LOW DOSE NALTREXONE

An Irish Family Physician's Clinical Experience

Washington DC
7th APRIL 2006

Dr. Phil Boyle MICGP. MRCGP

Resume – Dr. Phil Boyle

- Completed Family Physician training July 1997
- 2nd Feb 1998 opened private practice specialising in treatment of Infertility and miscarriage using NaProTECHNOLOGY and Fertility*Care* developed by Dr. Thomas Hilgers Omaha, NE, USA.
- To date have treated nearly 3,000 patients, many successfully after years on infertility, failed IVF or recurrent miscarriage

Resume – Dr. Phil Boyle

- Deliver public lectures on this pioneering new treatment
  - Slovakia, Italy, Portugal, Croatia, Switzerland,
  - UK, USA and Ireland
- Waiting List of 80 patients (6 months) for those seeking fertility treatment

Naltrexone

- Opioid Receptor Antagonist
  - Licensed Use
    - Morphine / Heroin Overdose
    - Alcoholism
  - Dose
    - 50mg tablet

Naltrexone

- Has been a part of NaProTECHNOLOGY infertility treatment for about 10 years

- Not used much in Ireland…until recently!

Naltrexone & NaProTECHNOLOGY

- Used to treat Endorphin Deficiency - Dr. Hilgers

- Need to confirm hormone deficiency in order to treat it
  - Beta Endorphin Blood tests
    - On Days 5,7,9 after ovulation each cycle

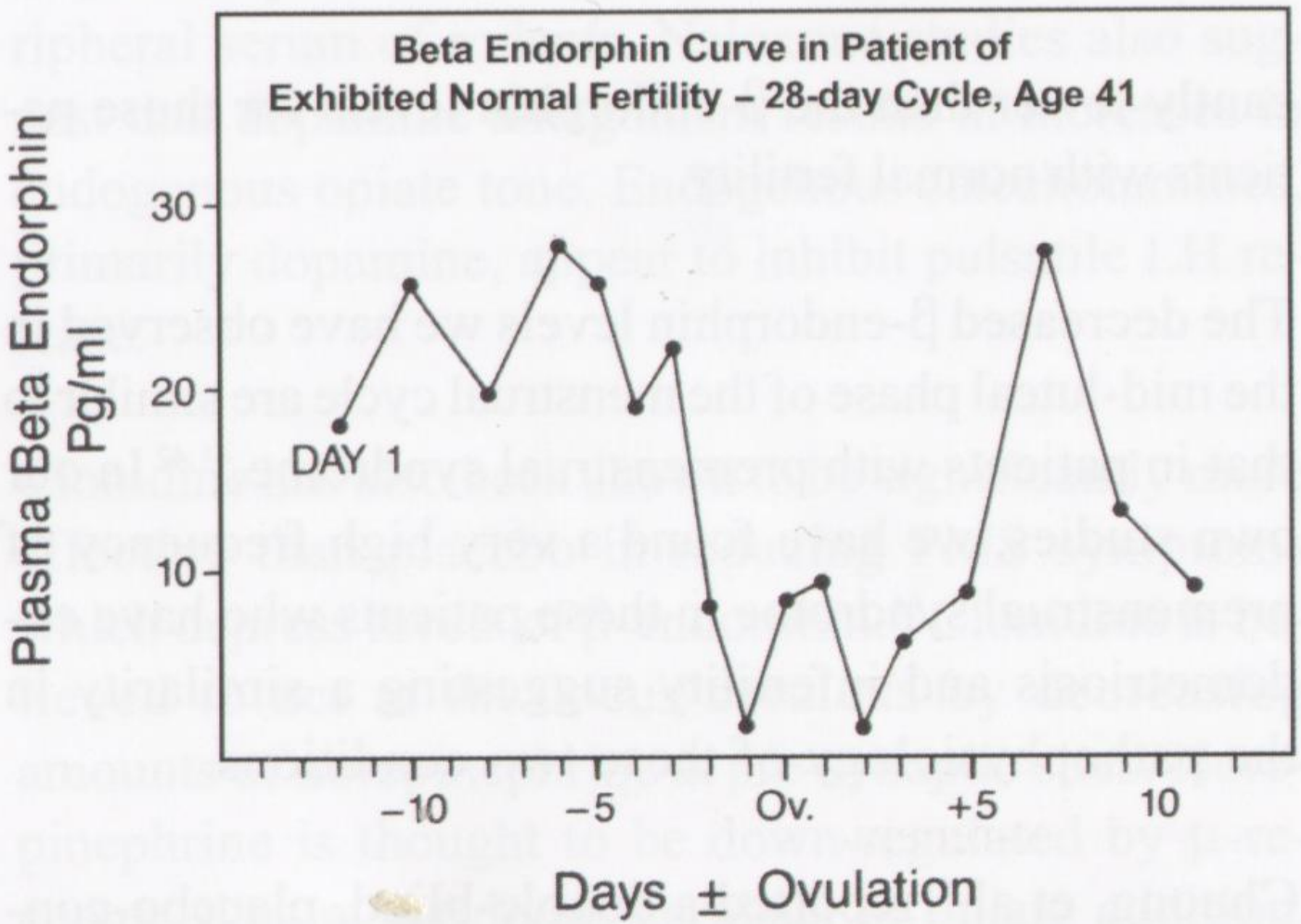


Figure 41-16: The measurement of plasma beta-endorphin levels in a patient with a 28-day cycle and exhibited normal fertility (From: Pope Paul VI Institute Research, 2004).

Naltrexone in low dose & NaPro

- Off label use
  1. Treat resistant PMS that does not respond to our usual hormonal treatment
  2. Improve fertility
     1. Used since early 1990's by Dr. Hilgers
     2. Adjunct to NaProTechnology Fertility treatment

Naltrexone in low dose & NaPro

- Compounding Pharmacist
  - Dose regieme
    - 0.25 mg 4 times daily for 10 Days
    - 0.50 mg 4 times daily for 10 Days
    - 1.00 mg 4 times daily for 10 Days
    - 2.00 mg 4 times daily for 10 Days
    - 4.00 mg 4 times daily for 10 Days
    - 8.00 mg 4 times daily for 10 Days

Table 29-19: Role of Low-dose and High-dose Naltrexone on Treatment Response to Targeted Hormone Support – Treatment of Premenstrual Syndrome (PMS)

Improvement Response	Without Naltrexone[1] n	%	With Low-dose Naltrexone[2,3] n	%
Marked	17	34.0	16	42.1
Moderate	26	52.0	12	31.6
Minimal	5	10.0	7	18.4
None	2	4.0	3	7.9
Totals	50	100.0	38	100.0

1. Includes 31 patients with progesterone support, 15 patients with HCG support, 3 patients with HCG and progesterone support and 1 patient on targeted E_2 support.
2. Includes 10 patients treated with progesterone support, 22 patients with HCG support, 5 patients on Naltrexone only and 1 patient on HCG and oral progesterone. Naltrexone maximum dose 2 mg PO QID.
3. p=.6888 (chi-square), when compared to no naltrexone.
4. Includes 10 patients on HCG support, 7 patients on progesterone support and 41 patients on naltrexone only. Dose was usually between 50 mg and 100 mg PO QD hs but ranged from 25 to 125 mg.
5. p<.0001, (chi-square) when compared to no naltrexone.
6. p=.0003, (chi-square) when compared to low-dose naltrexone.

Naltrexone

- Impossible to get Beta Endorphins measured in Ireland or UK
- Very delicate blood sample
- Perceived as a less important adjunctive treatment
- Difficult treatment to prescribe and explain to patients
- Difficult to get patient compliance

Low Dose Naltrexone - LDN

- 2002/3 – Mary Anne wanted her husband to take LDN for his MS
- "New treatment" found on Internet, recommended by a New York Neurologist
- Primary Progressive MS getting worse and not halted by interferons (unlicensed for this anyway!)

