

Entweder... oder...?



# Opiat-Therapie oder Blutegel bei Rheumapatienten?

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# Rheumatische Erkrankungen

- **Degenerative Erkrankungen**

(Arthrose, Rückenschmerz)

- **Entzündliche Erkrankungen**

(RA, Spondarthropathien, Kristallerkrankungen, reaktive Arthritiden, Juvenile Arthritis, Kollagenosen, Vaskulitiden)

- **Weichtelerheumatismus**

(Fibromyalgie, Enthesiopathien, Periarthropathien, Hyperlaxizitäts-Syndrom)

- **Knochenerkrankungen**

(Osteoporose, Osteomalazie, DISH)

# **Opioide bei nicht-malignen chronischen Schmerzen**

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- schlechte bis mässige Evidenz
- NW: Endokrinologie, Schmerzwahrnehmung,  
Immunologie, Kognition
- ungewollte Todesfälle
- multimodale Schmerzprogramme

# **Opioide und Toxizität**

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## **Objectives**

A dramatic increase in unintentional deaths  
from opioids has occurred over the past decade with strong inference that many of these deaths may be resulting from prescriber's error.

## Iatrogene Mortalität

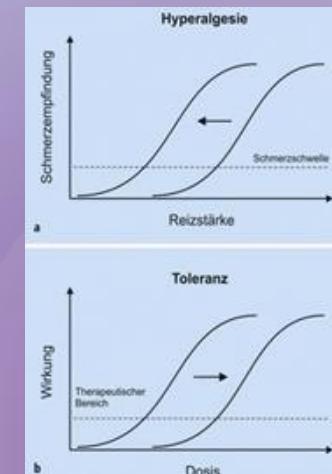
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- zweithäufigste Todesursache unter den ungewollten Todesfällen
- Mortalität erhöht sich um das 5fache
- Tagesdosis von 200mg Morphinäquivalent  
-> Sterblichkeit 2,2 – 2,9 fach höher

# Schmerzempfindung

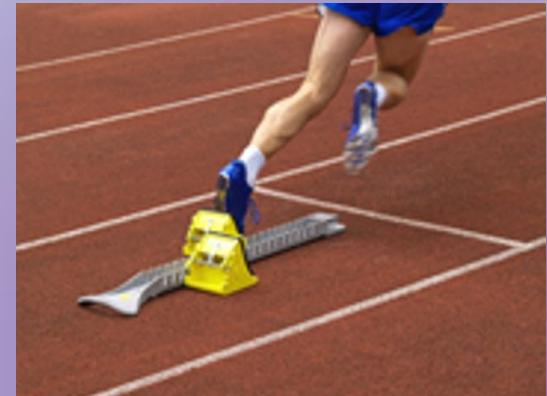
## zentrale Sensibilisierung

- Schmerzintensität Zunahme unter Therapie
- Schmerzausmass korreliert mit Dosis
- analgetische Dauer sinkt
- diffuser und schlechter charakterisierbar



# Kognition

- verminderte Aufmerksamkeit und Vigilanz
- Verschlechterung der Reaktionszeit



# Opioid-Rotation

An increasing number of deaths!



New paradigm for a potentially safer method of opioid rotation:

- Begin a downward **titration** of the original opioid by reducing the current dose by about 10–30%
- Use the new opioid at a dose that would normally be used in an opioid-naïve patient or at the **lowest available dose** for the formulation
- Slowly **reduce** the dose of the original total daily opioid dose by about 10–25% per week while increasing the dose of the new daily opioid dose by about 10–20% based on clinical need and safety (3–4 weeks)
- Provide sufficient **immediate-release** opioid throughout the rotation to prevent withdrawal and/or increased pain if the dosing changes prove insufficient
- This minimizes the risk of the **patient self-medicating** due to inadequate relief, which can be fatal

## 6275 subjects matched, 5 opioid groups

- The risk of cardiovascular events was similar across opioid groups 30 days after the start of opioid therapy, but it was elevated for codeine (RR, 1.62; 95% CI, 1.27-2.06) after 180 days.
- Compared with hydrocodone, after 30 days of opioid exposure the risk of fracture was significantly reduced for tramadol (RR, 0.21; 95% CI, 0.16-0.28) and propoxyphene (0.54; 0.44-0.66) users.
- The risk of gastrointestinal safety events did not differ across opioid groups.
- All-cause mortality was elevated after 30 days for oxycodone (RR, 2.43; 95% CI, 1.47-4.00) and codeine (2.05; 1.22-3.45) users compared with hydrocodone users.

### Conclusions:

The rates of safety events among older adults using opioids for nonmalignant pain vary significantly by agent.

