Low Dose Naltrexone

Novel uses for a licenced medication

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New Orleans, August 2013
Doctor Phil Boyle, MD

Dr. Boyle has listed no financial interest/arrangement that would be considered a conflict of interest.
Publications

- PubMed search “Low Dose Naltrexone” – 73 results
  - Pain Relief
  - Opioid, Alcohol and smoking cessation
  - Fibromyalgia
  - Crohn’s – Adults and children
  - Systemic Sclerosis
  - Cancer Treatment
  - Multiple sclerosis
Naltrexone Hydrochloride – Nalorex

• Growing number of novel uses for this licenced drug
• Nothing published on “Low dose Naltrexone” for Infertility, Miscarriage, PMS or Pregnancy
• But……High dose naltrexone….There is

http://www.medicines.ie/medicine/1664/SPC/Nalorex/
Naltrexone Hydrochloride – Nalorex

This is a licenced drug

- 50mg – 150mg per dose
- First synthesised in 1960s
- Licenced USA 1985 – Ireland 1991
- Adjunctive treatment of opioid dependence…and now alcohol dependence (unlicenced)
- Competitive inhibition of opioid receptors in both the central and peripheral nervous system
Special warnings and precautions for use

- Adverse reaction with opioids – severe – ensure no opioid use
- Confirm normal kidney and liver function
- Some elderly patients on 300mg naltrexone develop abnormal liver function tests
- No evidence of toxicity in volunteers receiving 800 mg/day for seven days
- Prolonged use at 50mg is acceptable……duration of treatment is not limited
Quantity matters.....

One glass of wine
Quantity matters.....

One glass of wine

One glass of wine
Naltrexone Hydrochloride – Nalorex

Clinical experience using low dose naltrexone 4.5mg since 2004

- Have not seen abnormal liver function
- It is not necessary to monitor liver function with low dose naltrexone

- BUT – never mix it with opioids – vomiting for hours – severe!
Naltrexone Hydrochloride – Nalorex

Animal studies do not suggest a teratogenic effect, but there is no experience of use during human pregnancy. The drug should only be used in pregnancy or lactation if considered essential by the physician.

Naltrexone has few, if any, intrinsic actions besides its opioid blocking properties.
Naltrexone Hydrochloride – Nalorex

Absorption – peak levels after 1 hour

Half Life of 4 hours

The duration of action of a drug is known as its half life. This is the period of time required for the concentration or amount of drug in the body to be reduced by one-half.
Naltrexone, Infertility

PubMed search – 10 publications

We will look at 4 interesting papers........
Steroids 2012

Medical management of metabolic dysfunction in PCOS.
“Naltrexone reduces appetite and modulates insulin release; its use in PCOS may reduce hyperinsulinemia.”

Duleba AJ. Reproductive Endocrinology and Infertility, Univ. of California


Fulghesu AM et al. Sacred Heart University, Rome, Italy - 2001

Naltrexone 50mg with pulsatile GnRH co-treatment is able to improve the ovarian responsiveness to ovulation induction in obese PCOS patients when compared to pulsatile GnRH alone.

This action seems to be related to a decrease of insulin secretion.

Successful induction of ovulation in normogonadotrophic clomiphene resistant anovulatory women by combined naltrexone and clomiphene citrate treatment.

Roozenburg BJ, van Dessel HJ, Evers JL, Bots RS.

- 22 patients with clomiphene resistant normogonadotrophic anovulation treated with naltrexone alone or in combination with clomid.
- 19 patients ovulation and resumption of a regular menstrual cycle
- 12 out of 19 a singleton pregnancy was observed…..2 of these miscarried

http://humrep.oxfordjournals.org/content/12/8/1720.full.pdf+html
All women resistant to clomiphene 150mg daily x 5 days – for 2 cycles

Treated with naltrexone 25 mg twice daily

Goal - complete opioid blockade – to treat hypothalamic inhibition of GNRH from excessively high endorphins

18 required clomiphene 100mg daily for 5 days

Continued treatment for 6 cycles
Treatment with naltrexone in hypothalamic ovarian failure: induction of ovulation and pregnancy.