Low Dose Naltrexone - LDN

- "Primum Non Nocere"
- "First do no Harm"
- Advised - nothing to lose by trying it

Low Dose Naltrexone - LDN

- Brother In Law, Noel on LDN for MS since 2002/3
- Mary convinced that at last the progression had stopped!

Low Dose Naltrexone - LDN

- Robert (MS Patient) commenced LDN in Galway on Mary's advice in 2003
- He gave a presentation in Galway in 2003.
- "Miraculous" Case Incredible response to treatment

Robert – LDN 2003

- Chronic Progressive MS AND Rheumatoid Arthritis
- Deteriorating despite Interferons
- Very tired all the time

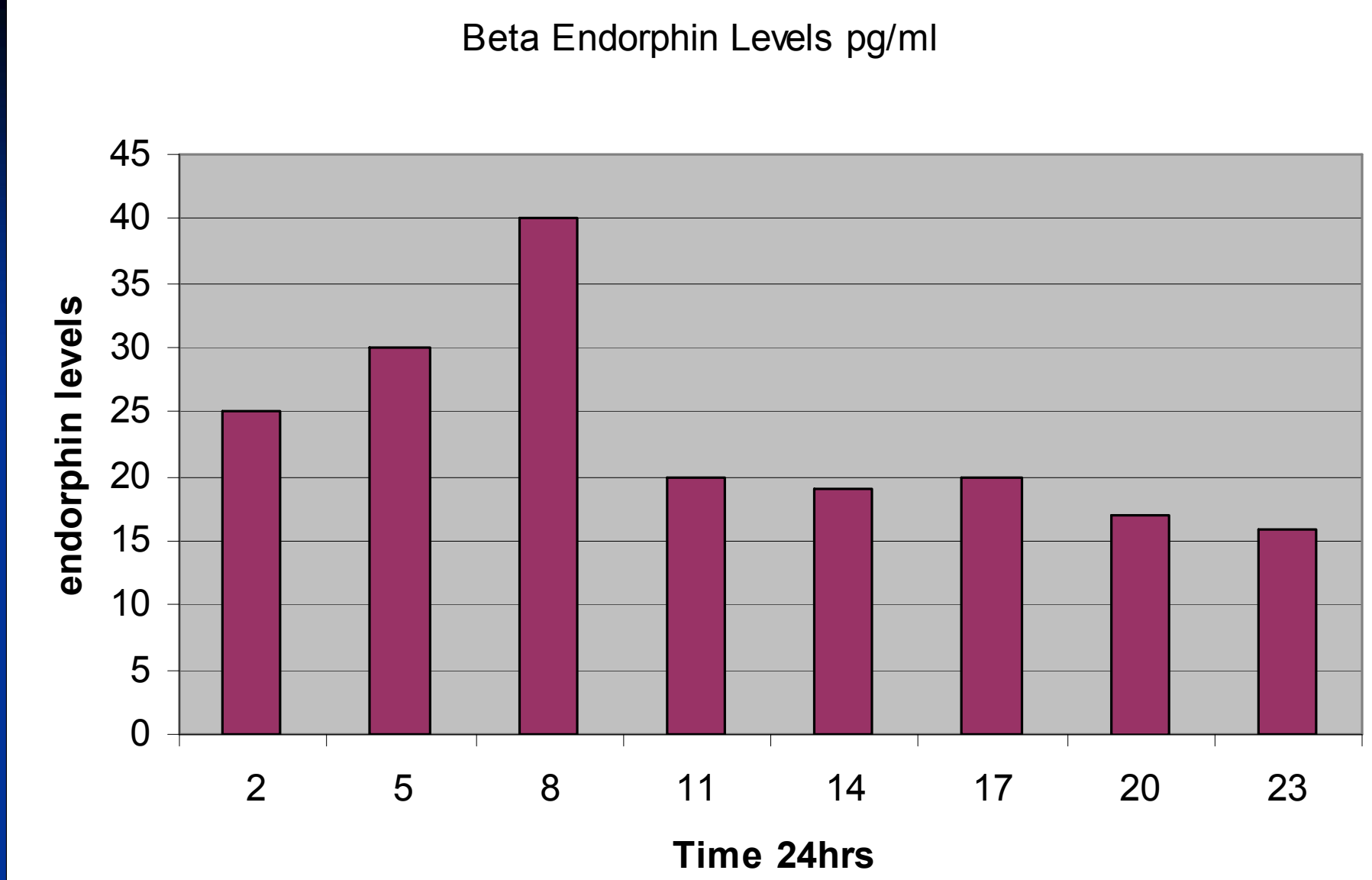
- Started LDN - DRAMATIC improvement in fatigue, joint pain
- No progression of MS since – except when LDN ran out!

A New Low Dose Naltrexone - LDN

- Unlicensed use ("off label use") Dr. Bahari
  - To treat Endorphin Deficiency
    - Improves immune function,
      - HIV
      - Auto-Immune disorders; Multiple Sclerosis, Rheumatoid Arthritis, Crohns Disease…etc
- 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.



ASSESSMENT OF BETA-ENDORPHIN AND MELATONIN CIRCADIAN RHYTHMS IN NORMOTENSIVE OBESE WOMEN OF REPRODUCTIVE AGE

Z. OSTROWSKA, et al. ENDOCRINE REGULATIONS, Vol. 31, 193 Œ 200, 1997

Low Dose Naltrexone - LDN

- A "No Brainer"
- Obviously fantastic treatment
  - Low toxicity – "first do no harm"
  - Inexpensive
  - Highly Effective
  - 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 doctors to even try it out!

Low Dose Naltrexone - LDN

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

- Too Risky!

Evidence Based Medicine

- What level of evidence is available to support a chosen treatment?
  - **Theoretical** √
  - **Clinical experience** √ **400 MS Pts, Dr. Bahari**
    √ **over 2000 pts in USA**
  - **Published trials in peer reviewed journal** X

Low Dose Naltrexone - LDN

- 5 Early Cases 2003-4
  - 1) Psoriatic arthropathy 44y male
    – No Improvement & No Harm
  - 2) Chronic Inactive Rheumatoid arthritis 55y female
    – No Improvement & No harm
  - 3) Acute early onset Rh. Arthritis 33y male
    – Dramatic Improvement
  - 4) Infertile patient with R.A 36y female, advised Methotrexate - Dramatic Improvement
  - 5) R.A. 66y male resist. to Methotrexate
    – Dramatic Improvement

3) Acute early onset Rh. Arthritis – Dramatic Improvement

- 33yrs. Married. Good health.
- Uncle with severe Rh Arth.
- Dec 03 gradual onset of finger and wrist pains – on and off for 12 months.
  - Low energy
  - Heartburn - severe
  - No Swollen joints –just pain and fatigue

3) Acute early onset Rh. Arthritis – Dramatic Improvement

- Seen by Rheumatologist
  - Blood results "Inconclusive"
- Plan
  - NSAIDS as required
- Progressive deterioration
    - Unable to play with 2 year old son after work
    - Very early to bed to rest
    - Especially tired and stiff in mornings

3) Acute early onset Rh. Arthritis – Dramatic Improvement

- LDN
  - Rapid improvement
    - No Fatigue
    - No Joint pain
    - No Heartburn
- Presently stable
  - Except when LDN runs out all symptoms return

Approached Local Rheumatologist

- Not Interested

  - **Cannot judge efficacy of new treatment with just one case**
  - **Probably Placebo**
  - **Risky experiment….if it does not work and joint damage occurs, potentially liable**

4) 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!)**

Methotrexate

- Methotrexate is classified as an anti-metabolite drug, which means it is capable of blocking the metabolism of cells
- helpful in treating certain diseases associated with abnormally rapid cell growth
  - Breast cancer, Psoriasis
- in treating rheumatoid arthritis, it seems to work by altering aspects of immune function which may play a role in causing rheumatoid arthritis.