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# Opioid-Mortalität

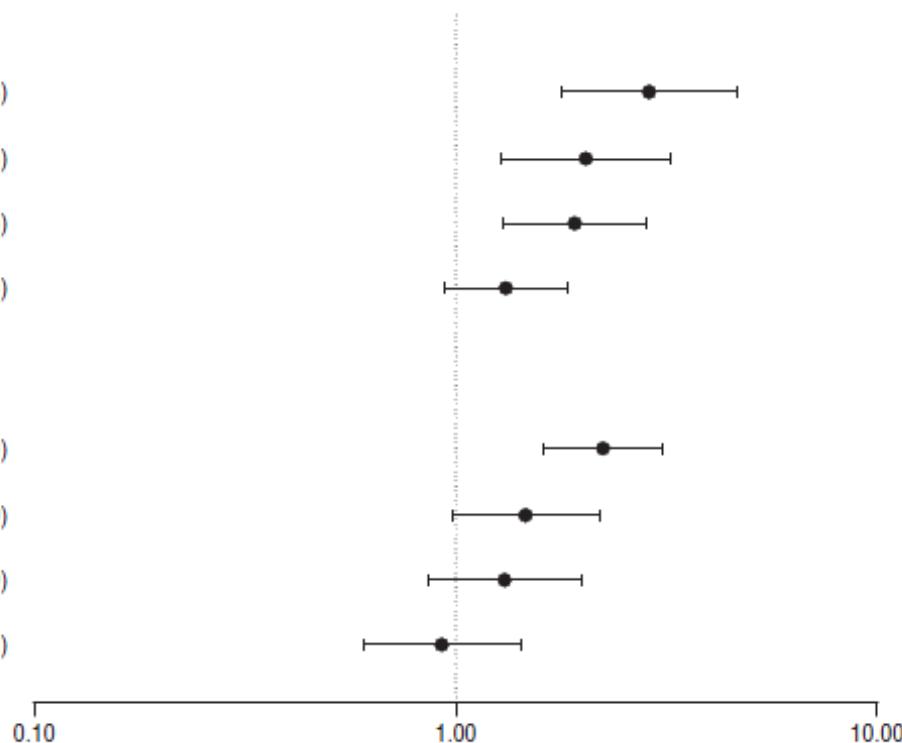
	Cases, n/N	Controls, n/N	Adjusted OR (95% CI)
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Primary analysis: overlapping opioid prescriptions  
(Reference: 1-19 mg morphine equivalents)

≥200 mg	116/498	223/1714	2.88 (1.79-4.63)
100-199 mg	82/498	181/1714	2.04 (1.28-3.24)
50-99 mg	97/498	273/1714	1.92 (1.30-2.85)
20-49 mg	118/498	514/1714	1.32 (0.94-1.84)

Secondary analysis: 120-d exposure window  
(Reference: 1-19 mg morphine equivalents)

≥200 mg	557/781	1319/2804	2.24 (1.62-3.10)
100-199 mg	64/781	303/2804	1.47 (0.98-2.19)
50-99 mg	52/781	300/2804	1.31 (0.86-1.99)
20-49 mg	41/781	366/2804	0.93 (0.60-1.42)



Among patients receiving opioids for nonmalignant pain, the daily dose is strongly associated with opioid-related mortality, particularly at doses exceeding thresholds recommended in recent clinical guidelines.

# Opioide bei nicht-malignen Schmerzen

## Limit FDA Approval for Noncancer Pain



maximum duration of 90 days for continuous (daily) use of opioids for noncancer pain

The following paragraph is a quote from that article:

*“Washington Department of Health officials, recognizing that opioid therapy will become increasingly difficult to obtain, proposed that chronic pain patients should explore alternative treatments for relieving pain, such as “physical therapy, yoga, massages or acupuncture.”*

# Opioide bei Frauen



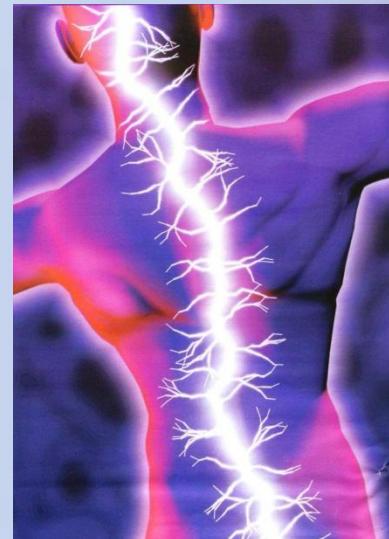
Long-term opioid use exposes women to unique risks, including **endocrinopathy**, reduced **fertility**, **neonatal** risks, as well as greater risk for **polypharmacy**, **cardiac** risks, **poisoning** and unintentional **overdose**, among other risks.

Risks for women appear to vary by age and psychosocial factors may be bidirectionally related to opioid use.

