TRIGEMINAL FOUNDATION
NERVE INJURIES
Helping to prevent, educate and mitigate

Launch of
Trigeminal FOUNDATION
Nerve injuries Website

trigeminalnerveinjuries.org

Wednesday July 11th
5.45 – 7.30 pm
Gordon Museum

http://trigeminalnerve.org.uk/

“to provide excellence in education, management and prevention of trigeminal nerve injuries related to dental surgery”
Post traumatic painful neuropathy
More common than you think!

BSOS 3 June 2013
Manchester

Tara.renton@kcl.ac.uk
Post traumatic trigeminal neuropathy

- Mechanisms
- Patient impact
- Prevention
- Management
Risk / Benefit

There is an element of risk inherent in all clinical decisions

+ Surgery nerve injury- risks of surgery
  70% of LN and IAN injuries present with neuropathic pain and many patients demonstrate post traumatic stress disorder in relation to the significant disability and these cannot be completely fixed – life long

- Surgery The risks may include the probability of an infection, pathology, distal seven caries and possibly systemic disease if surgery is not administered ?? ??

Dental extractions = most common NHS surgical procedure
Litigation against dentists
Peripheral sensory nerve injury
Causes of peripheral sensory nerve neuropathy

Diabetes
HIV
PHN
Chemotherapy
MS
Post surgical traumatic neuropathy
Parkinson’s
Malignancy
Drugs - Growth hormone injections
### Table 1: Estimated incidence of chronic postoperative pain and disability after selected surgical procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Estimated incidence of chronic pain</th>
<th>Estimated chronic severe (disabling) pain (&gt;5 out of score of 10)</th>
<th>US surgical volumes (1000s)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amputation²</td>
<td>30–50%</td>
<td>5–10%</td>
<td>159 (lower limb only)</td>
</tr>
<tr>
<td>Breast surgery (lumpectomy and mastectomy)³</td>
<td>20–30%</td>
<td>5–10%</td>
<td>479</td>
</tr>
<tr>
<td>Thoracotomy⁴⁻⁻⁷</td>
<td>30–40%</td>
<td>10%</td>
<td>Unknown</td>
</tr>
<tr>
<td>Inguinal hernia repair⁸⁻¹⁰</td>
<td>10%</td>
<td>2–4%</td>
<td>609</td>
</tr>
<tr>
<td>Coronary artery bypass surgery¹¹⁻¹³</td>
<td>30–50%</td>
<td>5–10%</td>
<td>598</td>
</tr>
<tr>
<td>Caesarean section¹⁴</td>
<td>10%</td>
<td>4%</td>
<td>220</td>
</tr>
</tbody>
</table>

*Gall bladder surgery not included, since preoperative diagnosis of pain specifically from gall bladder is difficult and persistent postoperative pain could therefore be related to other intra-abdominal disorders. †National Center For Health Statistics, Ambulatory and Inpatients Procedures, USA, 1996.

30% get persistent pain
10% are **severely** affected

? 0.4-5% of trigeminal severely affected
A Nociceptive pain
Pain caused by a non-inflammatory response to a noxious stimulus = Tissue damage

B Inflammatory pain

C Pathological pain
Neuropathic pain
Pain initiated or caused by a primary lesion or disease in the PNS or CNS = nerve damage

D Dysfunctional pain
REMEMBER it may be possible to have coincident combinations of A, B and or C types of pain
Mechanisms
Peripheral
Central
Peripheral
Na channels
Ca Channels
K Channels

Central
NMDA
AMPA
K Channel
a Peripheral nerve injury

- Dorsal root
- Dorsal root ganglion
- Spinal cord
- Ventral root
- Peripheral nerve

b Immune and glial cell reactions

Distal to the nerve lesion site

- Macrophage
- Schwann cells
- Mast cell
- T lymphocyte
- Regenerating nerve fibers

Dorsal root ganglion

- Sensory neuron
- Satellite cells
- Macrophage
- T lymphocyte

Spinal cord

- Sensory neuron
- Resident microglia
- Active microglia

Nerve X-Section

- Epineurium
- Perineurium
- Endoneurium

Nerve Fiber

- Myelin
- Axon
- Endoneurium
- Schwann Cell

Image credit: Kim Cressall
The neuro-immune balance in neuropathic pain: Involvement of inflammatory immune cells, immune-like glial cells and cytokines  
Paul J. Austin & Gila Moalem-Taylor  
Journal of Neuroimmunology  
Volume 229, Issue 1, Pages 26-50, 15 December 2010
OUT Trigeminal Nerve root-V ganglion

Mesencephalic V nucleus = proprioception

IN Trigeminal (V) Lemniscus-to VPM N thalamus - S1 and S2

Motor V nucleus = masticatory muscles

Pontine V nucleus = main sensory N touch

Spinal V nucleus subdivided vertically- Oralis / interpolaris / caudalis (Pain+ temperature)
Glial cells

2 types of cells in the brain—Neurons and Glial cells

Glia cells, named for the Greek word for "glue," hold the brain's neurons together and nourish them.

In neuropathic pain, epilepsy, ALS, Parkinson's and Alzheimer's, activated glial cells are associated with disease burden. Glial cells normally nourish and protect neurons.

Glia cells are central to the brain's plasticity — how the brain adapts, learns, and stores information. Almost all neurodegenerative diseases are glia-related pathologies,
Glutamate signalling - This excess in glutamate act on postsynaptic glutamate receptors (NMDA and AMPA), leading to and sustaining central sensitization. Moreover, under pathologic condition, glial cells are activated, representing a driving force for pain facilitation. AMPA = \text{a-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid}; \text{NMDA} = \text{N-methyl-D-aspartic acid}.
Changes in Thalamic anatomy and function in V pain

‘significant reduction in the N-acetylaspartate/creatine ratio, a biochemical marker of neural viability, in the region of thalamic volume loss’


Chronic pain: lost inhibition?
Henderson LA et al

Commentary

A new definition of neuropathic pain

1. Introduction

IASP has recently published a new definition of neuropathic pain according to which neuropathic pain is defined as “pain caused by a lesion or disease of the somatosensory system” (www.iasp-pain.org/resources/painDefinition). This definition replaces the 17-year old definition that appeared in the Classification of Chronic Pain published by IASP in 1994 [7], which defined neuropathic pain as “pain initiated or caused by a primary lesion, dysfunction, or transitory perturbation of the peripheral or central nervous system”. Even though the definition has not been changed dramatically, there are two important changes in the new version: (1) the word “dysfunction” has been removed and (2) a lesion or disease affecting the nervous system has been specified to be a lesion or disease of the somatosensory system.

