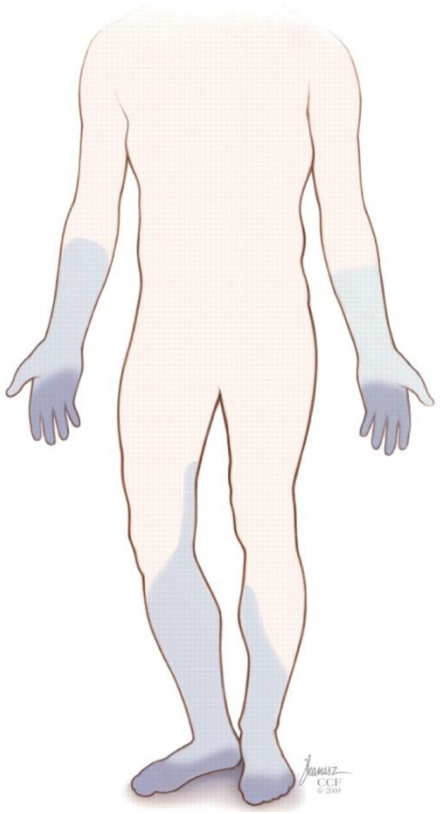
3 Klinische SDN Formen

- **Symmetrisch distal**
- **Asymmetrische Neuropathie**
- **Behandlungs-induzierte Neuropathie (Insulin Neuritis)**

SDN

Symmetrisch distal

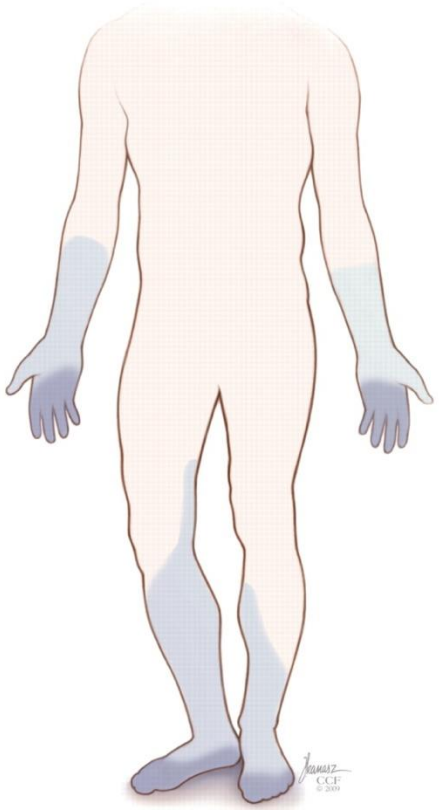
- Distal
- Schleichender Beginn
- Temperaturgefühl- brennend
- Nagend
- +/- andere sensible Symptome
- Ausgelöst durch
  - Bewegung, verlängertes Stehen
  - Nächtlich