# **Opioide oder Blutegel bei Rückenschmerzen**

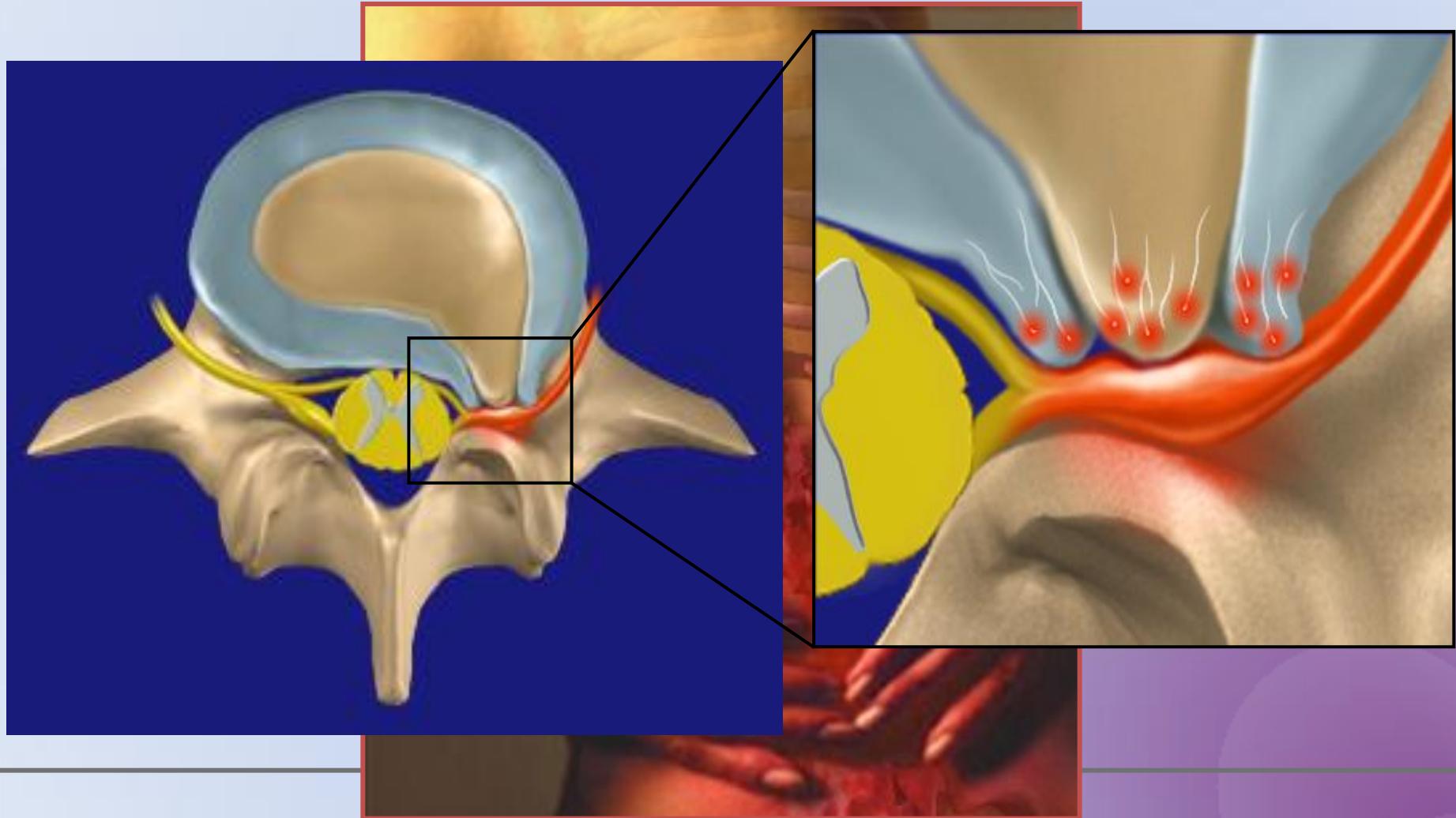
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## **Entweder ... oder ... ?**



Entweder... oder...?