Methotrexate

- can cause serious liver disease
- can suppress the body's immunity
- can impair fertility, decrease sperm count and cause menstrual dysfunction
- it can be toxic to the embryo and can cause fetal defects and spontaneous abortion (miscarriage)

Methotrexate

- The most frequent reactions include mouth sores, stomach upset, and low white blood counts. Methotrexate can cause severe toxicity of the liver and bone marrow, which require regular monitoring with blood testing.
- It can cause headache and drowsiness, which may resolve if the dose is lowered. Methotrexate can cause itching, skin rash, dizziness, and hair loss.

4) 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**

5) R.A. 66y male resist. to Methotrexate

- 66yrs. Married. Hypertensive. Hyperlipidaemia, Overweight, but good health.
- Dec 04 acute onset Rh Arth. First episode
  - Low energy x 3-4 months
  - "walking on stones"
  - Swollen painful joints –elbows, fingers, knees, ankles

5) R.A. 66y male resist. to Methotrexate

- Unable to shave, comb hair, get dressed
- Walking with crutches with great difficulty

5) R.A. 66y male resist. to Methotrexate

- March 05 – Aug 05
  - Methotrexate 10mg weekly
  - Mobic (Meloxicam) 15mg daily
- Progressive Deterioration
- July 05 advised TNF (Tumour Necrosis Factor) "Enbrel" injections – as methotrexate not working

ENBREL® (etanercept)

- **TNF – Potent Immunosuppressive treatment**

- **moderate to severe rheumatoid arthritis.**
- **moderate to severe juvenile rheumatoid arthritis**
- **active ankylosing spondylitis**
- **psoriatic arthritis**
- **moderate to severe chronic plaque psoriasis**

ENBREL® (etanercept)

- **IN POSTMARKETING USE, THE FOLLOWING SERIOUS ADVERSE EVENTS HAVE BEEN REPORTED:**

- **SERIOUS INFECTIONS AND SEPSIS, INCLUDING FATALITIES**
- **Cases of CNS demyelinating disorders** - MS
- **Rare cases of pancytopenia, including aplastic anemia, some fatal**

ENBREL® (etanercept)

- **In clinical trials of all TNF inhibitors, a higher rate of lymphoma was seen compared to the general population**
- In RA clinical trials, the most common adverse events were injection site reactions (37%), infection (35%) and headache (17%)
- In a JRA study (n = 69), infections (62%), headache (19%), abdominal pain (19%), vomiting (13%), and nausea (9%)

ENBREL® (etanercept)

- **Just because it is licensed does not mean it is safe!**

5) R.A. 66y male resist. to Methotrexate

- Aug 2005 Commenced LDN

5) R.A. 66y male resist. to Methotrexate

- Immediate dramatic improvement
- Walking without crutches after 2 weeks

- Continues well….r/v 10th Feb 06
- No Side Effects!

- Rheumatologist "Not Interested" in LDN

Low Dose Naltrexone - LDN

- Later Cases 2005-6

1. Bernadette, 26yo single girl – relapsing Remitting MS, Depression, PCOD
2. Mary, 34yo, Married 2 children Chronic Progressive MS
3. Fibromyalgia – 2 patients
4. ME - Chronic Fatigue

1. Bernadette, 26yo single girl MS, Depression and PCOD

- **Relapsing and remitting MS DX 1999 -**
  - **MRI, Lumbar Puncture, Optic Atrophy**
- **Irregular cycles DX PCOD**
- **RX: Glucophage, Cyclical Progesterone**

1. Bernadette, 26yo single girl MS, Depression and PCOD

- **Developed more MS symptoms**
  - **5 relapses in 6 years (1999-2005)**
  - **Aug 05 – advised Copaxin**

Copaxone

- **Copaxone is indicated for the reduction in frequency of relapses in ambulatory patients, (i.e. who can walk unaided) with relapsing, remitting multiple sclerosis (MS) characterised by at least two attacks of neurological dysfunction over the preceding two-year period.**

- **Copaxone is not indicated in primary or secondary progressive MS.**

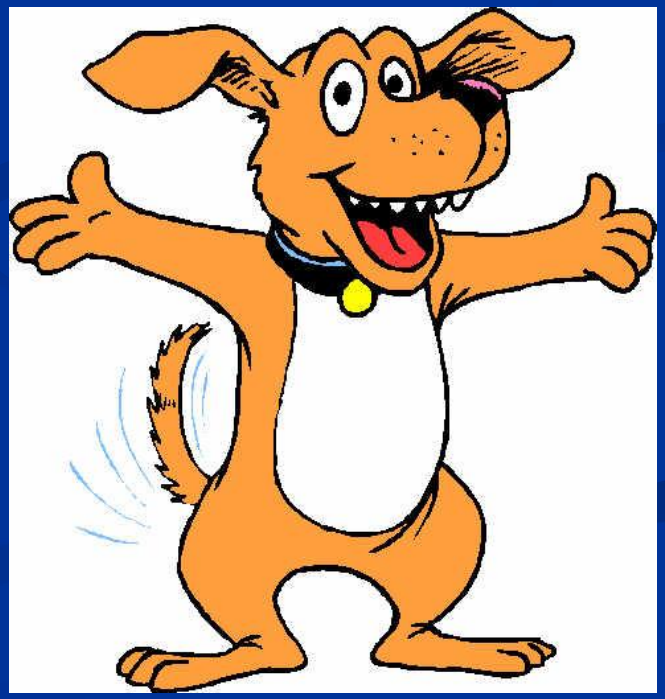
Copaxone

- Avoid Pregnancy
- vasodilatation (flushing), chest pain, dyspnoea, palpitations or tachycardia, may occur within minutes of a Copaxone injection
- Anxiety, Depression
- Dizziness
- Rash, Sweating

  - GREATER THAN 10% OF PATIENTS

1. Bernadette, 26yo single girl MS, Depression and PCOD

- **LDN commenced Oct 05**
  - **Improved energy, mood**
  - **No relapse since – Apr 06**
  - **Feels much better now**
    - **Increased energy**
    - **Improved mood**
    - **more regular cycles**



2. Mary, 34yo, Married 2 children Chronic Progressive MS

- MS DX 2001 – MRI and L. Puncture
- Oct 2005 – On Interferon for 5 years
  - Difficulty walking – Stick /Wheelchair
  - Extreme Fatigue
  - Reduced power arms, legs
  - Difficulty writing
  - ++ PMS - 7 days
  - Irregular cycles 60 days

Betaferon

- Betaferon is indicated for the treatment of patients with relapsing remitting multiple sclerosis and two or more relapses within the last two years. Betaferon is also indicated for patients with secondary progressive multiple sclerosis with active disease, evidenced by relapses

Betaferon

- **The efficacy of treatment for longer than two years has not been sufficiently demonstrated for relapsing-remitting multiple sclerosis**

- For secondary progressive multiple sclerosis efficacy for a period of two years with limited data for a period of up to three years

Betaferon

- Avoid Pregnancy
- Side Effects
  - At the beginning of treatment adverse reactions are common but in general they subside with further treatment. The most frequently observed adverse reactions are a flu-like symptom complex (fever, chills, headache, myalgia, arthralgia, malaise, or sweating) and injection site reactions.