2. Background

The history behind this change dates back several years with a long, and at times, heated debate about the inclusion of the terms mechanisms, with, neurological, and treatment of neuropathic pain, and increased understanding of pain mechanisms should put us in a better position to treat patients and design rational treatment strategies. There has indeed been progress since the last update of the neuropathic pain definition 17 years ago. For example, primary erythromelalgia and paroxysmal extreme pain disorder are both rare pain conditions for which we had no explanation 10 years ago, and therefore pain associated with these could not then have been classified as neuropathic. It is now clear that both disorders are due to specific and separable mutations in the SCN9A gene that codes for one of the many subtypes of neuronal voltage-gated sodium channels: the Na\textsubscript{v} 1.7 channel [1]. While these observations have not yet resulted in a specific or preventative treatment for the rare genetic pain states, there is now a clear target that can be addressed. Another pain condition that has seen progress is Fabry’s disease, which can now be treated with enzyme replacement therapy [6]. Biomarkers for an inflammatory component in neuropathic pain are also being discovered, and again, these may lead to new specific treatments. Other examples will certainly be added as our knowledge of diseases and their causes increases.
Painful Posttraumatic Trigeminal Neuropathy: A Recently Recognized Entity.

The Trigeminal nerve

Complex region
Consequences

Social function
Eating
Drinking
Speaking
Kissing
Make up / shaving
Sleeping
Issues specific to Trigeminal nerve

Consent
Closed injury
Most resolve
Type of nerve injury
Type of patient
Neuroplasticity

Current surgical management is inadequate
When a sensory nerve is damaged

**Pain**

* hyperaesthesia
  * allodynia pain with non noxious stimulus
    * pain on touch/cold/hot
  * hyperalgesia increased pain to painful stimulus

**Altered sensation**

* paraesthesia – pins and needles, formication, many descriptions
* dysaesthesia – uncomfortable sensations often burning

**Numbness**

* anaesthesia/hypoaesthesia
Neuropathic pain

The International Association for the Study of Pain introduced the term neuropathic pain, defined as “pain initiated or caused by a primary lesion or dysfunction in the nervous system.”

Grading system of "definite," "probable," and "possible" neuropathic pain has been introduced
The consequences of Trigeminal nerve injury
Profiling of patients presenting with posttraumatic neuropathy of the trigeminal nerve. Renton T, Yilmaz Z. J Orofac Pain. 2011 Fall;25(4):333-44
Consequences for the patient

620 patients with nerve injuries seen over 4 years at KCH

Pain
70% of Lingual or Inferior Alveolar Nerve injuries

Functional
Eating, speaking, drinking, sleeping, kissing, make-up, shaving, tooth brushing

Psychological
50% chronic pain sufferers are depressed
Informed consent
Informed consent

Less than 30% of patients are appropriately warned of nerve injury in high risk procedures
Neuropathic pain
Pain and altered sensation

70% of patients have pain
Psychological features

Depression
Anger
Post traumatic stress disorder
Victim of abuse
Loss of ability to trust

Kubler Ross
Patients perspective .......
When damage is done

If I Knew Then...

Its too late!
How do we avoid nerve injuries?
Third molar surgery
Third molar surgery
When is the Inferior alveolar nerves at risk?

- Local anaesthesia
- Third molar surgery (M3Ms)
- Implants
- Endodontics
- Orthodontics
- Orthognathic surgery
- Fractures
- Pathology
Elective removal of M3Ms

10 million M3Ms removed
USA per year 60% elective surgery

Costing $US 4.2 billion

11000 pts permanent nerve injury!

‘Silent epidemic’ of iatrogenic nerve injury


Mythology of 8s
Overall 12% associated with pathology
- same as appendicitis and cholecystitis
- 8% pericoronitis
- 3% caries lower 7s
- 0.048% resorption of adjacent tooth
- 0.0085% internal resorption
- 0.0165% cyst formation
Avoidance of surgery: Guidelines

UK  NICE

Indications

- untreated tooth decay
- abscess
- cysts or tumours
- disease of tissues around the tooth
- if tooth is in way of other surgery

USA  AAOMS 60% undertake M3M elective surgery
Justification for elective removal

**BUT should there be prophylactic extraction?**

- Periodontal defect
- Pre Heart valve surgery
- Pre Transplant surgery
- Pre chemotherapy
- Pre radiotherapy
- Pre Bisphosphonates
- Pre orthognathic surgery
- Pre long distance travel in at risk patients - Immunocompromised

- Risk of second molar caries?
International variance in Guidelines

Low intervention

- NICE Guidelines UK 2000
- Finnish Guidelines 2009
- Military Guidelines US UK Canada Australia
- AAOMS 2010 PROPHYLAXIS

High intervention

What has been the United Kingdom’s experience with retention of third molars?

NICE guideline effect on M3M surgery

Renton T, Al-Haboubi M, Pau A, Shepherd J, Gallagher J. What has been the United Kingdom’s experience with retention of third molars? JOMS 2012 in press

McArdle L & Renton T. The third molar debate – The impact of NICE guidelines. BDJ in press
Actual LA nerve injury incidence

GDP restorative procedures (LA)
1:14K
25% permanent

Oral surgery specialists
1:3.3K
29% permanent

Compare this with anaesthetic LA block procedures. NAP3 reports the estimated that nerve injury resulting from neuroaxial blocks (epidurals, spinals and combined epidural with spinals) resulted in sensory or motor nerve injury in 1 in 24-54K patients (and paraplegia or death in 1 in 50-140K patients)
Informed consent for M3Ms

Warn of principal complications of surgery and anaesthesia:
swelling, bruising, pain and trismus

Complications ...................... Be explicit!
Dry Socket 2-5%

Nerve damage (transient or permanent) 0.2% Perm 2% Temp
Remember if High risk 10 X more likely 2% Perm 20% temp
Inferior alveolar supplies skin of lip and chin, teeth and gums
Lingual supplies one half tongue, lingual gums
Nerve injury results in altered sensation, numbness and pain!

Time off work = 2 days - may need home help
Give printed post-op instructions and antibiotics & analgesics
Give your out of hours contact details -

GET WELL SOON LEAFLET for WISDOM TEETH - RCS England

http://www.rcseng.ac.uk/patient_information/get-well-soon/wisdom-teeth-extraction
Informed consent……

Get well soon leaflet
Conflicting LA info?