SDN

Symmetrisch distal

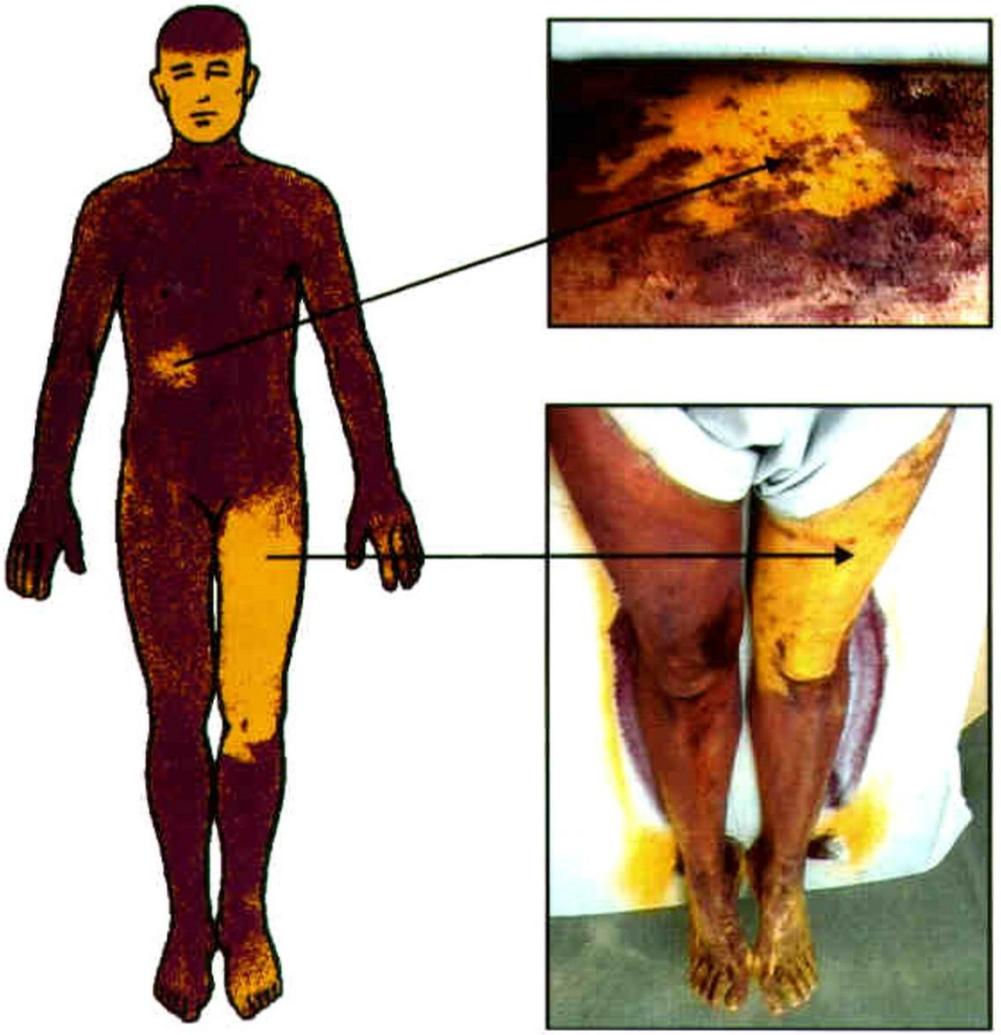
- Grosse Nerven Fasern +/-
- Reflexe können auslösbar sein
- Vibration/Berührung variabel
- Kleine Nerven Faser prüfen!
- Temperatur
- Schmerz (Spitz) (mechanische Allodynie!)



SDN

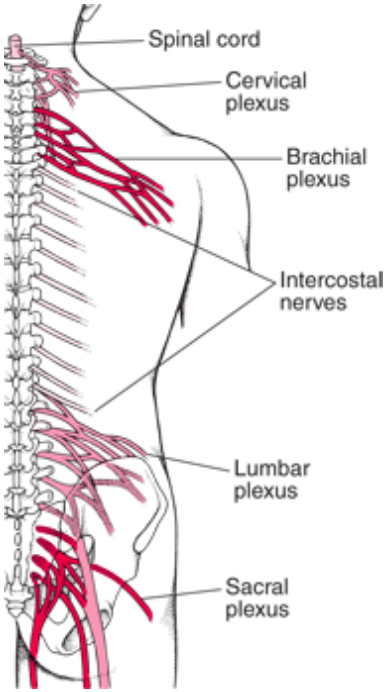
Asymmetrisch

- Radiculo-plexus-neuropathien
  - Lumbosakral
  - Thorakal
  - Zervikal Brachial



Radikuloplexus Neuropathie

- SCHMERZ initial Symptom
- Akut mit fokalem Beginn
  - Parese manifestiert 1-3 Tage
  - Maximaler fokal Defizit in 1 Woche
    - Thorakal
    - Lumbosakral
    - Zervikal



Brain 2012: 135; 3074–3088

Radikuloplexus Neuropathie

- Atrophie (n. Wochen) Hälfte aller Patienten
- Von 85 Patienten, benötigten 46 Opioid Analgesie zur Schmerz Kontrolle

Brain 2012: 135; 3074–3088

Radikuloplexus Neuropathie

- Schmerz Charakteristika (n=85)
  - Druck (n = 23), Brennen (n =14) Einschiessen/Lanzinieren (n=19)
  - Allodynie (n=16)
- Sensible Symptome
  - "positive" Symptome (Ameisenlaufen oder Paraesthesien) (n=41)
  - "negative" Symptome (Taubheit, Hypästhesie, Anästhesie) ungefähr gleich verteilt (n=35)