Wildt L, Leyendecker G, Sir-Petermann T, Waibel-Treber S.

University of Erlangen, Germany

66 women

• various grades of hypothalamic ovarian failure
• Normalisation of cycle in 49 women – 18 pregnancies
High Dose Naltrexone

- This appears to be a different mechanism of action compared to LOW DOSE NALTREXONE……..worth considering for excessive opioid production (Endorphins, Enkephalins……)
  - Clomiphene resistant
  - PCOD
  - Obese and very thin – extremes of weight
  - Highly stressed
Naltrexone, Infertility

Possible Mechanisms of action of High Dose Naltrexone

• Reduces insulin resistance
• Improves GNRH pulse frequency
  • Possibly by altering opioids where there is “an inappropriate increase in opioid tone”
Naltrexone, Pregnancy

PubMed search – 138 Publications

For doses up to 150mg Naltrexone has been proven safe for most adults except pregnant or nursing women…..and probably those with acute hepatitis;
Naltrexone, PMS

PubMed search – 1 publication

Clinical trial of naltrexone in premenstrual syndrome.
Chuong CJ, Coulam CB, Bergstralh EJ, O'Fallon WM, Steinmetz GI.

Department of Obstetrics and Gynecology, Mayo Clinic, Rochester, Minnesota.
Figure 29-8: Plasma $\beta$-endorphin changes (mean $\pm$ SE) in the perimenstrual period in PMS patients (solid line) and controls (dashed line). *$p<.05$ between groups (From: Facchinetti F, Martignoni E, Petraglia F, Sances MG, Nappi G, Genazzani AR: Premenstrual Fall of $\beta$-endorphin in Patients with Premenstrual Syndrome. Fertil Steril 47:570-573, 1987).
Naltrexone, PMS

20 women - double-blind, placebo-controlled, crossover study
Naltrexone 50mg – days 9-18 of cycle – to test inhibition of opiate withdrawal
Menstrual Distress Questionnaire ($100 for 50 copies)
The mean scores dropped 28 points on naltrexone (P = .016).
Naltrexone alleviates many PMS symptoms and may be an effective treatment for this syndrome……but Nausea, decreased appetite and dizziness
Naltrexone – opioid receptor antagonist

<table>
<thead>
<tr>
<th>Endogenous Opioid Peptides</th>
<th>Receptors CNS and PNS</th>
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</thead>
<tbody>
<tr>
<td>• Endorphins</td>
<td>• Epsilon (Endorphins)</td>
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<tr>
<td>• Enkephalins</td>
<td>• Delta (Enkephalins)</td>
</tr>
<tr>
<td>• Dynorphins</td>
<td>• Kappa (Dynorphins)</td>
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</tbody>
</table>

Naltrexone blocks all of the receptors

NaPro Textbook Ch 41p550, Hilgers TW.
Naltrexone – mechanism of action
Naltrexone – antagonism and rebound

Consider Letrozole –

1. Ovulation Induction and subsequent increase in oestrogen production
   • Letrozole – 20mg day 3 *one day of cycle* – rebound increase in oestrogen

2. Suppression of oestrogen production through aromatase inhibition
   • Letrozole 2.5mg *every day continuously* - a drop in oestrogen levels

*The same medication has a profoundly different effect depending on how it is given*
Naltrexone – antagonism and rebound

Consider Naltrexone –

1. Hoped to increase in endorphin production
   • Naltrexone 25mg bd for 10 days- (day 9-18) – rebound increase in beta endorphins

2. Suppression of endorphin production through
   • Naltrexone 25mg bd every day continuously - a drop in endorphin levels

*The same medication has a profoundly different effect depending on how it is given*
Naltrexone, PMS

Now Consider Low Dose Naltrexone 3-4.5mg nightly

- Naltrexone has a daily circadian rhythm
- Briefly and temporarily blocking endorphin receptors at night triggers a rebound stimulation of endorphins the following day
  - x 3-4 fold increase in Beta Endorphin Levels – B. Bihari
  - x 12-15 fold increase in enkephalin levels – J. Smith
- Vastly superior to naltrexone 25mg BD for 10 days (9-18) of cycle
Naltrexone, PMS

The International Institute for Restorative Reproductive Medicine
www.iirrm.org – We intend to do a clinical trial with LDN 3-4.5mg nightly
Interested doctors – please contact us!