# koexistierender Schmerz



## Zum Verständnis der Schmerzschlüsseltypen

### Noizeptiver Schmerz

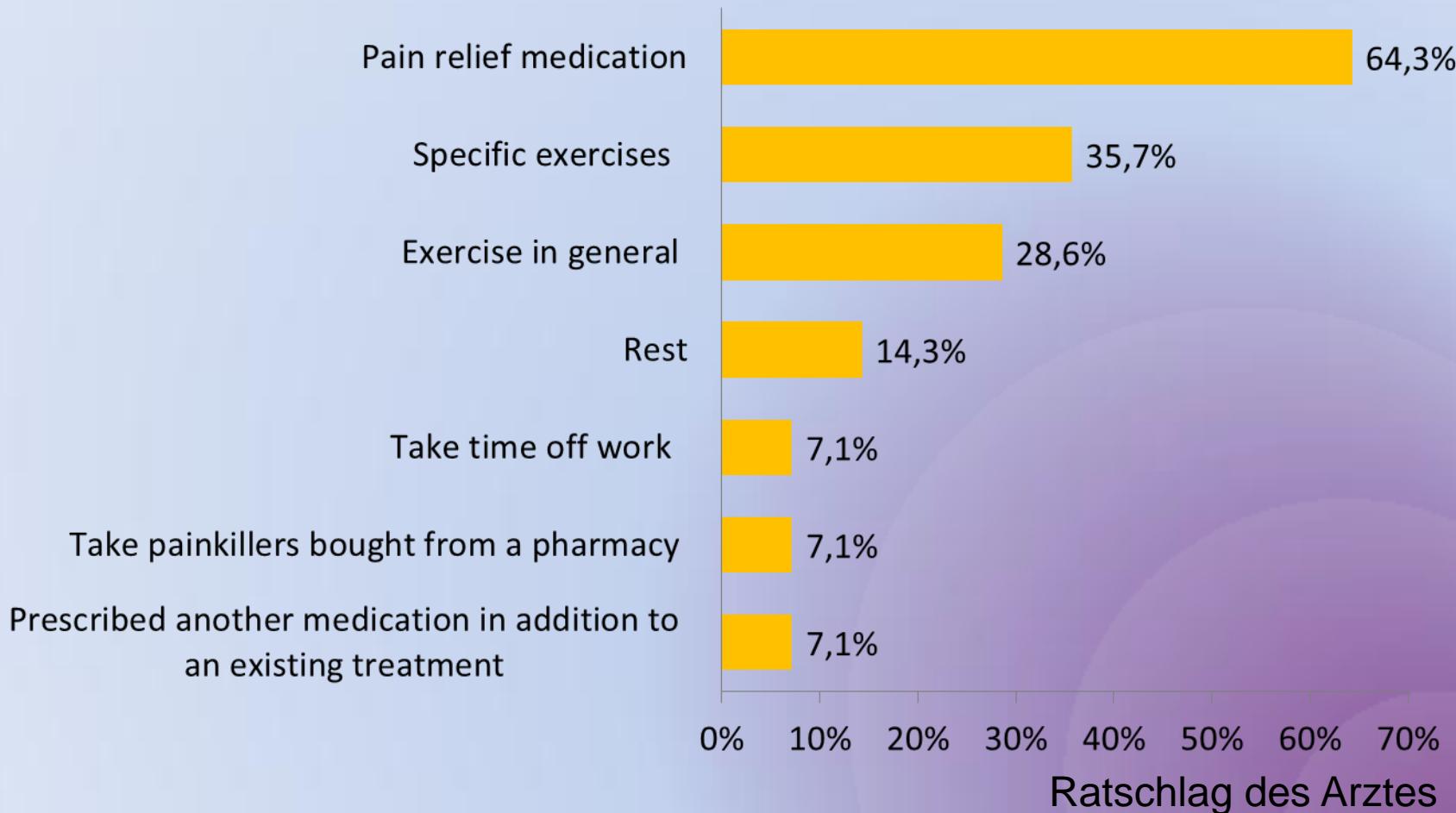
Durch eine inflammatorische oder nicht nicht-inflammatorische Antwort auf einen noxischen Stimulus verursachter Schmerz

### Neuropathischer Schmerz

Durch eine Primärläsion oder Dysfunktion im Peripheren oder Zentralen Nervensystem ausgelöster oder verursachter Schmerz

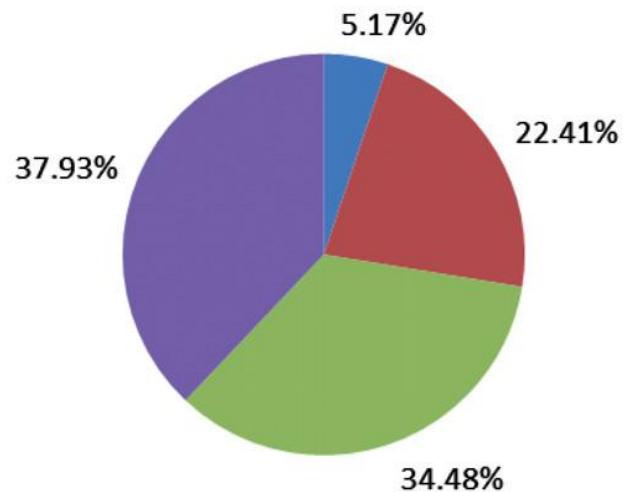


# Marktforschungsumfrage

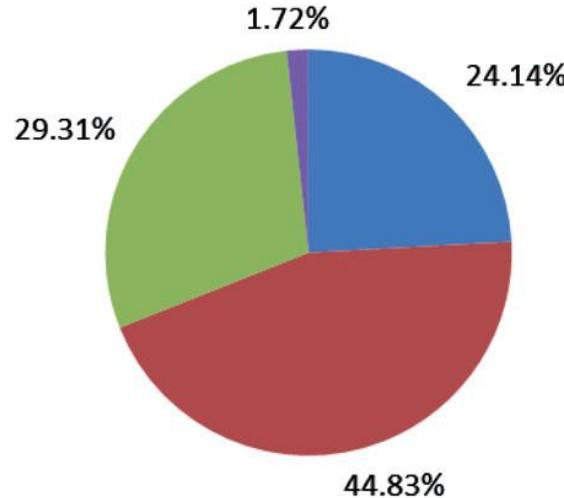


# Rückenschmerzen

**Pain Improvement**



**Function Improvement**

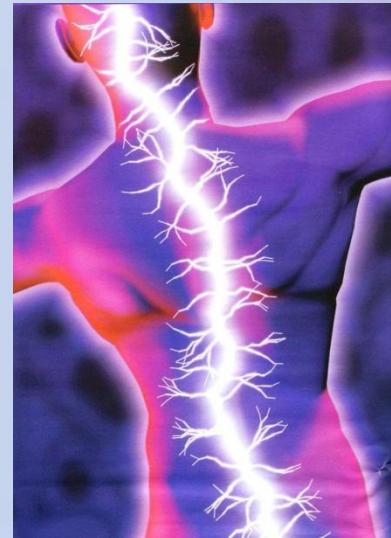


Prospective study of 3-year follow-up of low-dose intrathecal opioids in the management of chronic nonmalignant pain.