Brain 2012: 135; 3074–3088

Radikuloplexus Neuropathie

- >50% Patienten (44/85)
- Zusatzbeteiligung einer Körperregion
  - Lumbosakral (20/85)
  - Thorakal (16/85)
  - Wiederkehrend in 18/85

Brain 2012: 135; 3074–3088

Radiculoplexus Neuropathy

- Autonome Symptome: (ca 20%)
  - Hauptsächlich Orthostase
  - Alteration von Schwitzen
- Gewichtsverlust um 5 kg häufig (30 von 85)
- Assoz mit Phrenikus Neuropathie

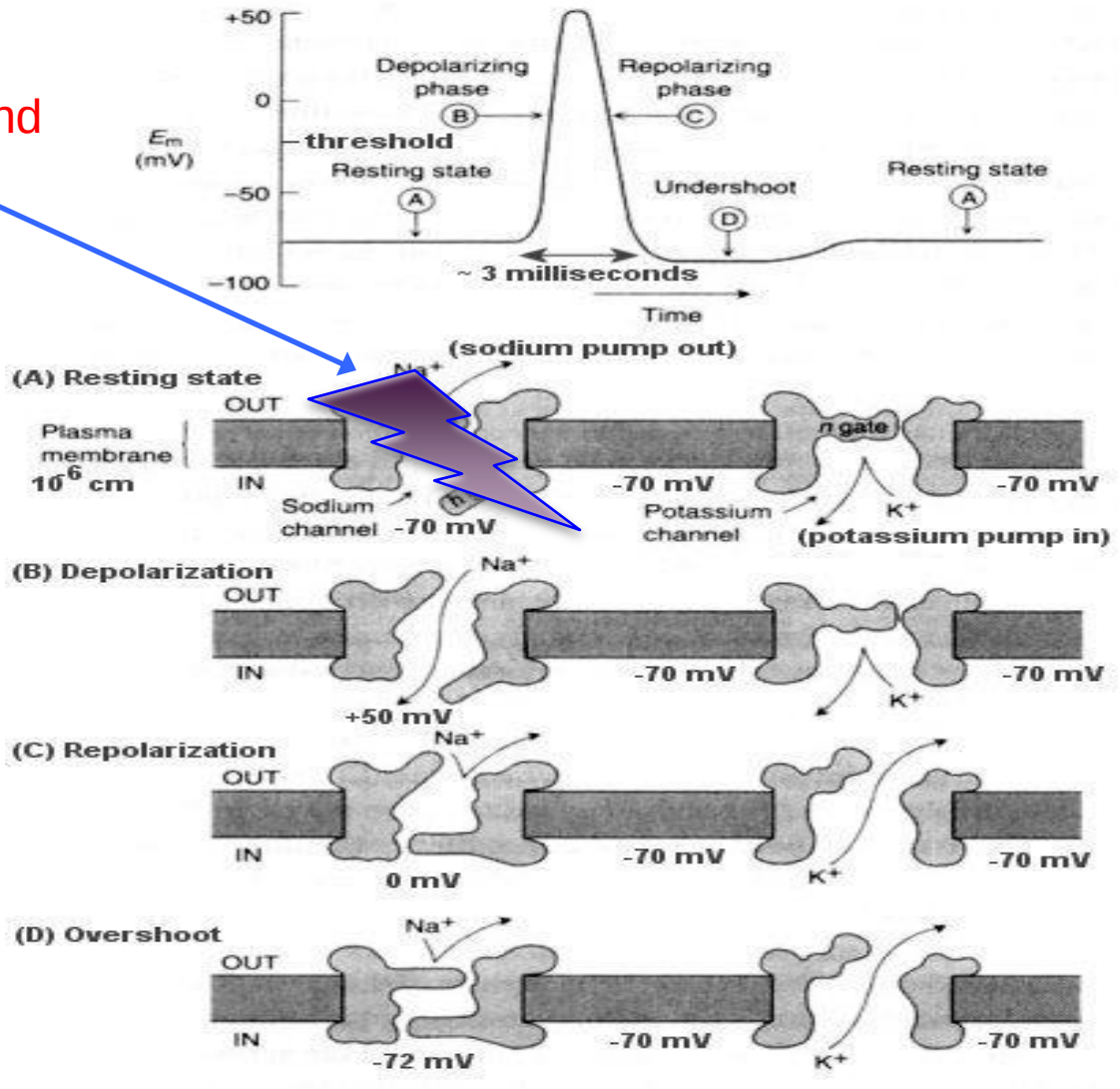
Pathophysiologie DSNP

Unterschiedlich

- **Methylglyoxal (Metabolit)**
  - Symmetrisch distal (Längen-abhängige Polyneuropathie)
- **Microvaskulitis**
  - Radikuloplexus Neuropathie

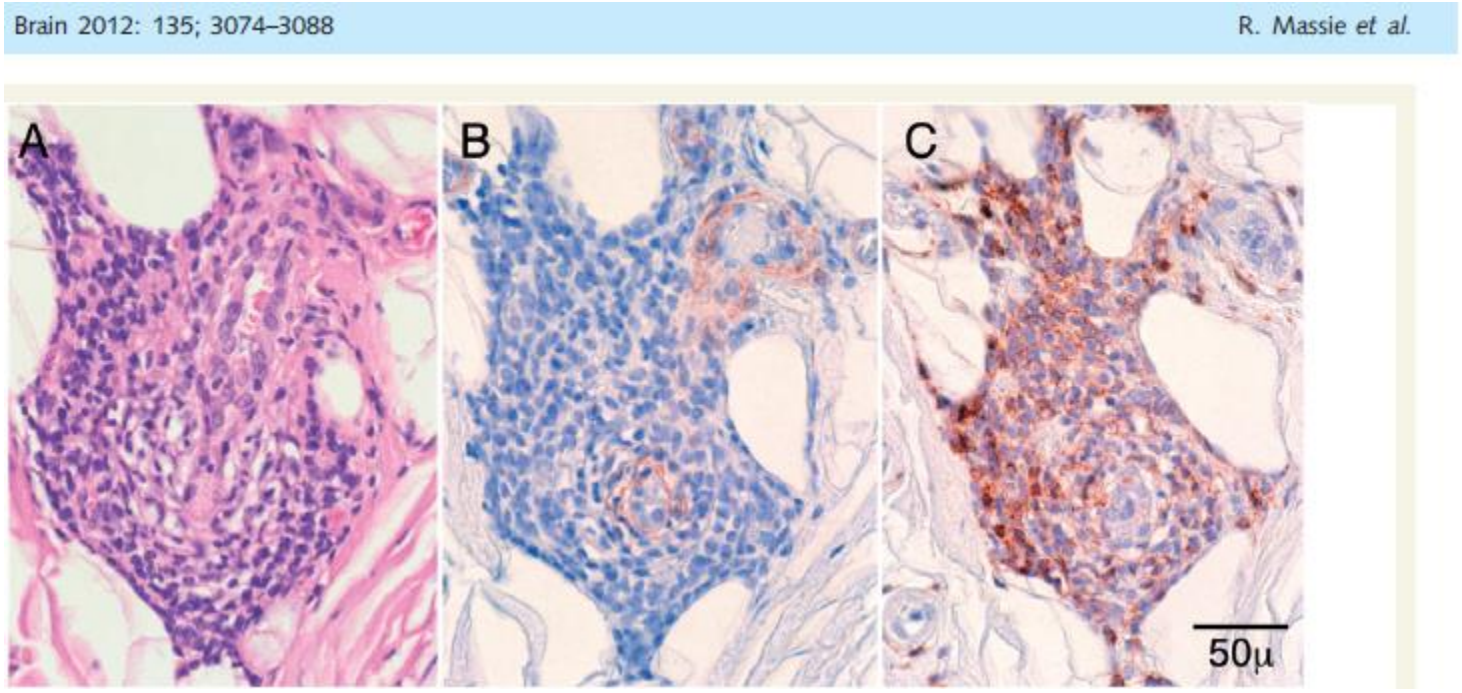
+ Erklärung für Schmerz via NA+ 1.8 Channel