Betaferon

- More Side Effects
  - Severe Anxiety, depression / Suicide
  - Insomnia, Dizziness
  - Injection site necrosis has been reported in patients using Betaferon. It can be extensive and may involve muscle fascia as well as fat and therefore can result in scar formation.
  - Many other side effects too numerous to mention!

Betaferon

- Asymptomatic Liver damage, in most case mild and transient, occurred very commonly in patients treated with Betaferon during clinical trials. As for other beta interferons, severe Liver injury, and death, has been reported rarely in patients taking Betaferon

2. Mary, 34yo, Married 2 children Chronic Progressive MS

- Plan
  - Stop Interferon!
  - After 7 days introduce LDN
- 1 Month later
  - Phone call – “walking without crutches”

2. Mary, 34yo, Married 2 children
Chronic Progressive MS

- Review 4 months later
  - Bright eyes, walking without stick, smiling
  - Dramatic improvement in energy and mood
  - Much less sleep needed
  - Sensation returned in feet
  - Delighted!

2. Mary, 34yo, Married 2 children Chronic Progressive MS

- Side effects 2 weeks "Brain Waking up"
  - Unable to sleep much for 2 weeks
  - Perfect Now! (March 06)

2. Mary, 34yo, Married 2 children Chronic Progressive MS

- Irish MS Society "Not Interested"
  - Active member – caution in discussing improvement
- Fear of Neurologist

- Tears in her eyes
  - "Thank your sister for her book!"
  - She has changed my life!

3. Fibromyalgia – 2 patients

- **Patient 1 – FM & Endometriosis**
  - **Cannot tolerate 1.5mg dose now on 0.25mg and building it up**
  - **Severe side effects – headache, nausea, sleep disturbance**
  - **Wait and see**

3. Fibromyalgia – 2 patients

- **Patient 2 – FM & Infertility**
  - **Took 2 months to notice gradual improvement in symptoms**
  - **Improved energy, Reduced pain**
  - **Severe recurrence of Symptoms when LDN ran out….(5 days..waiting for renewal)**

4. ME - Chronic Fatigue, 20yo female

- Interesting Family history of Autoimmunity
- Mum had endometriosis & patient has symptoms of very painful menses

4. ME - Chronic Fatigue, 20yo female

- LDN – Commenced Feb 06
  - Verbal review "Dramatic improvement" in energy levels

Low Dose Naltrexone - LDN

- Later Cases 2005-6

1. Patsy Polymyalgia Rheumatica
2. Sarah – Autoimmune polyendocrinopathy - (APCED)

Patsy Polymyalgia Rheumatica

- 68yo Man acute onset PMR
- Stopped Steroids
- Commenced LDN after 4 days
  - BUT …Deterioration in all symptoms after 2 weeks
  - Plan to stop LDN and recommence steroids if no improvement in another 2 weeks or if symptoms become much worse before that!

Sarah – Autoimmune polyendocrinopathy- (APCED)

- 8 years old
- No treatment available for her except symptomatic relief and replacement of hormone deficiencies
- Started LDN Nov 05
  - 0.5mg 1 week
  - 1.0mg 1 week
  - 1.5mg thereafter

Sarah – Autoimmune polyendocrinopathy- (APCED)

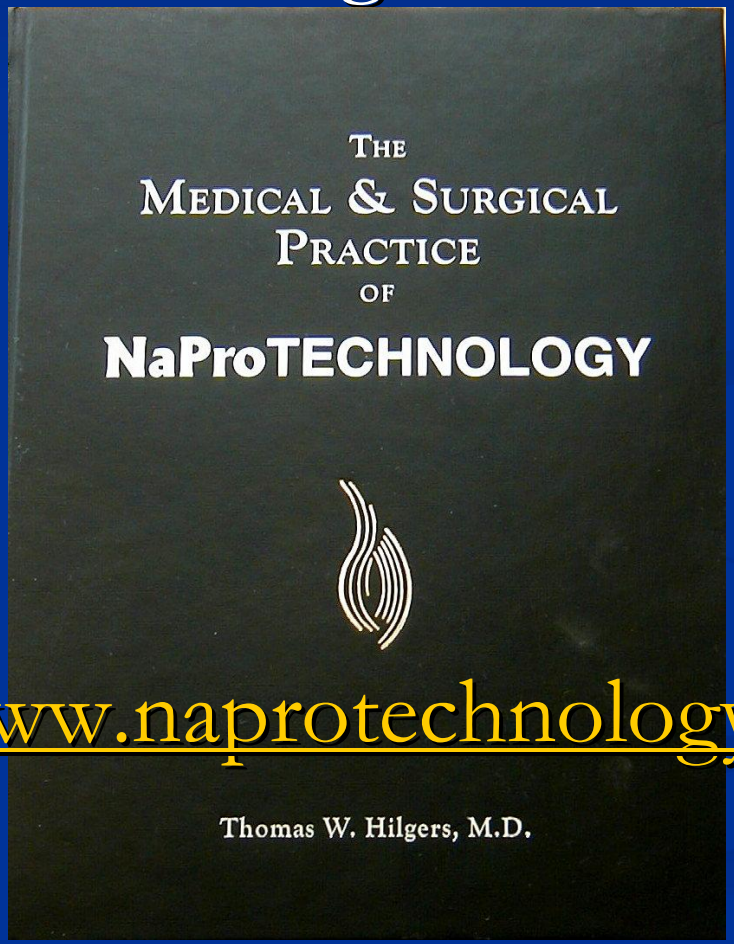
- Some improvement in energy and appetite
- BUT
  - Abnormal Liver Function
  - Low calcium

Admitted to hospital for calcium infusion

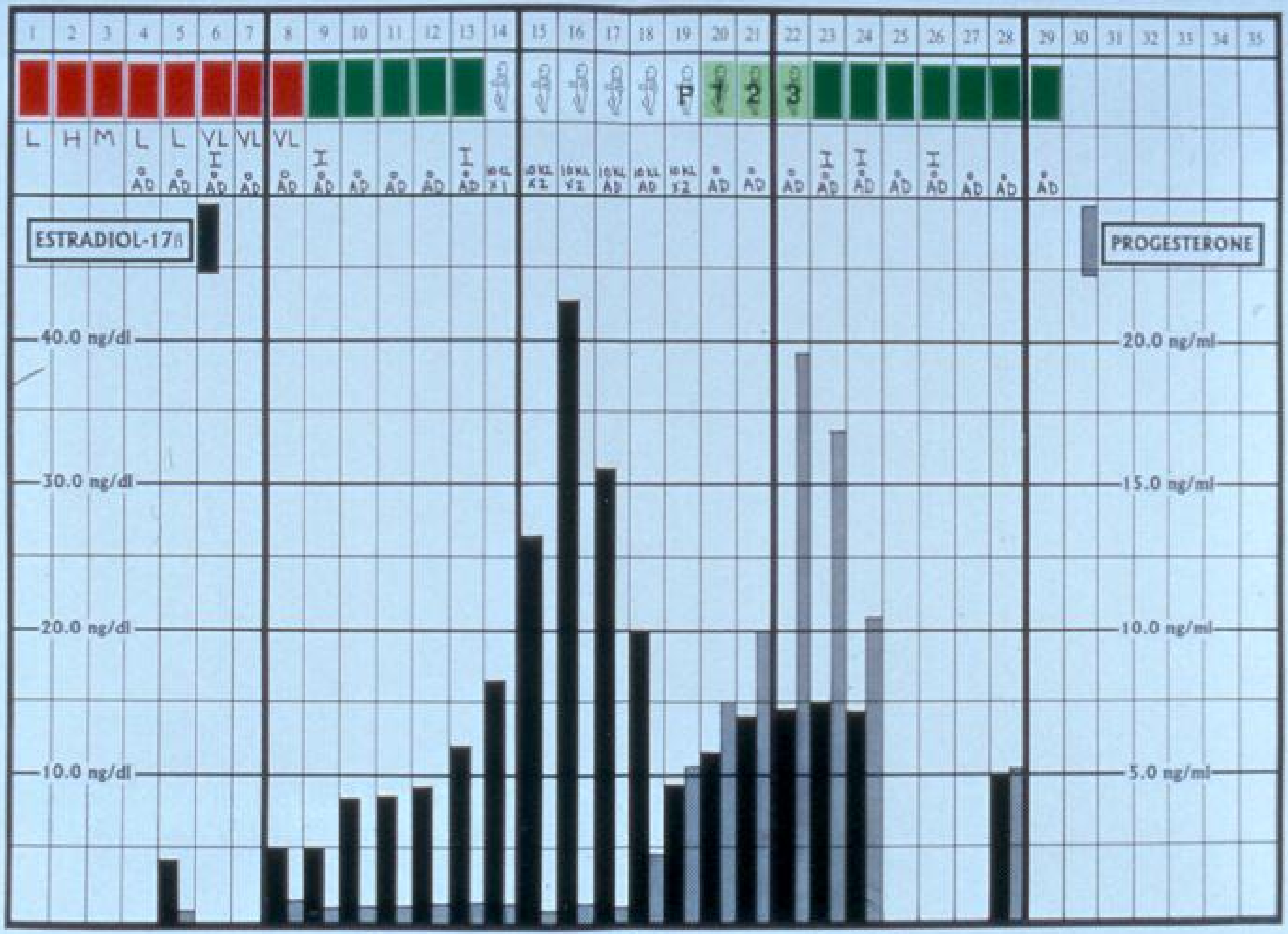
Stopped LDN…Next step??