• Clinical experience in treating PMS is 80% response
• Many say – I have my life back – I am me again!!
Low Dose Naltrexone

New uses of an old drug see www.lowdosenaltrexone.org

A proposed different mechanism of action

Naltrexone temporarily and briefly blocks opioid receptors, triggering a rebound increase in endogenous opioid production

Improving endogenous endorphins has multiple beneficial effects for endorphin deficient patients
Current concepts of beta-endorphin physiology in female reproductive dysfunction

Elevated or high levels of beta-endorphin have been associated with exercise-associated amenorrhea, stress-associated amenorrhea, and polycystic ovarian syndrome. .....(High Dose Naltrexone 25mg BD) PPVI, Omaha.

Depressed or low levels of beta-endorphin have been associated with PMS and menopause, (Endometriosis – Hilgers) .....(Low Dose Naltrexone 3-4.5mg nightly)

Galway, Ireland

Fertility and Sterility 1990. Seifer DB et al, Yale University School of Medicine

Figure 41-18: Plasma beta-endorphin levels during the luteal phase (Peak +7) in women of normal fertility versus those with infertility due to endometriosis ($p<.01$) (From: Pope Paul VI Institute research, 2004).
### Table 43-7: Incidence of Endometriosis in Patients with PCOD\(^1\) (N=55)

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>%</th>
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<tbody>
<tr>
<td>With endometriosis</td>
<td>28</td>
<td>50.9</td>
</tr>
<tr>
<td>No endometriosis</td>
<td>27</td>
<td>49.1</td>
</tr>
</tbody>
</table>

1. As determined at the time of laparoscopy.

Current concepts of beta-endorphin physiology in female reproductive dysfunction

Not a case of .....Either /Or

But rather Both / And

We should consider Naltrexone in both low and high dose
Endorphin Stimulation

• Immune modifying effect
  • Intestinal
  • Local effects
  • Central effects
• Mood enhancement
• Increased energy levels
Endorphin Stimulation

• **Immune modifying effect**
  - **Local effects** – Reduces pro-inflammatory cytokines Interleukin (2,6,12), TNF (Tumor Necrosis Factor) alpha, Gamma Interferon
  - Cause inflammation from wbc and macrophages
    Naltrexone influences mu, kappa and delta receptors locally
  - **Central effect** increases endogenous enkephalins (Metenkephalin) centrally to heal the bowel.

**Professor Jill Smith** – *Am J. Gastro 2007*. 
Endoscopic Improvement in Crohn’s Colitis with Naltrexone

**Figure A**: Shown is the rectum of a subject with active Crohn’s Disease before starting therapy with naltrexone 4.5 mg/day. The mucosa is ulcerated, edematous, and inflamed.

**Figure B**: Shows the same area of the rectum in the same patient four weeks after naltrexone therapy. The lining is now healed, ulcers resolved, and the mucosa is healthy.

Effect of LDN 4.5mg a day – treated 17 patients

- 89% improvement in Crohns Disease
- 67% in remission

- 70% -previous failed TNF alpha inhibitor – Infliximab (Remicade)
Effect of LDN 4.5mg a day – treated 17 patients

• 89% improvement in Crohn’s Disease
• 67% in remission
• 70% - previous failed TNF alpha inhibitor treatment –
• Infliximab (Remicade) $ 5,000+ per infusion - repeatedly for Crohn’s.
• LDN is $ 30-50 per month!
Probably Placebo!

You need a Randomized placebo-controlled trial.
Naltrexone promotes mucosal healing in active Crohn's disease: 2011

Randomized placebo-controlled trial.