Low-dose IT opioid can provide sustained significant improvement in pain and function for long-term follow-up in chronic noncancer pain.

Opiate oder Blutegel  
bei Rückenschmerzen

Entweder ... oder ... ?



# Multimodale Schmerzprogramme und Opiode

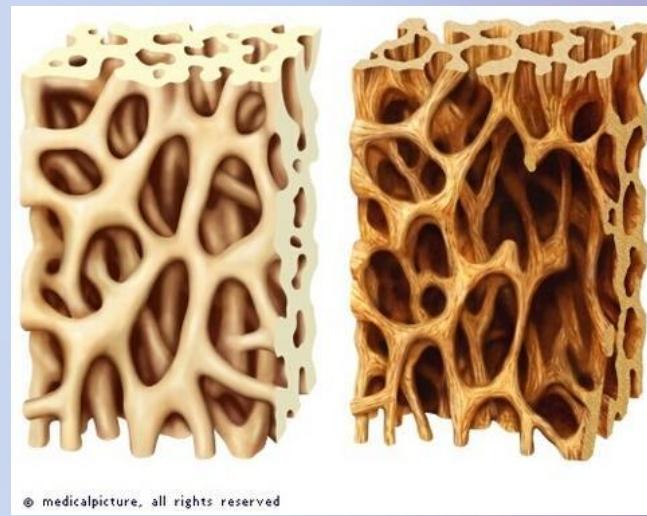
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- Ausschleichen gelingt in 90% der Fälle
- Verbesserungen auf physischer,  
emotionaler und sozialer Ebene

## Opioide oder Blutegel bei Osteoporose

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# Entweder ... oder ... ?



# Endokrinologie

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- osteoporotische Fraktur **6fach erhöhtes Risiko**
- Hemmung von LH und Testosteron
  - Hypogonadismus, Oligomenorrhoe/Amenorrhoe
- Störung Glukose-SW
- verstärkte hormonelle Stressantwort (ACTH)

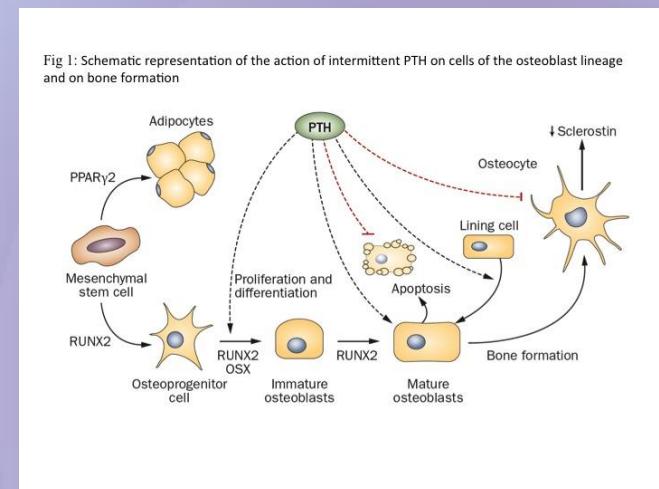
Entweder... oder...?

# Therapie

## Antiresorptiva

- Bisphosphonate  
Alendronat, Ibandronat, Risedronat, Zoledronat
- RANKL-Inhibitor  
Denosumab
- Selektive Östrogen-Rezeptor Modulatoren (SERM)  
Raloxifen, Bazedoxifen
- Hormonersatztherapie

## Knochenanabole Substanzen



**BASISTHERAPIE MIT VITAMIN D UND KALZIUM**

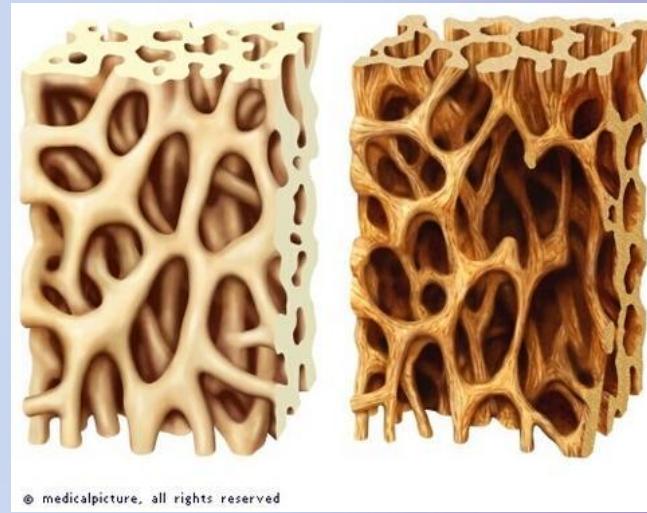
Entweder... oder...?

# Opiode oder Blutegel bei Osteoporose

Sorgfältige Indikationsstellung  
bei OP-Schmerz!