Methylglyoxal depolarisiert und induziert post-translational Modifikationen



Microvaskulitis

Radikuloplexus Neuropathie



Microvaskulitis im Nerven

Diagnose

Symmetrisch distal

- **Typisches klinisches Bild**
  - NLG kann normal sein
  - **Small fibre Tests**
    - Epidermal Nerve Faser Dichte (Haut Biopsie)
    - QSRT (Schweiss Test)
    - Stimulated Skin Wrinkling (Sympatischer Test)

Diagnose

Asymmetrisch

Radikuloplexus Neuropathy

- Typisches klinisches Bild
  - EMG
  - MRI Bildgebung der Radikuloplexus Anatomie oft K.M. anreichernd
  - CSF- erhöhtes Protein
  - Nerven Biopsie

Brain, 2012;135, 3074-3088

3 Klinische Haupt Formen

- Symmetrisch distal (Längenabhängige Neuropathie)
  - Distal symmetrische polyneuropathy (DSPN)

- Asymmetrische Neuropathie
  - Mononeuritis multiplex
  - Radikulo-Plexus-Neuropathien (RPN)

- Behandlungs-induzierte Neuropathie (Insulin Neuritis)

Behandlungs-induzierte Neuropathie (Insulin Neuritis)

Definition

- Akute neuropathische Schmerzen +/- autonomer Dysfunction
- Nach starker Verbesserung glykaemischer Kontrolle
- Abnahme HbA1c von 2% Punkten über 3 Monate

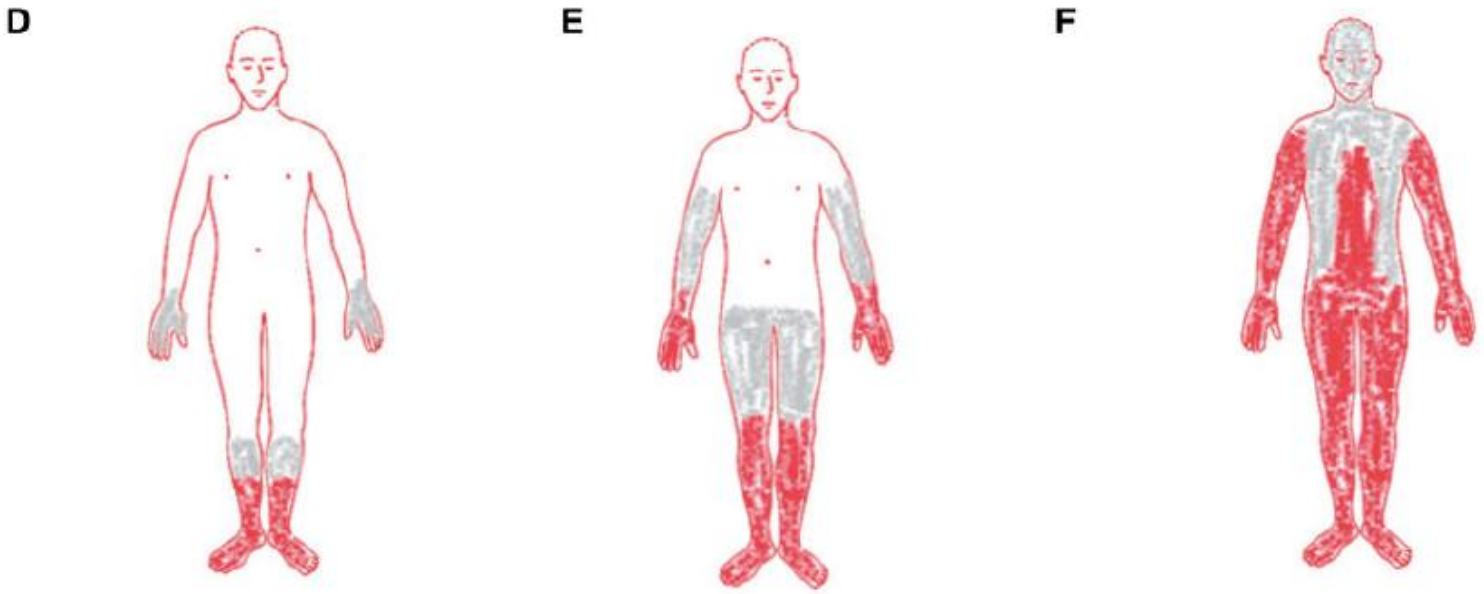
Brain, 2012;135, 3074-3088

Wie häufig?