Digestive Diseases and sciences 2011

Smith JP, Bingaman SI, Ruggiero F, Mauger DT, Mukherjee A, McGovern CO, Zagon IS.

Department of Medicine, The Pennsylvania State University, College of Medicine, GI Medicine H-045, 500 University Drive, Hershey, PA 17033, USA.

jsmith2@psu.edu
Effect of LDN 4.5mg a day – treated 40 patients for 12 weeks

- 88% Clinical response rate compared to 40% in Placebo group (P = 0.009)
- 78% endoscopic response compared to 28% in placebo group (P=0.008)
- 33% remission compared to 6% remission in placebo group

- Naltrexone improves clinical and inflammatory activity of subjects with moderate to severe Crohn's disease compared to placebo-treated controls.
Naltrexone promotes mucosal healing in active Crohn's disease: 2011

Randomized placebo-controlled trial.

Digestive Diseases and sciences 2011  Impact factor 2012  2.260
American Journal of Gastroenterology - Impact factor 2012  7.553

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3381945/
Probably Advertising Revenue

You need an expensive patented drug to publish your data!
Editor NEJM Forced to Resign in Dispute with the Medical Journal

July 27, 1999

Dr. Kassirer declined to provide specifics of the dispute beyond saying it involved sharp differences in "administrative and publishing issues."

……other editors said the dispute reflects tensions generated as the society seeks to generate more revenues to expand its influence in an increasingly competitive and political world of health care.
Clinical experience with LDN

- Started to prescribe it in 2004
Low Dose Naltrexone
LDN – plays an important part

• “NaProTechnology - A Multi-factorial approach to the chronic problem of Infertility” - P Boyle, J Stanford


• Paper from Kaunas, Lithuania June 2011
## Possible Diagnoses from NaProTechnology Evaluation

<table>
<thead>
<tr>
<th>Hormonal</th>
<th>Ultrasound</th>
<th>Surgical</th>
<th>Other</th>
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<tbody>
<tr>
<td>Low Progesterone</td>
<td>Immature follicle</td>
<td>Endometriosis</td>
<td>Limited (hostile) Mucus</td>
</tr>
<tr>
<td>Low Oestradiol</td>
<td>Partial rupture</td>
<td>Pelvic Adhesions</td>
<td>Adrenal Fatigue</td>
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<tr>
<td>Poor Follicular Function</td>
<td>Luteinised unruptured follicle</td>
<td>Blocked Fallopian Tubes</td>
<td>Chronic Endometritis</td>
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<tr>
<td>Corpus Luteum Insufficiency</td>
<td>Delayed Rupture</td>
<td>Hydrosalpinx</td>
<td>Endorphin Deficiency</td>
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<td>Polycystic Ovaries</td>
<td>Afollicularism</td>
<td>Fibroid</td>
<td>Food Intolerance</td>
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<tr>
<td>Reduced ovarian reserve</td>
<td>Absent Cumulus Oopherous</td>
<td>Polyp</td>
<td>Nutritional Deficiency</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Uterine Septum</td>
<td>Immune dysfunction</td>
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Fig. 3
LDN – plays an important part
Low Dose Naltrexone

Clinical Experience since 2004

• LDN is used to treat Clinical Endorphin Deficiency
• About 50% of fertility patients
• Safe to continue during pregnancy and breastfeeding
Clinical Endorphin Deficiency

1. PMS
2. Polycystic ovaries or Endometriosis
3. TEBB
4. Fatigue 2 or more of these
5. Low Mood
6. Anxiety
7. Sleep
8. Family History of Autoimmunity
Clinical Endorphin Deficiency

- Available from brochure
Side Effects

1. Vivid Dreams
2. Sleep Disturbance
3. Nausea for about 2 weeks
4. Headache
5. Dry Mouth over 95% acceptable
Drug Interactions

1. Morphine
2. Codeine
3. Alcohol

• Safe to combine with steroids
• Discontinue 2 days before surgery and resume after stopping pain relief
No longer an Experimental Treatment