Review Naltrexone use in NaProTECHNOLOGY

- Recent changes in treatment



www.naprotechnology.com



USE THESE SIGNS: P - PEAK • 1,2,3 - FERTILE DAYS FOLLOWING PEAK • I - INTERCOURSE

THE EFFECTIVENESS OF THE CREIGHTON MODEL TO AVOID PREGNANCY IN COUPLES OF NORMAL FERTILITY

Number of Couples Enrolled.....1,876

Number of Couple Months of Use..... 17,130

Number of Centers Participating..... 5

Omaha • St. Louis • Wichita • Houston • Milwaukee

METHOD EFFECTIVENESS.....99.5

USE EFFECTIVENESS.....96.8

Journal of Reproductive Medicine, 1998

Could the FertilityCare Charts be telling us <u>something more</u> ?


INFERTILITY
MISCARRIAGE
LOW PROGESTERONE
ABNORMAL BLEEDING
NAPROTRACKING® FOR A WOMAN'S HEALTH
USE THESE SIGNS: P - PEAK • 1,2,3 - FERTILE DAYS FOLLOWING PEAK • I - INTERCOURSE

AT its simplest level NaProTechnology uses a wide range of medical and surgical interventions to correct abnormal

1. Fertility*Care* Charting patterns
2. Subtle hormonal deficiencies
3. Ovulation defects
4. Surgical / structural abnormalities

Naltrexone in High Dose

- Compounding Pharmacist
  - Dose regieme
    - After 8.00 mg 4 times daily,
    - 32mg at single dose at night (QD hs)
    - 50mg QD hs
- Much Better Results!!

Table 29-20: Effect of High-dose Naltrexone on P+7 Serum β-Endorphin Level (N=15)

Status of Naltrexone	β-Endorphin Level (pg/mL)
Before naltrexone	15.9
On naltrexone	22.1[1]

1. p=.025, equal variance t-test.

Table 29-19: Role of Low-dose and High-dose Naltrexone on Treatment Response to Targeted Hormone Support – Treatment of Premenstrual Syndrome (PMS)

Improvement Response	Without Naltrexone[1] n	%	With Low-dose Naltrexone[2,3] n	%	With High-dose Naltrexone[4,5,6] n	%
Marked	17	34.0	16	42.1	19	90.4
Moderate	26	52.0	12	31.6	1	4.8
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5. p<.0001, (chi-square) when compared to no naltrexone.
6. p=.0003, (chi-square) when compared to low-dose naltrexone.

Psychiatric disorders

- Improvement
  - Depression
  - Bipolar disorder
  - Obsessive compulsive disorder

- Patients often discontinue psychiatric Medications…gradually under suppervision!

PMS

- Present in 75 % of women with Infertility or recurrent miscarriage
- Is there a common link?

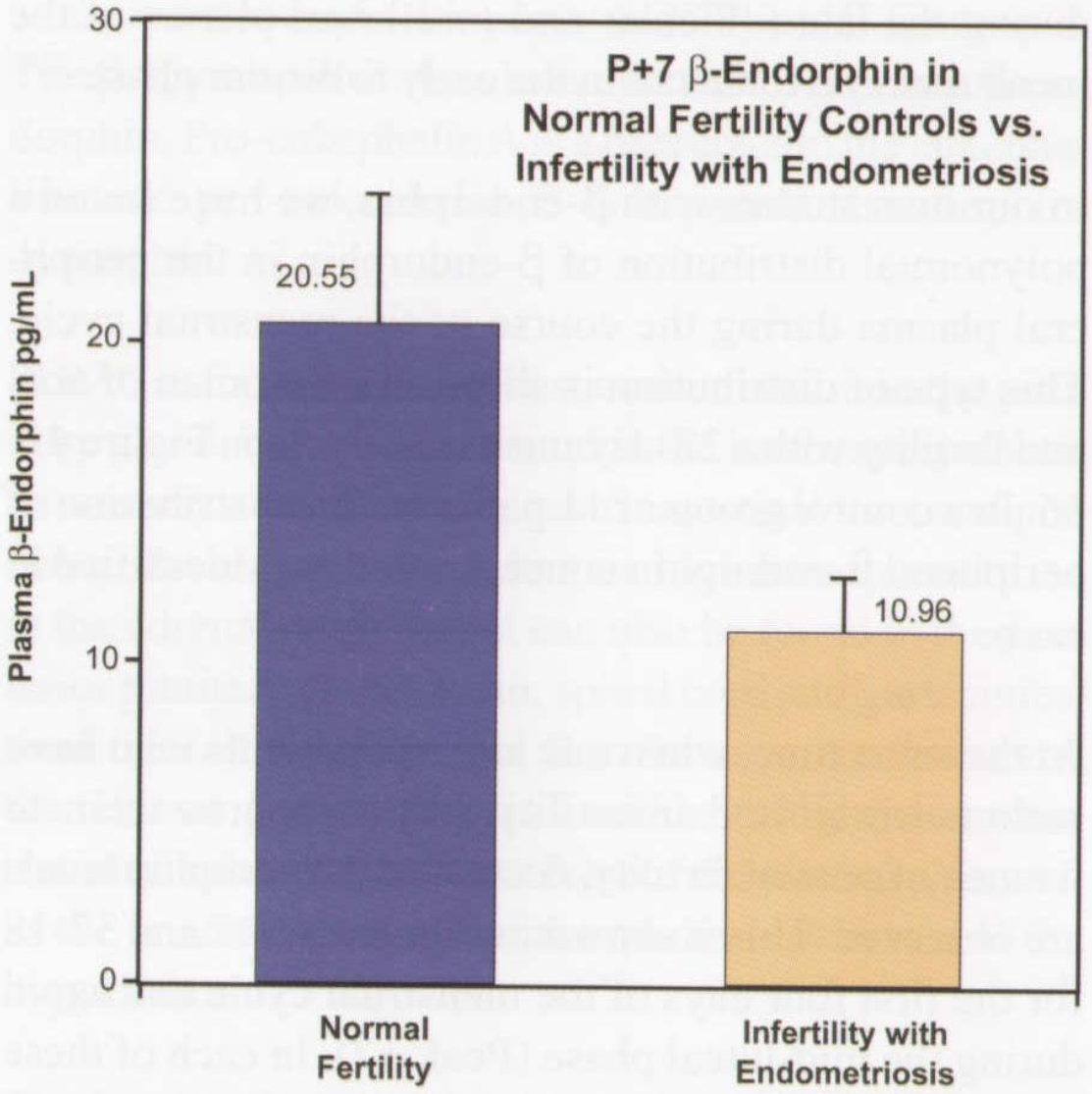

Figure 41-18: Plasma beta-endorphin levels during the luteal phase (Peak +7) in women of normal fertility versus those with infertility due to endometriosis ($p<.01$) (From: Pope Paul VI Institute research, 2004).