Articaine and lignocaine

Abstracted from

Kedar K.

Question: What is the efficacy and safety of articaine compared to lignocaine for molar and mandibular infiltration and block anesthesia in patients presenting for routine dental treatments?

Data sources: Cochrane Central Register Trials, EMBASE, MEDLINE, and Pre-Print Health and Medical Complete, the metasearch of the cumulated database and a leading manufacturer.

Study selection: Randomly controlled trials with patients requiring non-complex routine dental treatments comparing 2% articaine (615,000 units/mL) with 2% lignocaine (615,000 units/mL) for molar and mandibular infiltrations and block anesthesia were included. The primary outcome measure was anesthetic success, defined as complete anesthesia without any pain or paresthesia, and secondary outcomes included overall patient satisfaction.

Dissertation and synthesis: Following data extraction, a meta-analysis was performed using Stata software. A single study was included.

Results: Eight studies were included in a meta-analysis. Articaine is somewhat less likely than lignocaine to achieve anesthetic success in the lower jaw, by a relative risk of 0.85 (95% CI 0.75, 0.96, P = 0.008). There was no difference in post-injection adverse events between articaine and lignocaine with a relative risk of 1.15 (95% CI 0.99, 1.32, P = 0.06). However, articaine injection results in a higher percentage of patients experiencing the sensation, after the anesthetics, with a weighted mean difference of 4.5 (95% CI 2.5, 6.6, P < 0.001). Conclusion: The results of this systematic review do not provide support for the argument that articaine is more effective than lignocaine in providing adequate anesthesia in the lower jaw, leading to a possible increase in the risk of adverse events.

Trigeminal nerve injury associated with injection of local anesthetics

Needle lesions or neurotoxicity?

Local anesthetics typically are considered safe for use in healthy people. However, injection-related trigeminal nerve injury reflected in neurosensoric disturbance (NSD) does occur. Such NSDs occur, and patients with NSD are referred to as prolonged paresthesia. A detailed clinical examination may reveal a variety of signs and symptoms of neurological discomfort, such as hypoesthesia, anesthesia, dysesthesia, alldynia, spontaneous pain and abnormalities related to gustation.

Estimates of the incidence of local anesthetic-related trigeminal nerve injury are not available.
Successful extractions in Incisors-premolars 90%
M1Ms  60%
M2Ms  75%

Prospective audit 380 extractions by dental UGs
- no palatal blocks given
- Articaine infiltration
- Lidocaine IDB rescue

87% success!
Prevent Local anaesthesia induced nerve injuries?

Avoid multiple blocks
No IDBs under GA
Avoid high concentration (Articaine) IDBs
Stick to Lidocaine ID blocks for now!

Is the future Articaine as infiltration only with no ID blocks????????

M3M SURGERY
Lingual nerve risk factors in surgery

Prospective case series 1384 patients undergoing third molar surgery (n=2134)

Significant risk factors associated with lingual nerve injury

- Difficulty of surgery
  - Patient age
  - Depth of application
- Surgeons surgical skill
  - Scoring of lingual plate
  - Exposure of the nerve

Ouch!
No flap Section tooth
Routine use of the ‘buccal’ approach?

99% US oral surgery practitioner
52% after defining the buccal approach

Surgical approach methods

Avoid envelope flaps!

**Buccal approach**
- Robinson and Smith 1996
- Deeply impacted (horizontal) teeth
  - Buccal bone removal
  - Cut off crown (decoronate)
  - remove roots
    - Elevate or
    - Divide parallel and divergent roots
    - loosen and remove with luxator
Triangular Buccal flap
Video of ‘proper’ buccal approach
‘Episiotomy’ buccal relief
‘Episiotomy’ buccal relief
NO to distal bone removal
Kiesselbach and Chamberlain 1988

Lingual nerve
NO to distal bone removal
Kiesselbach and Chamberlain 1988

Lingual nerve
Spot the lingual nerve!
Is the M3M high risk?
Prevention of Inferior alveolar nerve injuries
Remember other teeth can be high risk crossing IDC.
Inferior alveolar nerve injury in M3M surgery

Risk

- 0.5% of cases permanently
- 2% of cases temporarily

BUT if the teeth are superimposed on the IAN canal

- 20% temporary
- 2% permanent

Risk factors

- increased age
- difficulty of surgery
- proximity to the IAN canal

USA-If a lower third molar is high risk -----CBCT
IAN - Radiographic factors

OLD
- Diversion of the canal
- Darkening of the root
- Interruption of the canal LD

NEW
- Juxta-apical area
- Deviation of canal
- Narrowing / darkening of roots
Assessment nerve ‘at risk’

Crossing lamina dura of IAN canal on plain film?

Associated radiographic signs?

Consider CBCT
Tooth sectioning

If the tooth is **high risk** and non vital then roots should be sectioned to minimise IAN injury.
Coronectomy

- Prospective randomised study 196 M3M procedures
- Factors associated with failed coronectomy
  - Female patient
  - Conical roots
  - Age

128 patients
196 teeth

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Temp IAN</th>
<th>Perm IAN</th>
<th>AO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical removal 102 teeth</td>
<td>20%</td>
<td>2%</td>
<td>11%</td>
</tr>
<tr>
<td>Coronectomy 56</td>
<td>0%</td>
<td>0%</td>
<td>9%</td>
</tr>
<tr>
<td>Attempted coronectomy 36</td>
<td>9%</td>
<td>0%</td>
<td>10%</td>
</tr>
</tbody>
</table>

Renton T et al. A prospective randomized study assessing coronectomy versus removal in third molar surgery. BJOMS 2005
Avoid root removal?
Role CBCT in localising IAN

Localising IAN proximal to lower teeth

DISTANT from nerve???????
Role CBCT localising IAN

Localising IAN proximal to lower teeth

PROXIMAL to nerve
DO not rely on radiologists report

Read the CBCT your self!

CBCT Radiation dose reduction
Remove the tooth or coronectomy?

Distant- remove 'Snake like' or Perf-Coronectomy
Less than 10% of high risk M3Ms need coronectomy
Coronectomy
Coronectomy Risks

Intra-operative mobilisation of M3M roots
Early post operative infection
Late post operative infection (with eruption)
Second surgery

• Article first published online: 14 JUN 2010 DOI: 10.1111/j.1752-248X.2010.01079.x
Coronectomy on other teeth
Algorithm for coronectomy decision.