**Nein**

## Entweder ... oder ... ?



## **Opioide oder Blutegel bei Periarthropathien**

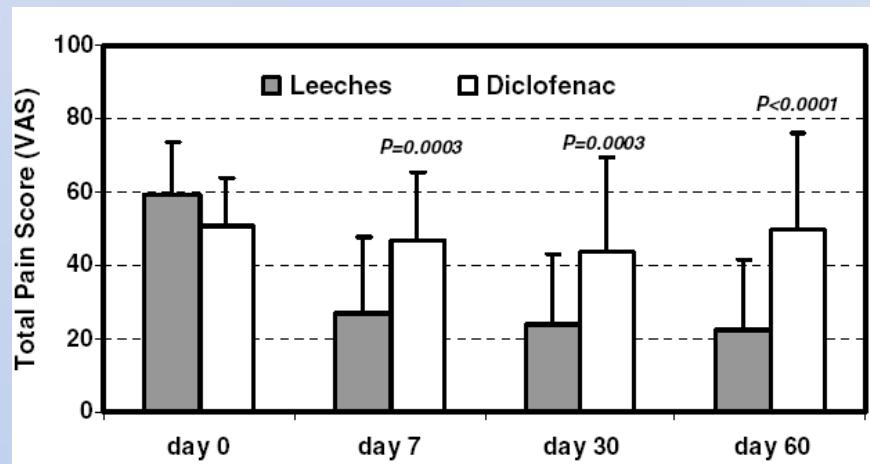
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# **Entweder ... oder ... ?**





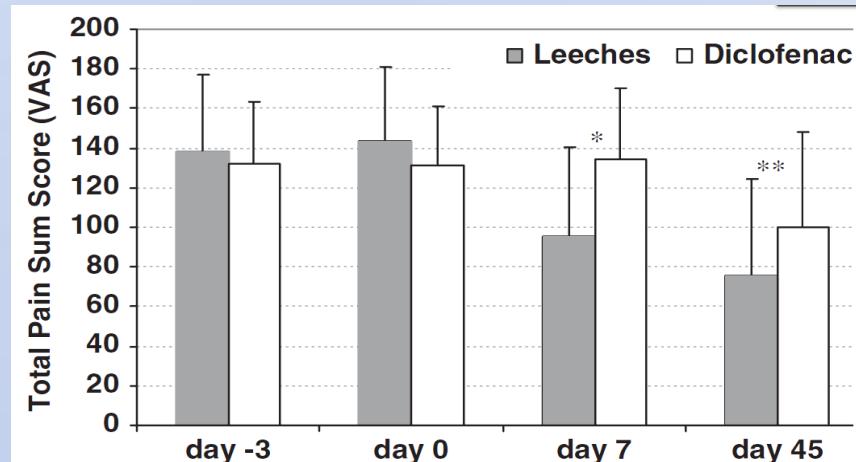
# Blutegel



- n = 32 randomisiert (MCP I)
- VAS, DASH, SF-36
- Kraft nahm bereits nach 7 Tagen zu (relevant)
- Schmerz ↓
- anhaltender Effekt bis Studienende (60 Tage)



# Blutegel



- n = 40 randomisiert (Epicondylopathia)
- VAS, SF-36
- Kraft nahm bereits nach 7 Tagen zu (relevant)
- Schmerz ↓
- anhaltender Effekt bis Studienende (45 Tage)



# Blutegel

Table 1 Main outcome parameters (mean  $\pm$  1 standard deviation, \* $p < 0.001$  double-sided Mann–Whitney-U-test).

		Day 0	Day 3	Day 7	Day 21
Group 1	L.I.	12.07 $\pm$ 4.24	9.17 $\pm$ 4.80	9.2 $\pm$ 4.66	9.37 $\pm$ 5.10
	VAS [cm]	5.89 $\pm$ 2.40	4.55 $\pm$ 2.60	4.30 $\pm$ 2.65	4.16 $\pm$ 2.67
Group 2	L.I.	11.66 $\pm$ 3.42	10.88 $\pm$ 3.56	11.27 $\pm$ 3.56	11.63 $\pm$ 3.05
	VAS [cm]	5.63 $\pm$ 2.35	5.09 $\pm$ 2.18	5.36 $\pm$ 2.31	5.61 $\pm$ 2.61

- n = 52 randomisiert (Periarthropathia genu)
- VAS, Lequesne-Index
- Funktion nahm bereits nach 3 Tagen zu (relevant)
- Schmerz ↓
- anhaltender Effekt bis Studienende (21 Tage)