- 10.9%
- In einer Studie an einem Diabetes Zentrum
- Von 954 Patienten die auf diabetische Neuropathie untersucht wurden, 104 mit Behandlungs-induzierter Neuropathie

Schmerz Muster

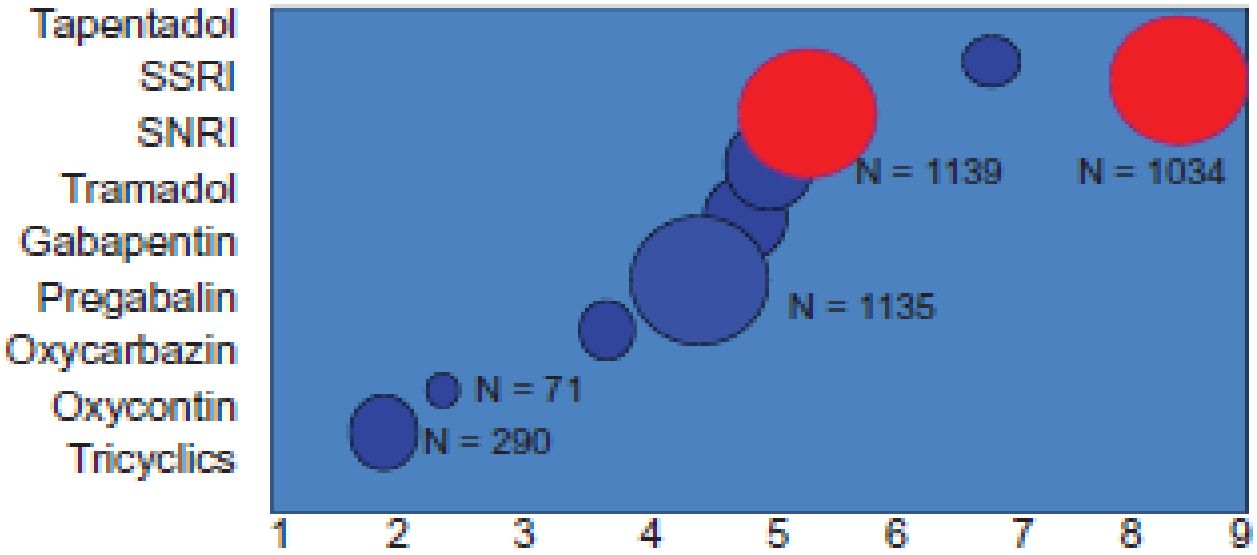
Behandlungs induzierte Neuropathie



Behandlung

- **Symptomatisch**
  - Antidepressiva (neu/klass)
  - Antikonvulsiva (neu/klass)
  - Opiode
- **Krankheits modulierend**
  - Steroide
  - IVIG

Symptomatische Behandlung (alle sub-Typen)



$$NNT = \frac{1}{\frac{n_{(goal-achieved-active)}}{n_{(total-active)}} - \frac{n_{(goal-achieved-active)}}{n_{(total-placebo)}}}$$

Figure 1 Efficacy analysis of drugs used for painful diabetic neuropathy.
Note: Copyright © 2012, MDTEXT.COM, INC. Reproduced with permission from Endotext.org [homepage on the internet]. Darmouth: Chapter 31 – Diabetic Neuropathies; 2012 version [updated September 26, 2012]. Available from: http://www.

Therapie

Table 1 Odds ratios for efficacy and withdrawal, numbers needed to treat (NNT) and numbers needed to harm (NNH)

Drug class	Odds ratio – efficacy	Odds ratio – withdrawal (2ry to AE)	NNT	NNH
Tricyclics	22.2 (5.8–84.7)	2.3 (0.6–9.7)	1.5–3.5	2.7–17.0
Duloxetine	2.6 (1.6–4.8)	2.4 (1.1–5.4)	5.7–5.8	15.0
Traditional anticonvulsants	5.3 (1.8–16.0)	1.5 (0.3–7.0)	2.1–3.2	2.7–3.0
New generation anticonvulsants	3.3 (2.3–4.7)	3.0 (1.75–5.1)	2.9–4.3	26.1
Opioids	4.3 (2.3–7.8)	4.1 (1.2–14.2)	2.6–3.9	9.0

Abbreviation: 2ry to AE, secondary to adverse events.