- **FURTHERMORE……**

Table 43-7: Incidence of Endometriosis in Patients with PCOD[1] (N=55)

	n	%
With endometriosis	28	50.9
No endometriosis	27	49.1

1. As determined at the time of laparoscopy.

From: Pope Paul VI Institute research. 2004.

Infertility
Endometriosis and PCOD

- Could they have a similar underlying cause of disease?

- Could it be something to do with
  - endorphin deficiency

Infertility
Endometriosis and PCOD

- PCOD – Elevated Insulin

- Greatly improved with naltrexone (Higher doses)

Ch 43 PCOD, Hilgers, MED and Surg Practice of NaProTECHNOLOGY

88. Fulghesu AM, Ciampelli M, Fortini A, et al: Effect of Opioid Blockade on Insulin Metabolism in Polycystic Ovarian Disease. Hum Reprod 10:2253-2257, 1995.

89. Givens JR, Kurtz BR, Kitabchi AE, et al: Reduction of Hyperinsulinemia and Insulin Resistance by Opiate Receptor Blockade. J Clin Endocrinol Metab. 64:377-382, 1987.

90. Fulghesu AM, Lanzone A, Cucinelli F, et al: Long-Term Naltrexone Treatment Reduces the Exaggerated Insulin Secretion in Patients with Polycystic Ovary Disease. Obstet Gynecol. 82:191-197, 1993.

91. Lanzone A. Fulghesu AM, Fortini A, et al: Effect of Opiate Receptor Blockade on the Insulin Response to Oral Glucose Load in Polycystic Disease. Hum Reprod. 6:1043-1049, 1991.

92. Lanzone A, Fulghesu AM, Cucinelli F, et al: Evidence of a Distinct Derangement of Opioid Tone in Hyperinsulinemic Patients with Polycystic Ovary Syndrome: Relationship with Insulin and Luteinizing Hormone Secretion. J Clin Endocrinol Metab. 80: 3501-3507, 1995.

93. Fulghesu AM, Ciampelli M, Guido M, et al: Role of Opioid Tone in the Pathophysiology of Hyperinsulinemia and Insulin Resistance in Polycystic Ovarian Disease. Metabolism. 47:1-5, 1998.

Infertility
Endometriosis and PCOD

- Could they have a similar underlying cause of disease?

- Could it be something to do with
  - endorphin deficiency

    or
  - abnormal immune function?

Immune Deficiency and Infertility

It has been thought for a number of years that endometriosis may be associated with some type of alteration in cell-mediated immunity.[83] In fact, *endometriosis fulfills all the classic characteristics of an autoimmune disease*—polyclonal B cell activation, tissue damage, multi-organ involvement, female preponderance, familial occurrence, and increased concurrence with other autoimmune diseases.[84]

In women with endometriosis, there is a defect in natural killer cell activity, and the natural killer cell activity of the peritoneal fluid mononuclear cells is decreased in endometriosis. This correlates significantly with the severity of the disease in both the peripheral blood and the peritoneal fluid of women with endometriosis.[85,86]

Substantial evidence indicates that endometriosis shares many similarities with autoimmune diseases. The theory of an altered immune system and endometriosis suggests that changes in cell-mediated immunity and/or humoral immunity may contribute to the development of the disease. Many investigators now are looking at immunomodulaters and inflammatory modulators as possible innovative treatments for endometriosis.[87-89]

Chapter 39, p500

Hilgers

Med & Surg practice of NaProTechnology

83. Dmowski WP, Steele RW, Baker GF: Deficient Cellular Immunity in Endometriosis. Am J Obstet Gynecol. 141: 377-383, 1981.

84. Gleicher N, El-Roeiy A, Confino E, Friberg J: Is Endometriosis an Autoimmune Disease? Obstet Gynecol. 70: 115-121, 1987.

85. Oosterlynck DJ, Cornillie FJ, Waer M, Vandeputte M, Koninckx PR: Women with Endometriosis Show a Defect in Killer Activity Resulting in a Decreased Cytotoxicity to Autologous Endometrium. Fertil Steril. 56: 45-51, 1991.

86. Oosterlynck DJ, Meuleman C, Waer M, Vandeputte M, Koninckx, PR: The Natural Killer Activity of Peritoneal Fluid Lymphocysts is Decreased in Women with Endometriosis. Fertil Steril. 58: 290-295, 1992.

87. Johnson KM: Endometriosis: The Immunoendocrine Factor. The Female Patient. 21: 15-34, 1996.

88. Nothnick WB: Treating Endometriosis as an Autoimmune Disease. Fertil Steril. 76: 223-231, 2001.

It has also been recently identified that there are high concentrations of anti-ovarian antibodies associated with polycystic ovaries. This suggests that an immune reaction is associated with this condition. This also suggests the possibility that polycystic ovaries may have an autoimmune component to it.[19]

19. Ali AFM, Fateen B, Ezzet A, et al: Polycystic Ovary Syndrome as an Autoimmune Disease: A New Concept. Obstet Gynecol 95:48S, 2000.