• It is a licensed drug but at a much higher dose (50mg) for a different indication – drug addiction
• A growing number publications at LDN Website
  – MS, Crohn’s and fibromyalgia
• A proven potent immune modifying treatment through a double blinded randomized placebo controlled trial 2011
Low Dose Naltrexone

Dosage

• 3mg nightly
  or
• 4.5mg nightly
Low Dose Naltrexone

• Needs to be specially compounded as
• Fast release preparation
  – Not lactose or calcium carbonate filler
  – Preferably microcrystalline filler (avicel)
• Suppliers listed
  – www.lowdosenaltrexone.org
Clinical Experience

1. Case C – 3 previous failed IVF cycles
2. Six recurrent miscarriages
Case C

- Gravida 1 (with IVF), Para 0, 5 Years of primary infertility
- Female age 38, Male age 38
- Mild Endometriosis
- 12 previous cycles of clomid
- 3 attempts at IUI
- 3 previous failed IVF
Case C – NPT Diagnoses

• Endometriosis
• Oligoasthenozoospermia
• Clinical endorphin deficiency
• Low progesterone and oestradiol – combined poor follicle function and corpus luteum insufficiency Obvious from Chart
• Food Intolerance to eggs
Pre-menstrual Spotting with low progesterone levels
Case C – NPT Treatments

• Clinical endorphin deficiency - significant
  • Naltrexone 4.5mg nightly

• Food Intolerance to eggs
  • Change in diet
Case C – NPT Treatments

- Endometriosis
  - Laparoscopy and diathermy June 2008
- Oligoasthenozoospermia
  - CoEnzyme Q10 200mg daily
  - Tamoxifen 20mg daily
  - FertilityPlus for men
  - Lifestyle – (cigarettes, alcohol, caffeine, stress)
Case C – NPT Treatments

- Low progesterone and oestradiol – combined poor follicle function and corpus luteum insufficiency
- Clomiphene 150mg daily x 3 days, starting on day 3 of the cycle with HCG 5000 iu mid cycle to facilitate follicle rupture and HCG 2,500 iu on days 3, 5 and 7 after ovulation
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
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**Laparoscopy**

**Positive Test!**
Case C – NPT Pregnancy Treatments

- Positive pregnancy test in September 2008
- Cyclogest 400mg pv nocte until 14 weeks
- Naltrexone 4.5mg nocte until 38 weeks
Case C – NPT Pregnancy outcome

• They had a healthy baby boy by normal vaginal delivery weighing 3.400kg in June 2009, when mum was 40 years old.
Case C – repeat attempt

• Second attempt in February 2010
• Same treatment approach successfully conceived by September 2010.
• Delivered a second healthy boy at term 19th May 2011
  – Mum 42 years old.
Case C – Comments

• We continued Naltrexone throughout pregnancy in this case because the patient felt dramatically better preconception with treatment.
• It appears she had significant endorphin deficiency which needed ongoing treatment.
• Over 200 pregnancies with naltrexone.
Case 2

• 6 Recurrent Miscarriages
G.C. - 6 Miscarriages

- Presented Feb 2005
- Female 33yrs.  Male 40yrs.
- G6 SA6 from Oct 02 – Jan 05
  - Miscarriage at 5 to 9 weeks each time
G.C. - 6 Miscarriages

• Dx:
  • Balanced Translocation Ch 7 and 18
  • 30% miscarriage risk every time
  • 5% risk abnormal baby

• Additional Dx:
  • Uterine Fibroid – 2 x 3cm anterior fibroid
G.C. - 6 Miscarriages

- Normal clotting
- Normal day 21 progesterone
- Unexplained why 6 miscarriages?
<table>
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<tr>
<th>Date</th>
<th>Day</th>
<th>Time</th>
<th>Temp</th>
<th>Cycle</th>
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<th>LH</th>
<th>LH FSH</th>
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**REMARKS:**
- Taking a supplement for my monthly cycle.
- Cycle was not normal.
- Bad PHS
- FSH? (Blood)
- Ventolin + steroid
- Dimmer