- Is the tooth vital?
- Is the patient non-immuno compromised?
- Is the tooth crossing BOTH IDC lamina dura?

NO

- REMOVE THE TOOTH

YES

CBCT findings:
Are the roots perforated by the IDC or an IAN branch?
Is the IAN intricately associated with indented M3M root?
Is there missing lingual plate related to root and the adjacent IDC?

NO

- Are the roots proximal but separate from the IDC?
- During decoronation do the roots move?

YES

INTENTIONAL CORONECTOMY
How else can we ‘knacker’ the ID nerve?
Inferior alveolar nerve - Endo
Other considerations
Toxicity of commonly used dental products

BioOss

Socket Medicaments
  • Alvogyl, Whiteheads varnish, Corsodyl and Surgicel (pH 5.8)

Endo Medicaments
  • Formocresol (pH 12.45 +/- 0.02)
  • Sodium hypochlorite (pH 11-12)
  • Calcium hydroxide (CalyxI) (pH 10-14)
  • Antibiotic-corticosteroid paste (Ledermix) (pH 8.13 +/- 0.01)
  • Neutral (pH 7.35-7.45)
  • Eugenol (pH 4.34 +/- 0.05)
  • Iodoform paste (pH 2.90 +/- 0.02)
Inferior alveolar nerve - Endo

30 hours to remove endo overfill OR tooth
Post operative protocol endodontics

- **Post operative LCPA**
  - Overfilled? Remove endo/tooth
- **Routinely check on patient early post op** <24 hours
- If pt has **neuropathy immediately** after LA has worn off;
  - **REMOVE Endo/tooth**
    - Extract tooth
    - Apicectomy nerve decompression
    - Steroids and NSAIDS
  
Refer
Implant related nerve injuries

The incidence of implant related inferior alveolar nerve (IAN) nerve injuries vary from 0-40%. Bone graft harvesting is also associated with IAN injuries


10% of patients presenting with iatrogenic trigeminal nerve injury in 2000 now 37% in 2011
Post-implant neuropathy of the trigeminal nerve. A case series.

T. Renton, A. Dawood, A. Shah, L. Searson and Z. Yilmaz

Background The incidence of implant-related inferior alveolar nerve injury in implant patients has increased in recent years. The incidence of inferior alveolar nerve injury has remained static in the UK over the last 20 years, however, the incidence of inferior alveolar nerve injury has increased as a result of implant surgery and endodontic therapy.

Aims This study prospectively reviewed thirty cases from the dental implantology and periodontology department at a specialist nerve injury clinic. Methods Neurosensory examination of the perception, pain profiling and functional difficulties. Details were recorded for each case. Results were analyzed against a control population. All subjects were aware of signing consent forms for the surgery in 11 cases. No clinical evidence of nerve injury was found in any of the patients. Over 10% of patients were referred after six months. Films showed a 30% increase in mean pain scores, 16% in CBCT (10%) and 5% in radiographic evidence of nerve injury. No problems included bleeding and neurofibromatous symptoms. Further analysis is required to determine the true incidence of implant-related trigeminal injuries.

Conclusions Awareness of the incidence of neuropathic pain following implant surgery is required to prevent further injuries.

INTRODUCTION

Trigeminal nerve injury is a frequent problematic consequence of dental surgical procedures with major medico-legal implications.1 The incidence of lingual nerve injury has remained static in the UK over the last 20 years, however, the incidence of inferior alveolar nerve injury has increased as a result of implant surgery and endodontic therapy.2

Altered sensation and pain in the oro-facial region may interfere with eating, speaking, kissing, swallowing, applying make-up, tooth brushing and drinking. In fact, just about every social interaction we take for granted.3 These injuries therefore have a significant effect on the patient’s quality of life and the restoration of these injuries may lead to further significant psychological effects.4

The interior alveolar canal has a greater risk for injury to the lingual nerve (LN), as it is in a bony canal, predisposing to trauma and a higher level of nerve damage.5 Dental surgeons are not being vigilant when carrying out implant surgery and are failing to inform patients about the risks of nerve damage, a study in the British Dental Journal says.

Researchers from King’s College London Dental Institute analysed 30 patients with nerve injuries and found problems with pain, speech, eating and kissing.

There are rare reports of implant related IAN injuries,4 but these are not normal reports of periodontal injuries.5 Another study of injuries after implant surgery may be too late for many other peripheral sensory nerve injuries. We now understand that after three months, permanent central and peripheral changes occur within the central nervous system subsequent to injury, which are unlikely to respond to surgical intervention.6

The incidence of implant related IAN’s varies from 0-33.2% (Table 1).7-9 Bone grafting of patients seen at the specialist pain clinic, hoping to form recommendations to reduce injury related to implant surgery.

METHODS

Subjects

A total of 287 patients with trigeminal nerve injuries collected over three years were included in this study. The majority of patients had undergone implant surgery.

REFERENCES

1. King’s College London Dental Institute, Bessemer Road, London, SE5 8PB (www.dental.kcl.ac.uk)
Implant related nerve injury

Planning
Preparation
Placement
Post operative
Advanced implant surgery
• Bone harvesting
IRTNI issues ........

• Consent
• LA protocol
  • Articaine as infiltration only with no ID blocks?
    Peterson 2004; Heller & Shankland 2001
• Planning
• Placement
• Post operative care
• Management of IRTNI
• Post implant pain
Planning

What radiography?
- Cone Beam CT Scan

Planning
- Software
  - Simplant

Assessment of IAN position
Safety zone >2mm IAN canal
? Should be >4mm

What is the actual position of nerve???????
Planning imaging

What radiography?
- Cone Beam CT Scan

Planning
- Software
  - Simplant

Assessment of IAN position
Safety zone >2mm IAN canal
? Should be >4mm

IAN plotted on Simplant using 5 points!
80% of clinicians questioned get technician to draw in
Can you read the full CBCT??
Implants: Are you sure you know where the nerve is?
Beware the mental foramen!!!

Adequate imaging?
Here or there?
Mental Loop
Drill length versus implant length?

Drill longer than your implant length?

Beware!

Use Drill stops!!
Signs of Intra-operative nerve injury

- Pain on injection of LA
- Brisk persistent bleed
- Sudden pain during implant bed preparation or placement

Any protrusion into the IDC or breech, will result in acute and often severe neuralgic type pain intra-operatively.