NNH macht den Unterschied aus!

Table 2 Summary of American Academy of Neurology recommendations

Evidence level	Recommended
Level A	Pregabalin 300–600 mg/day
Level B	Gabapentin 900–3600 mg/day
	Duloxetine 60–120 mg/day
	Amitriptyline 25–100 mg/day
	Venlafaxine 75–225 mg/day
	Sodium valproate 500–1200 mg/day
	Dextromethorphan 400 mg/day
	Morphine titrated to 120 mg/day
	Tramadol 210 mg/day
	Oxycodone 37 mg/day (max 120 mg/day)
	Capsaicin, 0.075% QID
	Isosorbide dinitrate spray
	TENS × 3–4

Level A Prägabalin

Not recommended

Oxcarbazepine

Lamotrigine

Lacosamide

Clonidine

Pentoxifylline

Mexiletine

Magnetic field treatment

Low-intensity laser therapy

Reiki therapy

Zusatz Therapie

Radikuloplexusneuropathie & Behandlungs induzierte PNP

- Mikrovaskulitis Rx
- Evidenz Level C/D

  Kasuistiken mit positivem Effekt
- Intravenöse Steroide, (1 g Puls Therapie)
  - Dauer, Dosis?
- Plasmapherese
- IVIG

Zusammenfassung

- Schmerzhafte Diabetische Neuropathie
  - 30% Diabetiker
- Drei Hauptformen
  - Symmetrisch Distal
  - Radikulo Plexus Neuropathie
  - Behandlungs-induzierte Neuropathie
- Verschiedene pathophysiologische Mechanisme

Danke für die Aufmerksamkeit!