**Note:**
- P = Peak
- 1, 2, 3 = Fertile Days Following Peak
- L = Intercourse
- BE = Breast Self-Exam
G.C. - 6 Miscarriages

• **Additional Problems with NPT**
  • Moderate PMT symptoms for 7 days
  • Abnormal bleeding
  • Low Progesterone on P+7

• Query “Some immune factor?”
Rx: Pre-conception

Letrozole 2.5mg for 5 days from day 3

Luteal HCG 2,500 P+3,5,7,9
|    | 1  | 2  | 3  | 4  | 5  | 6  | 7  | 8  | 9  | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 |
|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| P  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| E  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |

P – 86.3 nmol/l
E - 677 pmol/l

P – 59.7 nmol/l
E - 676 pmol/l

P – 78.1 nmol/l
E - 950 pmol/l
P – 86.3 nmol/l
E - 677 pmol/l

P – 59.7 nmol/l
E - 676 pmol/l

P – 78.1 nmol/l
E - 950 pmol/l

+ive test
G.C. - 6 Miscarriages

• **Rx: Post-conception**
  - Gestone 200mg im twice weekly
  - HCG 5000 sc twice weekly
  - Prednisolone 5mg daily
G.C. - 6 Miscarriages

- **Rx: Post-conception**
  - Gestone 200mg im twice weekly
  - HCG 5000 sc twice weekly
  - Prednisolone 5mg daily

- Continued treatment until 35 weeks
G.W. - 6 Miscarriages

- Baby Boy @ 37 weeks gestation
- 6th March 2006
- 5lb 5oz
- NVD – with Vacuum

- Mum and Baby are well!
G.C. - 6 Miscarriages with LDN

• Returned for another attempt Aug 2006
G.W. - 6 Miscarriages

- Conceived subsequently again
  - With treatment pre-conception
  - Adjusted treatment
  - LDN (Low Dose Naltrexone)
G.W. - 6 Miscarriages

• Previous Problems
  Needed to continue treatment throughout pregnancy
  Low Progesterone persisted
  Baby smaller than avg. 5lb 5oz
G.C. - 6 Miscarriages

- Add New Immune modifying treatment
  - LDN – Low Dose Naltrexone 4.5mg nightly
G.W. - 6 Miscarriages

- Hoped
  Less need to continue progesterone treatment throughout pregnancy
  Better Progesterone levels
  Bigger baby
Cyclogest
Twice daily
Progesterone Levels in Normal Pregnancy
(N = 145)

Patient's Name:

<table>
<thead>
<tr>
<th>G</th>
<th>P</th>
<th>LMP</th>
<th>ETC</th>
<th>ETA</th>
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<td>17. 6. 05</td>
<td>3. 5. 06</td>
<td>26. 4. 06</td>
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Weeks Gestation

Pope Paul VI Institute
National Reproductive Hormone Laboratory
Cyclogest
Twice daily
G.W. - 6 Miscarriages

- Successful pregnancy
  - Female 7lb 3 oz
  - Full term
  - NVD Sept 2007
A New Low Dose Naltrexone - LDN

- **Compounding Pharmacist**
  - **Dose**
    - 1.5mg, 3.0mg or 4.5 mg fast release tablet nightly before sleeping (9pm -2am)
A New Low Dose Naltrexone - LDN

- This will give a 3 fold increase in beta endorphin levels.
A New Low Dose Naltrexone - LDN

- Improving Endorphin Levels
  - Has a “Stimulatory effect” on the immune system
  - Improves immune function
A New Low Dose Naltrexone - LDN

- Improving Endorphin Levels
  - Halts the progression of **HIV**
  - Halts the immune system when it begins to attack “SELF” (Auto-immune illness)
  - Reduces Lifetime risk of developing cancer
Low Dose Naltrexone - LDN

- Obviously fantastic treatment
  - Low toxicity – “first do no harm”
  - Inexpensive
  - Seems Effective Clinically
  - Easy to take
  - No Need for specialised Physician training
  - Few Ethical issues

- Anticipate widespread use and acceptance very quickly
Low Dose Naltrexone - LDN

- Surprise!!