Intra-operative risk factors

Sudden ‘give’ during preparation

Extrusion of debris into canal

Intra-operative IAN bleed

Do not place implant immediately delay 2-3 days
Post operative protocol - implants

- Routinely check on patient early post operatively at 6 hours

- If patient has neuropathy immediately after local analgesia has worn off:
  - **REMOVE** the implant in less than 24 hours
  - Steroids and NSAIDS
  - Refer
Post operative protocol - implants

- Routinely check on patient early post operatively at 6 hours

- If patient has neuropathy immediately after local analgesia has worn off:
  - **REMOVE** the implant in less than 24 hours
  - Steroids and NSAIDS
  - Refer
When it goes wrong
If nerve injury does happen
What next?
Say sorry

Not an admission of guilt just shows empathy!

You should already have had a conversation about the risks!
Managing the patients expectations

Is MUCH easier when good preoperative consent has been undertaken!
Diagnosis and Classification of Neuropathic Pain

Epidemiology and Impact of Neuropathic Pain

Neuropathic pain—“pain arising as a direct consequence of a lesion or disease affecting the somatosensory system” according to the NeuPSIG (Special Interest Group on Neuropathic Pain) definition—is a challenge to health care. This common type of pain is often underdiagnosed and undertreated, and it is associated with suffering, disability, impaired quality of life, and increased cost.

The exact prevalence of neuropathic pain is not known. Two population-based studies from Europe reported the prevalence of pain of predominantly neuropathic origin or pain with neuropathic characteristics to be 8% and 7%, respectively. In both studies neuropathic pain was more severe than other types of pain. A German study reported that 37% of patients with prolonged low back pain had predominantly neuropathic pain. Depression, anxiety, and sleep disorders were significantly more prevalent in patients with neuropathic pain compared to those with nociceptive pain.
Temporary or permanent?

- **Mechanism**
- **Duration**
- Identify the extent of injury
  - Size neuropathic area
  - Subjective function
  - Mechanosensory function
  - Disability
  - Pain / discomfort

**Patient’s story and expectations?**

Renton T, Thexton A, SJ Crean, Hankins M. Simplifying assessment of recovery of the lingual nerve from injury. BDJ 2006 10:569-573


Assessment of neuropathy

Mechanosensory
- Neuropathic area
- Subjective function
- Light touch
- Sharp blunt

PAIN VAS
- At rest
- Dynamic allodynia
- Cold allodynia
- Capsaicin

Thermo sensory

Biopsy
Table 2
Definitions of common features suggestive of neuropathic pain

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paresthesia</td>
<td>An abnormal sensation, whether spontaneous or evoked</td>
</tr>
<tr>
<td>Dysesthesia</td>
<td>An unpleasant sensation, whether spontaneous or evoked</td>
</tr>
<tr>
<td>Hypoesthesia</td>
<td>Decreased sensitivity to stimulation (tactile or thermal; both are frequent)</td>
</tr>
<tr>
<td>Hyperesthesia</td>
<td>Increased sensitivity to stimulation (tactile or thermal; both are rare)</td>
</tr>
<tr>
<td>Hypoalgesia</td>
<td>Diminished pain response to a normally painful stimulus</td>
</tr>
<tr>
<td>Hyperalgesia</td>
<td>An increased response to a stimulus that is normally painful</td>
</tr>
<tr>
<td>Alodynia</td>
<td>Pain due to a stimulus that does not normally activate the nociceptive system</td>
</tr>
</tbody>
</table>
Would be good if..........

- Pulpakanal (Zahnmark)
- N. alveolaris inf. (Unterkiefernerv)
- Zystischer Tumor
Diagnosis of the degree of TNI injury based on patient presentation is NOT possible!
What do we treat?

Pain or discomfort?

Functional problems?

Psychological impact...can't cope!

Questions? / Expectations?

- Normal sensation will NEVER return after 3-6 months
- Will not increase risk of cancer or other pathology

Managing iatrogenic trigeminal nerve injury: a case series and review of the literature.
Managing iatrogenic trigeminal nerve injury: a case series and review of the literature


Abstract. This study describes the management of 216 patients with post-traumatic iatrogenic lingual nerve injuries (LNIs; \( n = 93 \)) and inferior alveolar nerve injuries (IANIs; \( n = 123 \)). At initial consultation, 6% IANI and 2% LNI patients had undergone significant resolution requiring no further reviews. Reassurance and counselling was adequate management for 51% IANI and 55% LNI patients. Systemic or topical medication was offered as pain relief to 5% of patients. Additional cognitive behaviour therapy (CBT) was offered to 8% of patients. Topical 5% lidocaine patches reduced pain and allodynia in 7% of IANI patients, most often used without any other form of management. A small percentage of IANI
Management tools

Counselling

- LA, Orthognathic, Fracture
- Endo or implant injuries > 30 hours
- TMS injuries older 6 months
- Reaffirm nerve injury is permanent
- Reassurance and explanation

Medical symptomatic therapy (pain or discomfort)

- Topical agents for pain
- Systemic agents for pain

Surgical exploration

- Remove implant or endo material within 24 hours
- Explore IAN injuries thro socket less than 4 weeks
- Explore LN injuries before 12 weeks
A small percentage of IANI patients (4%) received a combination of therapies involving CBT, surgery, medication and 5% lidocaine patches.
Management of affective / behavioural problems

All patients were ‘counselling’

Liaison psychiatry

Development of a tailored Cognitive behavioural therapy programme

Patient website NEW

Patient days NEW

50% Chronic pain sufferers are depressed

Wesseley S 2010
Medications

Neuralgic pain
• Oxcarbazepine
• Neurontin pregabalin
• Gabapentin

Burning chronic pain
• Nortriptyline > Amitriptyline

5% pts persisted with systemic meds
18% IANI used topical medication
Pharmacological Management of Neuropathic Pain

Background

Neuropathic pain may arise as a consequence of a lesion or disease affecting the somatosensory system.\(^1\) Neuropathic pain is estimated to afflict as much as 7–8% of the general population in Europe.\(^2,3\) Classical examples include diabetic polyneuropathies, postherpetic neuralgia, trigeminal neuralgia, central poststroke pain, and spinal cord injury pain, although traumatic/postsurgical neuropathies and painful radiculopathies represent common conditions in the general population.\(^4\)