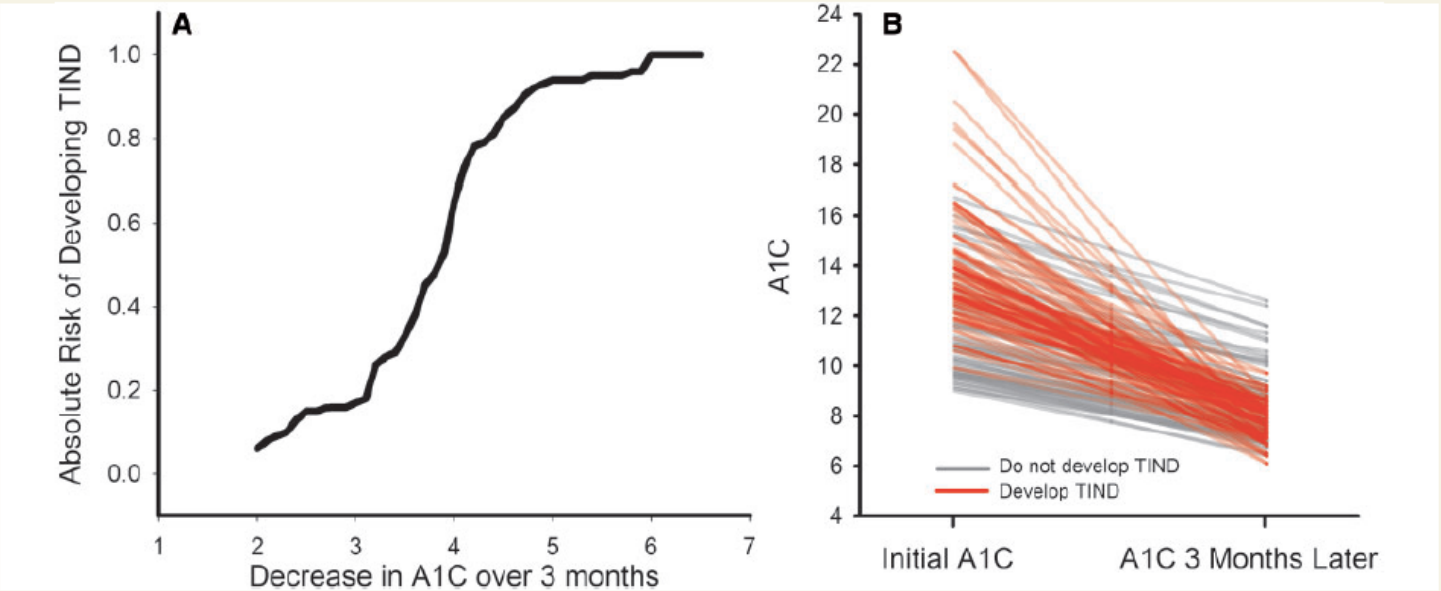


Figure 3 Risk of developing TIND. (**A**) A survival curve plotting the total number of patients (n = 168) with a decrease in HbA1c of ⩾2% over 3 months. The absolute risk of developing TIND is plotted against the change in HbA1c over a 3-month period of time. (**B**) Individual data lines for all 168 individuals with a change in HbA1c ⩾2% over 3 months. Individuals that develop TIND are shown with red lines and those that do not develop TIND are shown with grey lines.

Section of Physical Medicine

President—Basil Kiernander, M.R.C.P.

Meeting
November 11, 1959

The Blood Supply of the Brachial Plexus

By Sajida Abdullah, M.Sc., M.B.,[1] and Ruth E. M. Bowden, D.Sc., M.B.
London

Clinical observation suggests that vascular insufficiency might contribute to the onset of brachial neuritis associated with disease of the cervical spine. Omissions and discrepancies in the literature of the detailed general and vascular anatomy of the plexus (Abdullah, 1958) prompted yet another study of the subject. The findings summarized here are based on studies of 118 plexuses of dissecting-room cadavers and 8 fœtal and 30 adult plexuses injected with Neoprene latex (the adults ranged from 49 to 87 years of age). Movements of dural sheaths, spinal cord and nerve roots in relation to bone were observed in four unfixed fœtuses (26, 27, 32 and 34 weeks respectively), a male of 14 and a female of 19 years.

The blood supply of the brachial plexus is dependent upon the subclavian artery and its derivatives, but there is some disagreement about the precise branches involved (Adamkiewitz, 1886; Bartholdy, 1897; Tonkoff, 1898; Bergmann and Alexander, 1941). Amongst the vessels cited are the vertebral, the ascending and deep cervical and the superior intercostal arteries, and all these vessels were observed to play some part (Fig. 1). The origin of the vertebral artery may vary and frequently the left is somewhat larger than the right vessel (Thane, 1899; Adachi, 1928) (Fig. 2); both may undergo gross distortion as a result of osteoarthritic changes in the spine (Biemond, 1951; Hutchinson and Yates, 1956). The main vessels supplying the plexus were symmetrically arranged

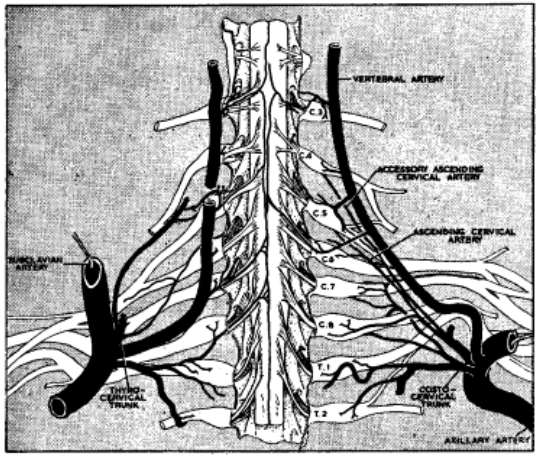


Fig. 1 (*Case* 2).—Anterior view of the blood supply of the right and left brachial plexuses. The proximal ends of both subclavian arteries have been retracted and displaced upwards and laterally to display the origin of branches more clearly. (Drawn by A. Besterman.)

[1]Present address: The Fatimah Jinnah Medical College for Women, Lahore, West Pakistan. The work reported here was supported by a Grant from the Medical Research Council and formed part of a thesis entitled "Studies on the Anatomy of the Human Brachial Plexus with special reference to its Blood Supply" for which the degree M.Sc. was awarded by the University of London.