- Huge resistance among many doctors to even try it out!
Doctor Resistance

- Unlicensed for Auto-immune disorders
- Experimental treatment
- Not “evidence based” medicine
- Doctors not covered by medical insurance

- Too Risky!
Infertile 36y female with R. Arth.

- Diagnosis of PCOD and 10 years of Infertility, previous success in our programme
- First episode of Acute onset of R. Arth.
  - When trying to conceive for the second time
- Diagnosed by Rheumatologist
- Resistant to NSAIDS
- Advised – Methotrexate (then cannot conceive!)
Infertile 36y female with R.Arth.

- **LDN**
  - Rapid 80% improvement in symptoms
  - No Side effects
  - Conceived after 2 cycles of LDN and other fertility treatment

- Successful pregnancy
Case Presentations

- Premenstrual Syndrome
- Severe Bipolar Disorder
- The Future......Pre-Treatment!
Endometriosis 27 yr old single female

- Dx Age 18
  - 5 laparoscopies
  - Oral Contraceptive Pill
  - Zoladex x 3 years – made pain bearable

- Deferred University studies
Endometriosis 27 yr old single female

- Depression
- Profound fatigue
- Underactive thyroid
- Anxiety
- Joint pain
- Severe PMS 7 days each cycle & brown menstrual bleeding

Hospitalised repeatedly for investigation and treatment of pain
Endometriosis 27 yr old single female

- 2007 – Started NaPro
- LDN 4.5mg nightly
- Diet – based on IgG antibody testing
Endometriosis 27 yr old single female

- It has completely changed my life
- For the first time in a long time, I can say I have a life
Endometriosis 27 yr old single female

- Depression - gone
- Profound fatigue - gone
- Underactive thyroid - on a lower dose of medication
- Anxiety - gone
- Joint pain - gone
- Severe PMS 7 days each cycle – now 2 days and mild
- brown menstrual bleeding - gone
- Pain -
Endometriosis 27 yr old single female

- A complete transformation has occurred physically, mentally and emotionally.
- For the first time in my life I feel like a complete human being and not a multitude of symptoms.
- I was helpless and a hopeless case before this treatment.
Bipolar Disorder - 28 year old female

- On Lithium for 10 years
- Previously hospitalised
- Trying to conceive and wean off lithium
- Part of treatment included LDN
- Delivered 3 years ago 2010 – Never had a relapse
- Maintained on LDN
The Future……

- 31yo G0 P0 – 1st Visit Feb 2008
- Engaged – wedding July 2008
  - +++PMS, Fatigue,
  - +FH – Sister PCOS
- Not Sexually Active
- Not trying to conceive ...yet!
The Future......

- Peak +7
  - Low Progesterone
  - Low Oestradiol

- Endorphin Deficiency
The Future......

- Treatment
  - Cyclogest Peak +3 for 10 nights
  - Naltrexone 4.5mg
The Future......

- Treatment
  - Improved Progesterone
  - PMS gone
  - Energy and mood improved

- But.....still abnormal bleeding...
The Future......

- Ultrasound May 08.............
22 + 14 + 8
The Future……

- Ultrasound  May 08
  - PCOS
  - Endometrial Polyp
- Surgical referral
  - Hysteroscopy & Polypectomy July 08
The Future......

- Healthy and Happy
  - PMS, Energy

- Normal Chart
  - Bleeding, Mucus

- Normal hormones
  - Progesterone, Oestradiol
HONEYMOON BABY!
8 Weeks and 1 day
EDD April 2009
The Future…..

Problem was identified and solved
.....even before it officially existed!

What would have happened
without LDN and
NaProTechnology?
The Future…..for LDN

It is safe….

- Doctors need to consider the mounting clinical and published evidence in favour of LDN!
- Proven Immune modifying treatment Placebo RCT.
Restore normal function
Any Questions?

Dr. Phil Boyle