The management of patients with chronic neuropathic pain is challenging,\(^4,8\) despite several attempts to develop a more rational therapeutic approach.\(^8,9\) Most studies have been performed in postherpetic neuralgia (PHN) and painful diabetic neuropathy (PDN). These trials mainly studied the effects of monotherapy and were placebo controlled. Outcome measures were generally restricted to a global assessment of pain by
Fig. 1. Combined number-needed-to-treat (NNT) values for various drug classes in all central and peripheral neuropathic pain conditions (not including trigeminal neuralgia, cancer-related neuropathic pain, or radiculopathies). The circle sizes indicate the relative number (given in parentheses) of patients who received active treatment drugs in trials for which dichotomous data were available. It is important to note that because studies on tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and opioids are mainly crossover trials and studies on SNRIs and gabapentin or pregabalin are mainly parallel-group design studies, a direct comparison of NNT values across drug classes cannot be made. Adapted from Finnerup et al. Abbreviations: BTX-A = botulinum toxin A; ns = absolute risk difference not significant; SNRIs = mixed serotonin-norepinephrine reuptake inhibitors.
Centrally acting agents

Levetiracetam

Topiramate
Novel peripheral strategies

Topical LA patches
• 12 patients

Botox injections

Peripheral local anaesthetic block
Check effect on local musculature- Facial nerve

Experience so far

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>TN</td>
<td>2</td>
</tr>
<tr>
<td>PTN</td>
<td>4</td>
</tr>
<tr>
<td>AO</td>
<td>2</td>
</tr>
<tr>
<td>Headache</td>
<td>21</td>
</tr>
</tbody>
</table>


Injection of botulinum toxin type A (BOTOX) into trigger zone of trigeminal neuralgia as a means to control pain.
Medical and psychological management of 74% patients
Remember

If there is NO response to anti inflammatory drugs
Consider neuropathic pain

www.kcl.ac.uk
Baffled????

Does the reaction seem disproportionate to the cause?

Psychometrics……………………………

• Liaison Psychiatry
• Clinical psychology
Surgical intervention

Why do we operate?
When do we operate?
What technique should be used?
How do we assess the outcome?
Why only surgery?
Surgery on less than 8% of patients
Why is the timing of nerve repair so paramount?

Peripheral consequences of nerve injury

Central consequences of nerve injury

Improved outcomes

- Susarla et al 2007
- Ziccardi 2007
Nerve surgery

Exploration

Decompression

Neuroma in continuity (NIC) excision and re-approximation

End neuromata EN) excision and re-approximation with minimal tension
Surgery – Management

Tell the patient of permanency of nerve injury

Adjunctive care prior to referral occurred in several patients

Surgery

3 patients had their implants removed within 30 hours
10 patients had their implants removed 3 days and 6 months

Psychological

13 patients were consulted and reassured
Cognitive behavioural therapy was of benefit to 7 patients

Medications including

Tricyclic antidepressants
Pregabalin
Topical 5% lidocaine patches (Versatis)
Benzoncaine topical LA cream
LA with botox injections.

<table>
<thead>
<tr>
<th>Adjunctive care</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>16</td>
</tr>
<tr>
<td>Medication immediate post op</td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>2</td>
</tr>
<tr>
<td>Steroids</td>
<td>1</td>
</tr>
<tr>
<td>Removed implant after 4 days</td>
<td>6</td>
</tr>
<tr>
<td>Removed within 3 days</td>
<td>3</td>
</tr>
<tr>
<td>Specialists seen</td>
<td>1</td>
</tr>
<tr>
<td>Neurologist</td>
<td>1</td>
</tr>
<tr>
<td>Pain specialist</td>
<td>1</td>
</tr>
<tr>
<td>Specialist GDP</td>
<td>1</td>
</tr>
</tbody>
</table>

Management procedure:
Reassurance with explanation of symptoms alone 13
Reassurance and TCA 2
Reassurance and CBT 1
Reassurance and Versatis 2
Reassurance, TCA and CBT 1
Reassurance, TCA, CBT and LP 4
CBT 1
CBT, TCA, PG and Botox 1
LP and TCA 1
Versatis and TCA 2
Versatis and TCA 1
Lingual nerve

- Retromolar approach
Surgical procedures for LNI patients

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exploration and decompression</td>
<td>11</td>
</tr>
<tr>
<td>Release of scar tissue, excision of neuroma and re-anastomosis of the nerve</td>
<td>7</td>
</tr>
<tr>
<td>Nerve appears normal</td>
<td>1</td>
</tr>
</tbody>
</table>
# Novel Management of nerve injuries

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Duration</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known/suspected nerve section</td>
<td></td>
<td>Immediate exploration</td>
</tr>
<tr>
<td>TMS IANI – retained roots</td>
<td>&lt;30 hours</td>
<td>Immediate exploration</td>
</tr>
<tr>
<td>Implant</td>
<td>&lt;30 hours</td>
<td>Remove implant</td>
</tr>
<tr>
<td>Endodontic</td>
<td>&lt;30 hours</td>
<td>Remove tooth / overfill</td>
</tr>
<tr>
<td>Implant / Endodontic</td>
<td>&gt;30 hours</td>
<td>Treat therapeutically</td>
</tr>
<tr>
<td>TMS IANI large neuropathic area, pain and disability</td>
<td>&lt;3 months</td>
<td>Consider exploration</td>
</tr>
<tr>
<td>TMS LNI – large neuropathic area, pain and disability</td>
<td>&lt;3 months</td>
<td>Consider exploration</td>
</tr>
<tr>
<td>TMS IANI –</td>
<td>&gt;6 month</td>
<td>Treat therapeutically</td>
</tr>
<tr>
<td>TMS LNI–</td>
<td>&gt;6 month</td>
<td>Treat therapeutically</td>
</tr>
<tr>
<td>LA, fracture, orthognathic, other surgery</td>
<td></td>
<td>Treat therapeutically</td>
</tr>
</tbody>
</table>
No sit and wait policy!

Urgent intervention is required for;

• Suspected nerve injury
• IANIs
  • Third molar surgery
  • Implant
  • Endo
Post op problems
Homecheck

Always check on your patient after LA wears off for M3Ms /Implants

Extreme post op pain may be an indication of nerve injury

You have 30 hours to manage implant or endo nerve injuries

Report
Key messages... changing practice

We cannot ‘fix’ patients with these nerve injuries

We can prevent most of these nerve injuries

We can improve informed consent - Hyperaesthesia and pain are more likely than numbness

Lingual nerve / inferior alveolar nerve injuries are NOT mainly temporary? DO NOT SIT AND WAIT for resolution

Home check will facilitate timely urgent intervention
Reporting complications

CQC

Dentists or patients are reminded of the requirements to notify the Care Quality Commission of injuries to the nervous system that last longer than 21 days. These can be reported to the Commission using the form which can be found at www.cqc.org.uk under “Organisations we regulate”.

www.kcl.ac.uk
Thank you

Zehra Yilmaz

Launch of
Trigeminal FOUNDATION
Nerve injuries Website

trigeminalnerveinjuries.org

Wednesday July 11th
5.45 – 7.30 pm
Gordon Museum

http://trigeminalnerve.org.uk/

“to provide excellence in education, management and prevention of trigeminal nerve injuries related to dental surgery”
Any Questions?