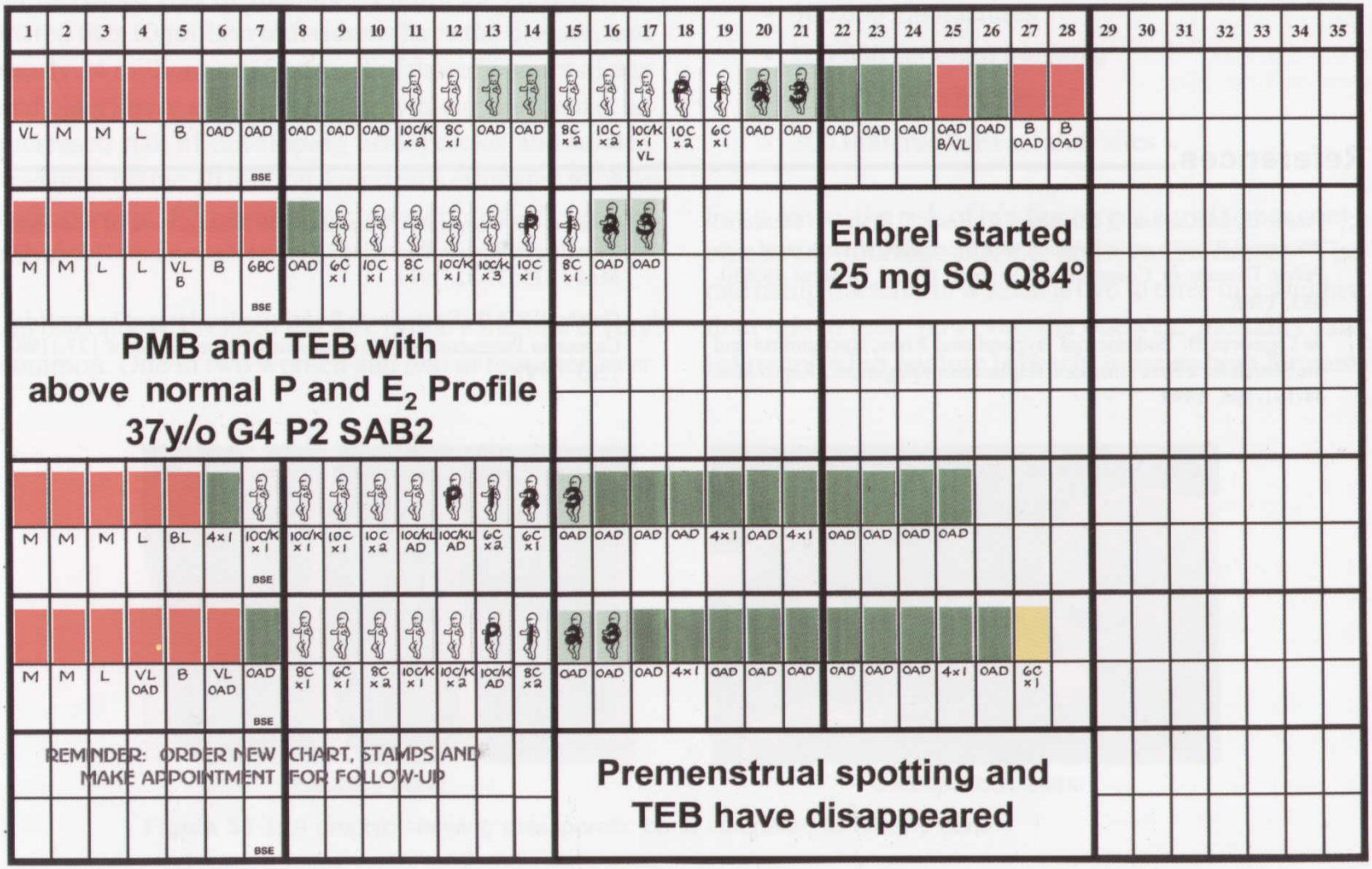

Figure 32-22: This is the same patient as in Figure 32-21. The premenstrual spotting is shown in the first cycle of charting. She was treated by a reproductive immunologist with Enbrel 25 mg SQ every 84 hours. On treatment with Enbrel, her premenstrual spotting and tail-end brown bleeding disappeared (From: Pope Paul VI Institute research, 2004).

Dr. Alan Beers – Immunologist in Chicago, treats recurrent miscarriage

Low Dose Naltrexone - LDN

- Irish Fertility Patient 2004
  - Nothing was working after 15 months of different treatments
  - Poor cycle, poor hormones, horrible PMS resistant to HCG
- Clinical Experiment
  - Trial of LDN 4.5mg Nocte 2004

Case Presentations - LDN

1. **Ailish – Nothing else was working**

OCT '04

	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
TAMP			F	F	F	F																												E 197 P 81	
Date	11/10	12/10	13/10	14/10	15/10	16/10	17/10	18/10	19/10	20/10	21/10	22/10	23/10	24/10	25/10	26/10	27/10	28/10	29/10	30/10	31/10	1/11	2/11	3/11	4/11	5/11	6/11	7/11	8/11	9/11	10/11	11/11	12/11	13/11	
DESCRIPTION	VL OAD	M	M	L OAP	VL OAD	B OAD	B BE OAD	B OAD	B OAD	OAD	OAD	OAD	I OAD	I OAD	I 10HL X 2	I 10HL X 2	I 10K X1	10K X 1	OAD	OAD	OAD	OAD	OAD I	OAD	OAD BT	OAD	OAD I	OAD	OAD I	OAD	OAD	OAD	OAD	CAD	
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DESCRIPTION	H	M	L OAD	B OAD	B OAD	B OAD	OAD BE	OAD I	OAD	OAD I	OAD	OAD	I 10HL X 2	I 10HL X 2	I 10HL X 1	OAD	OAD	OAD	OAD	I OAD	OAD	OAD	OAD	OAD	I OAD BT	OAD	I OAD	OAD	I OAD	OAD	OAD	TSH Free T4	378 15 8
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Date	15/12	16/12	17/12	18/12	19/12	20/12	21/12	22/12	23/12	24/12	25/12	26/12	27/12	28/12	29/12	30/12	31/12	1/1	2/1	3/1	4/1	5/1	6/1	7/1	8/1	9/1	10/1	11/1	12/1	13/1	14/1	15/1	16/1		
DESCRIPTION	H	M	VL OAD	B OAD	B OAD	I OAD	BE OAD	I OAD	OAD	I OAD	OAD	OAD	10K X1	OAD	10KL X2	I OAD	10KL X 1	I OAD	OAD	OAD	OAD	I OAD	OAD	I OAD BT	OAD	I OAD	OAD	OAD	OAD	OAD	OAD	OAD	OAD		
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Date	17/1	18/1	19/1	20/1	21/1	22/1	23/1	24/1	25/1	26/1	27/1	28/1	29/1	30/1	31/1	1/2	2/2	3/2	4/2	5/2	6/2	7/2	8/2	9/2	10/2	11/2	12/2	13/2	14/2	15/2	16/2			P Procrin	107-3 356
DESCRIPTION	L OAD	H	M	L OAD	B OAD	OAD I	OAD BE	OAD	OAD I	OAD	OAD I	OAD	OAD I	OAD	10KL 10BL I	OAD	OAD	I OAD	OAD	OAD	OAD	OAD	OAD	OAD	OAD	OAD	I OAD	OAD	OAD	I OAD	OAD				
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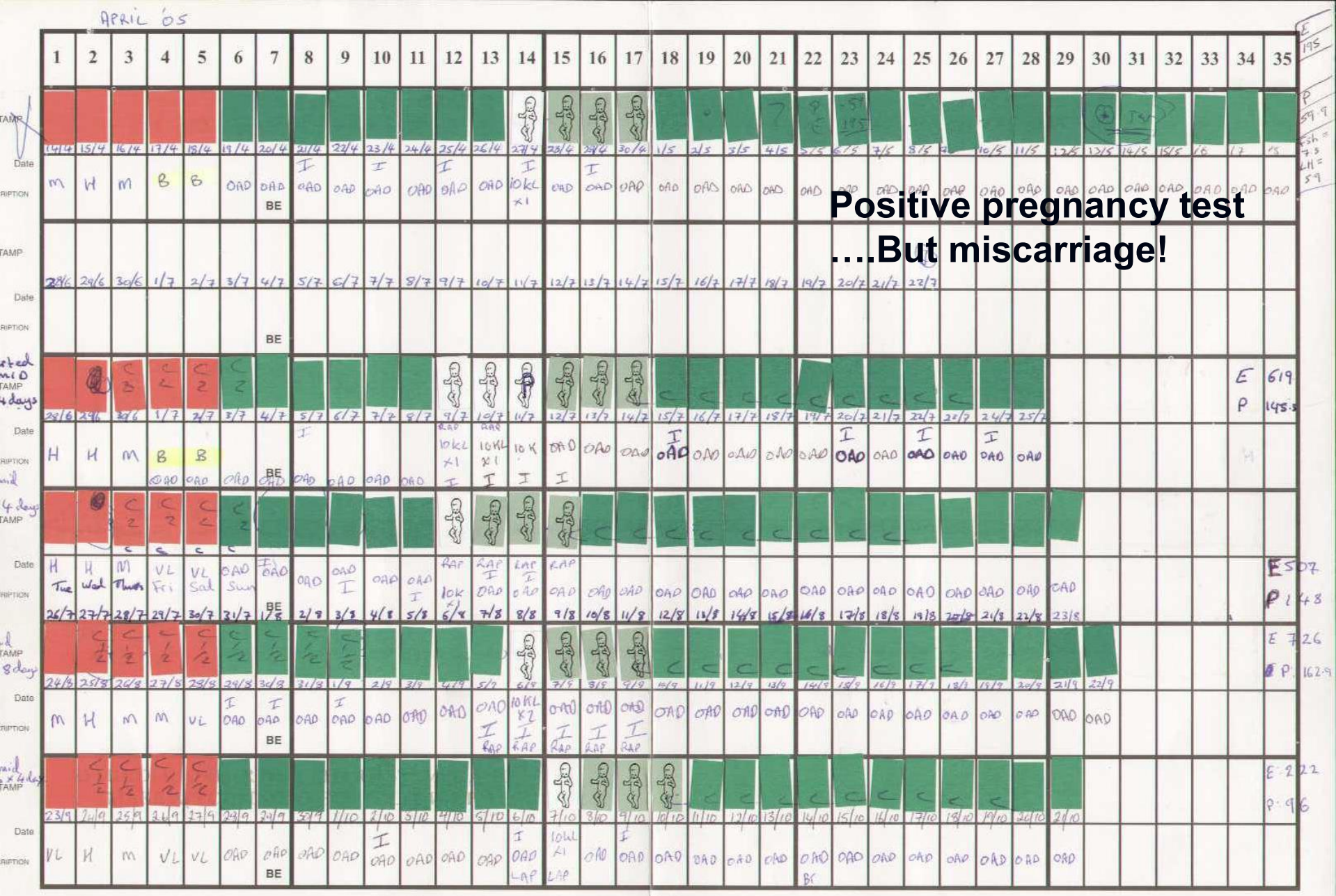
Date	16/3	17/3	18/3	19/3	20/3	21/3	22/3	23/3	24/3	25/3	26/3	27/3	28/3	29/3	30/3	31/3	1/4	2/4	3/4	4/4	5/4	6/4	7/4	8/4	9/4	10/4	11/4	12/4	13/4						
DESCRIPTION	M	H	M	L	B		BE				I 8K X2	I 8K X2	10KL X1	I 10KL X1	I 10K X1	OAD	I OAD	OAD	OAD	OAD	I OAD	OAD	I OAD	OAD	I OAD	OAD	OAD	OAD	OAD						