Op...ide oder Blutegel  
bei Periarthropathien

**Entweder ... oder ... ?**



## **Opioide oder Blutegel bei RA**

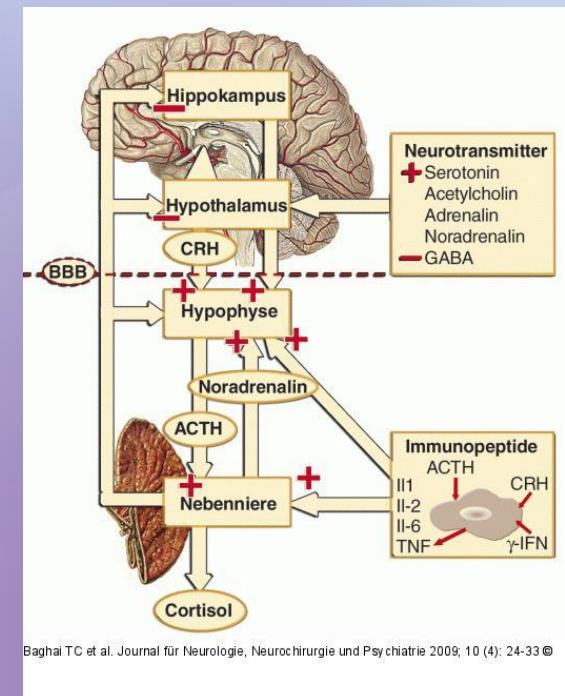
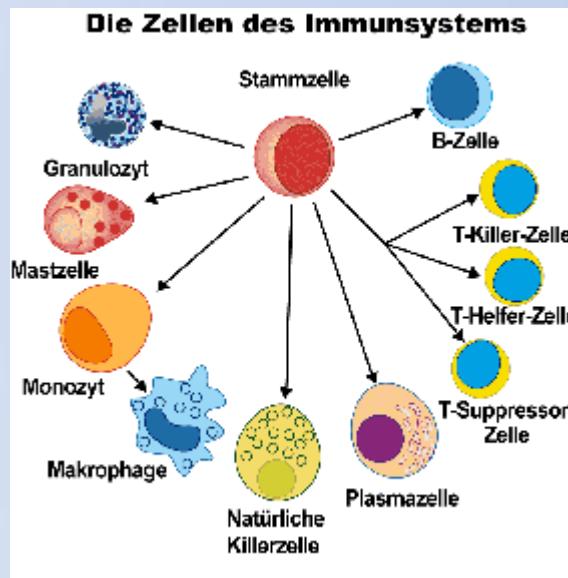
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**Entweder ... oder ... ?**



# Endokrinologie/Immunologie

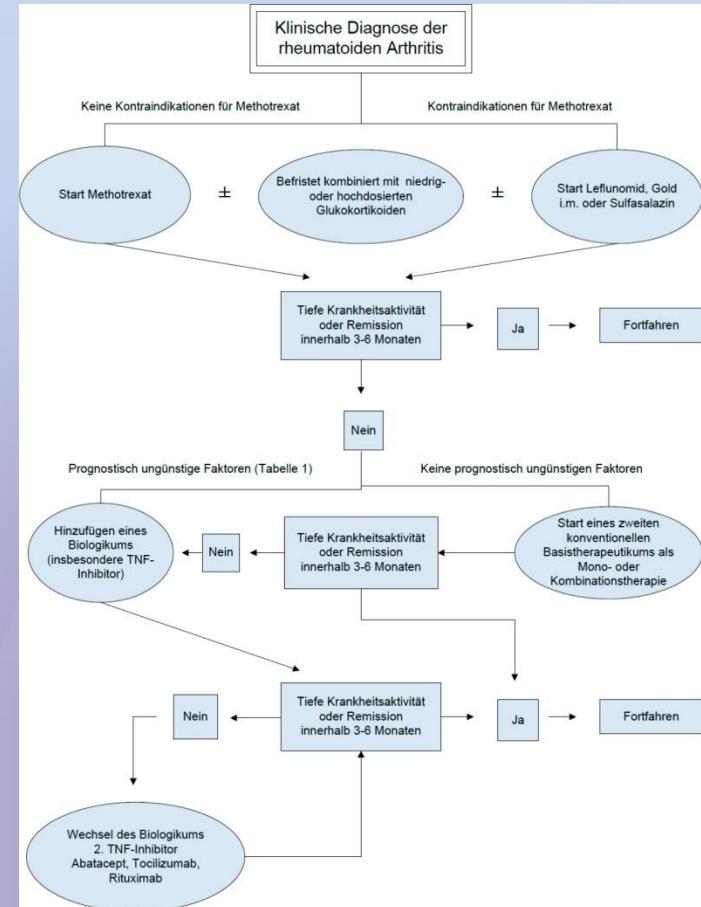
- indirekte Inhibition über Hypothalamus-Hypophysen-Nebennieren-Achse
- direkte Inhibition auf Immunzellen