TRIGEMINAL FOUNDATION
NERVE INJURIES
Helping to prevent, educate and mitigate

Launch of
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“A to provide excellence in
education, management
and prevention of
trigeminal nerve injuries
related to dental surgery”

Trigeminalnerve.org.uk
Where do drugs work?

- NSAIDS peripheral block – cyclooxygenase
- Paracetamol: ? central block – cyclooxygenase
- Opiates central block of NMDA receptors
- Local analgesia blocks all sodium nerve channels (motor and sensory)
- Sedation blocks central GABA receptor pathway = anxiolytic
Acute dental pain

Pre or post surgical

GOLD STANDARD

- Paracetamol  500mgs – 1g  QDS PO
- Ibuprofen  400-800mgs  QDS PO
- Take together SYNERGISM

Pharmacologic rationale for the treatment of acute pain.
Hargreaves KM, Troullos ES, Dionne RA
### Efficacy of analgesics expressed as need to treat (ntt)

<table>
<thead>
<tr>
<th>Medicine</th>
<th>ntt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diclofenac</td>
<td>2.3</td>
</tr>
<tr>
<td>Ibuprofen 400</td>
<td>2.6</td>
</tr>
<tr>
<td>Morphine</td>
<td>3.3</td>
</tr>
<tr>
<td>Ibuprofen 200</td>
<td>4.4</td>
</tr>
<tr>
<td>Paracetamol + dextropropoxyphene</td>
<td>3.3</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>4.8</td>
</tr>
<tr>
<td>Tramadol</td>
<td>5.2</td>
</tr>
<tr>
<td>Aspirin codeine</td>
<td>5.6</td>
</tr>
<tr>
<td>Dextropropoxyphene</td>
<td>7.7</td>
</tr>
<tr>
<td>Tramadol</td>
<td>8.3</td>
</tr>
<tr>
<td>Dihydrocodeine</td>
<td>9.7</td>
</tr>
<tr>
<td>Codeine</td>
<td>10.7</td>
</tr>
</tbody>
</table>
Chronic OFP

LA block

• If pain does not go then pain must be centrally mediated (not peripheral)

Conventional analgesics do not work
Chronic pain medication

Local Analgesics
- Topical / systemic

Antidepressants
- Selective Serotonin Reuptake Inhibitors (SSRI)
- Selective Norepinephrine Reuptake Inhibitors (SNRI)
- Monoamine Oxidase Inhibitors (MAOI)
- Noradrenergic and Specific Serotonin Antidepressants

Antiepileptics
- Tegretol – carbamazepine
- Oxcarbazepine
- Lacosamide
- Alpha 2 delta ligands - Pregabalin / Gabapentin

NMDA antagonists
- Opioids / opiates / ketamine

Others
- Capsaicin
- Alpha lipoic acid 600mg/day
Medications for Chronic pain

Neuralgic pain
- Oxcarbazepine
- Neurontin pregabalin
- Gabapentin

Burning chronic pain
- Nortriptyline > Amitriptyline

5% pts persisted with systemic meds
18% IANI used topical medication
Chronic pain management

PAIN

PERIPHERAL Altered ion channel expression and activity

SPINAL calcium channel activity

WIND UP

5HT

CENTRAL Decreased descending fascilitation inhibition

TCA / SNRI Duloxetine Venlafaxin

Clonidine NMDA antagonist

Lidocaine Lacosamide Carbamazepine

Gabapentin Pregabalin

TCA / SNRI Duloxetine Venlafaxin

Clonidine NMDA antagonist

www.kcl.ac.uk
Lidocaine

Na Channel blocker
Diagnostic blocks
Topical patches
  • Versatis 5% Lidocaine
IV for severe breakthrough
Conventional surgical management

CUT SLASH FREEZE or BURN!
Conventional surgical management

CUT SLASH FREEZE or BURN!
Non pharmacological methods
Psychological
Interpersonal strategies

• Communication
  • reassurance
  • sympathy
  • understanding
• Caring
• Comfort
• Consideration
• Clinical Competence
Psychological factors in pain

20-50% of patients respond to Placebo!

Increased anxiety / neuroticism / psychiatric morbidity
  - All predictive of persistent pain post operatively

Cognitive behavioural therapy decreases pain in burns patients

Increased use of OTC NSAIDs for headache with associated stress and poor physical fitness
Anxiolysis
Non pharmacological
  • Interpersonal skills - reassurance
  • Hypnosis
  • Acupuncture
  • TENS

Pharmacological anti-anxiety treatments
  • Single drug sedation (conscious)
  • Multiple drug sedation (deep)
  • Anaesthesia
Alternative analgesic therapies

Homeopathic
  - Arnica reduces bruising and swelling

Hypnotherapy
  - self hypnosis
  - induced hypnosis

Counselling
  - Chronic pain patients may need counselling to improve their coping strategies

CBT

Biofeedback
  - training in changing function to reduce pain

Tens shown to reduce the discomfort of ID blocks
Management – Alternative
Self empowerment Counselling

- Laughter
- Distraction
- Stress management – relaxation
- Exercise
- Social support
- Hypnosis
- Acupuncture
- Aromatherapy
- Pets
- Hobbies
The future

Diagnose and Measure pain with fMRI

Neural crest stem cells
  • Nerves
  • Immune cells
Manage the Pain Process

Bio psycho social Model

Nociception
Sensation
Behaviour
Suffering

Social / cultural
Age, gender, race, peer support, familial expectation

Cognitive / conceptual
Memories past experience, secondary gain, threat perception

Emotional / psychological
Depression, anxiety, stress, fear, anger
Manage the Pain Process

Nociception

Sensation

Behaviour

Suffering

LA, Spinal Block
Membrane stabilising drug

Cognitive / conceptual
Memories past experience, secondary gain, threat perception

Social / cultural
Age, gender, race, peer support, familial expectation

Emotional / psychological
Depression, anxiety, stress, fear, anger

Sedation, CBT
CBT
Management

• Inflammatory or neuropathic pain?
• Patient factors
• Environment

• Investigations
  • Psychological
  • Medical
  • Surgery
  • Combination
Management tools

Counselling
• Reassurance and explanation

Medical symptomatic therapy (pain or discomfort)
• Topical agents for pain
• Systemic agents for pain

Surgical intervention
• LA diagnostic / therapeutic block Greater occipital nerve block
• Cryo/glycol/thermocoag/gamma knife
• MVD microvascular decompression
Management of affective / behavioural problems

- All patients were ‘counselling’
- Liaison psychiatry
- Development of a tailored Cognitive behaviour therapy programme
- Patient website NEW
- Patient days NEW
- 50% Chronic pain sufferers are depressed Wesseley S 2010
- CBT was offered to 8% of patients
Management of affective or behavioural problems

Liaison psychiatry

Cognitive behavioural therapy

Findings

PTSD

Victim of abuse

50% Chronic pain sufferers are depressed

Wesseley S 2010 156

Tara Renton Premier symposium  2010
Chronic pain management

- Peripheral: Altered ion channel expression and activity
- Spinal: Calcium channel activity
- Central: Decreased descending facilitation/inhibition

Drugs:
- Lidocaine
- Lacosamide
- Carbamazepine
- Gabapentin
- Pregabalin
- TCA / SNRI (Duloxetine, Venlafaxin)
- NMDA antagonist (Clonidine)
- 5HT inhibitors (Duloxetine, Venlafaxin)

Wind Up (Pain)
Drugs for chronic pain

As of June 2005 only five drugs had been approved by the Food and Drug Administration to treat neuropathic pain:

-- gabapentin, marketed by Pfizer as Neurontin, the gold-standard drug used in over 50 percent of cases and originally developed to treat depression;

-- lidocaine, marketed by Endo Pharmaceuticals as Lidoderm, a local anesthetic;

-- carbamazepine, originally marketed by Novartis as Tegretol, an anti-convulsant;

-- duloxetine, an anti-depressant marketed as Cymbalta by Eli Lilly, and

-- pregabalin, also marketed by Pfizer as Lyrica, another anti-depressant. Neurontin recently lost its patent protection in the United States, and a number of generic versions are now available.

Most of these drugs need to be taken four times a day, opening a space for a pharmaceutical that requires less from the patient.
Chronic pain medication

Local Analgesics
- Topical / systemic

Antidepressants
- Selective Serotonin Reuptake Inhibitors (SSRI)
- Selective Norepinephrine Reuptake Inhibitors (SNRI)
- Monoamine Oxidase Inhibitors (MAOI)
- Noradrenergic and Specific Serotonin Antidepressants (NaSSA)

Antiepileptics
- Tegretol – carbemazepine
- Oxcarbazepine
- Lacosamide
- Alpha 2 delta ligands - Pregabalin / Gabapentin

NMDA antagonists
- Opioids / opiates / ketamine

Others
- Capsaicin
- Alpha lipoic acid 600mg/day
Antidepressants

- TCAs
- Selective Serotonin Reuptake Inhibitors (SSRI)
- Selective Norepinephrine Reuptake Inhibitors (SNRI)
- Monoamine Oxidase Inhibitors (MAOI)
- Noradrenergic and Specific Serotonin Antidepressants (NaSSA)
Tricyclic Antidepressants

• Tricyclic antidepressants were introduced in the late 1950s and early 1960s.
• They block the reuptake of norepinephrine by the presynaptic cell, thereby increasing its concentration in the synaptic cleft.

• Tricyclic antidepressants include:
  – nortryptiline (PamelorTM)
  – maprotiline (LudiomilTM)
  – desipramine (NorpramineTM)
  – amitryptiline (ElavilTM)
  – clomipramine (AnafranilTM)
  – imipramine (TrofranilTM)

• Side effects
  • affect heart rate and blood pressure
  • postural hypotension
  • Tachycardia (rapid heart rate)
  • dry mouth, urinary retention and blurry vision
  • Physicians must monitor the patient closely for toxic side effects.
  • Tricyclic antidepressants are nonselective inhibitors of norepinephrine reuptake because their chemical structures look like norepinephrine.
Selective Serotonin Reuptake Inhibitors (SSRI)

introduced in the mid-1980s. SSRIs block the transport of serotonin back into the presynaptic cell, increasing stimulation of the postsynaptic cells.

SSRIs include the following drugs:

• **fluoxetine** (Prozac™)
• **paroxetine** (Paxil™)
• **sertraline** (Zoloft™)
• **fluvoxamine** (Luvox™)
• **citalopram** (Celexa™)
• **escitalopram** (Lexapro™)

some patients may experience more side effects with one type of SSRI than with another. Most of the time, patients have to take antidepressants more than once per day.

*fluoxetine* has a longer half-life -- it remains in the body longer, so patients can usually take it once a day. This lowers the chance of missing a dose. At high doses, paroxetine and sertraline will interfere with dopamine and serotonin neurotransmission.
Serotonin-Norepinephrine Reuptake Inhibitors (SNRI) introduced in the mid-1990s block the reuptake of both serotonin and norepinephrine by binding to the transporters of these neurotransmitters on the presynaptic cell. SNRIs include:

- bupropion (Wellbutrin™) -- blocks dopamine and norepinephrine reuptake as well
- duloxetine (Cymbalta™)
- venlafaxine (Effexor™)

Side effects of these drugs are similar to, but less than, those of SSRIs. Bupropion and duloxetine, in particular, have minimal side effects in the areas of sexual dysfunction and weight gain.
Monoamine Oxidase Inhibitors (MAOI)

- An enzyme called monoamine oxidase can degrade serotonin and norepinephrine in the synaptic cleft and presynaptic cell. MAOIs block this degradation, increasing the concentration of the neurotransmitters.
- MAOIs include:
  - phenelzine (Nardil™)
  - tranylcypromine (Parnate™)
  - selegiline (Eldepryl™)
  - isocarboxazid (Marplan™)
  - moclobemide (Manerix™)
- can interfere with norepinephrine - cardiovascular side effects.
- patients must limit their consumption of foods containing tyramine because the drugs interact with tyramine to cause hypertension.
- Tyramine can be found in foods like soy sauce, sauerkraut, chicken and beef livers, aged cheese, sausage, cured meat and fish, yogurt, raisins, figs and sour cream. Patients also have to refrain from consuming alcohol when on these antidepressants. Because of these interactions, doctors do not prescribe this class of antidepressants as frequently as others.