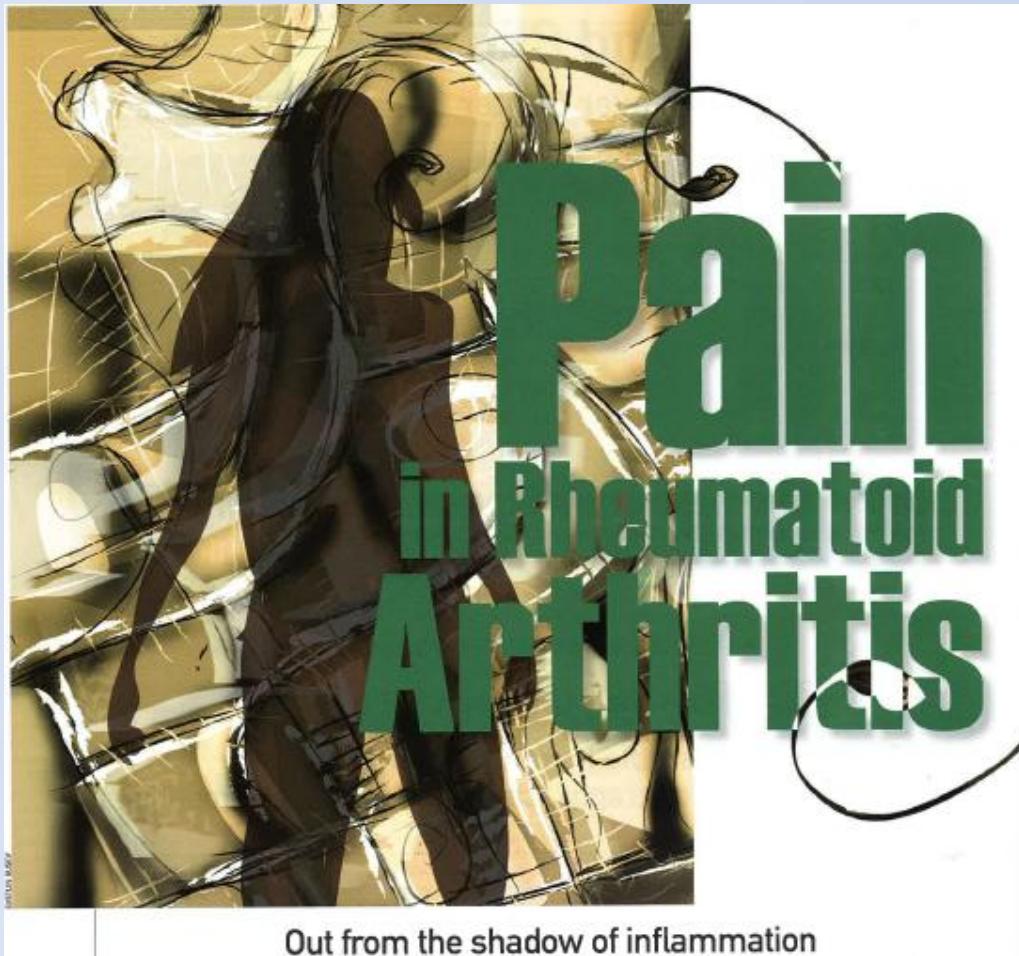
Entweder... oder...?

# Therapie der RA

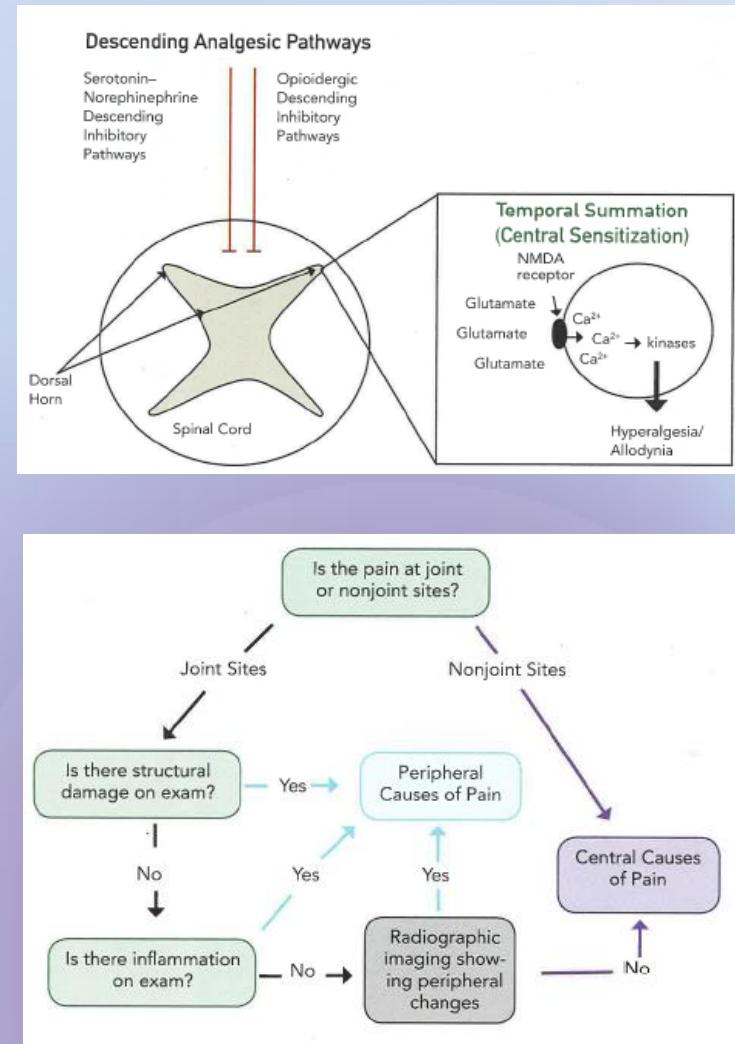
- Medikamentöse Therapie
- Physiotherapie
- Ergotherapie
- Rheumachirurgie



Entweder... oder...?



The Rheumatologist, October 2011



Entweder... oder...?

Opiode oder Blutegel  
bei RA **Nein**

Sorgfältige Indikationsstellung  
bei RA-Schmerz!

Entweder ... oder ... ?