Started LDN

USE THESE SIGNS: P = PEAK • 1.2.3 = FERTILE DAYS FOLLOWING PEAK • I = INTERCOURSE BE = BREAST SELF-EXAM


APRIL '05
Positive pregnancy test
….But miscarriage!
USE THESE SIGNS: P = PEAK • 1.2.3 = FERTILE DAYS FOLLOWING PEAK • I = INTERCOURSE
BE = BREAST SELF-EXAM

Ailish - LDN

- Dramatic, Immediate Clinical improvement, relief of severe intractable PMT
- Conceived 2 months later!?!
- Very Low levels of Estradiol on P+7, ….Miscarried

Ailish - LDN

- Recent Laparoscopy found moderately severe endometriosis
- Waiting for a successful pregnancy still, but now feels fantastic, and confident of success

LDN – Criteria for use with infertility

- Feb 2005 – LDN on clinical observation
  - Persistent PMS
  - Personal or Family History AI Disorder
  - Endometriosis

LDN – Criteria for use with infertility

- With Clinical experience and practicing the "ART" of medicine, by listening to my patients…..I added more categories of suitable candidates

- NaProTechnology is especially suited to trying new treatments as the charting system gives real-time daily biological feedback on the effect of treatment

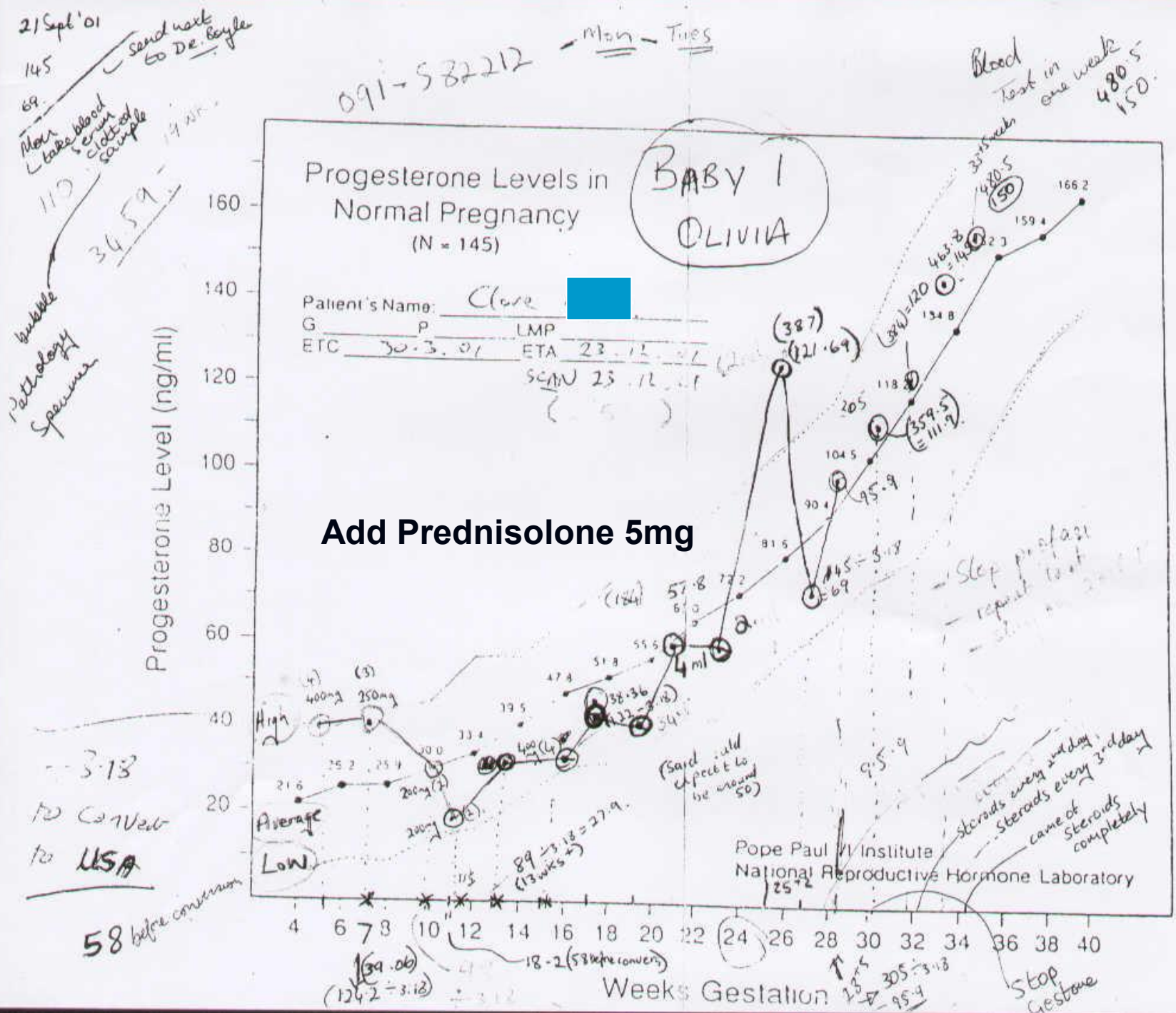
LDN – Criteria for use with infertility

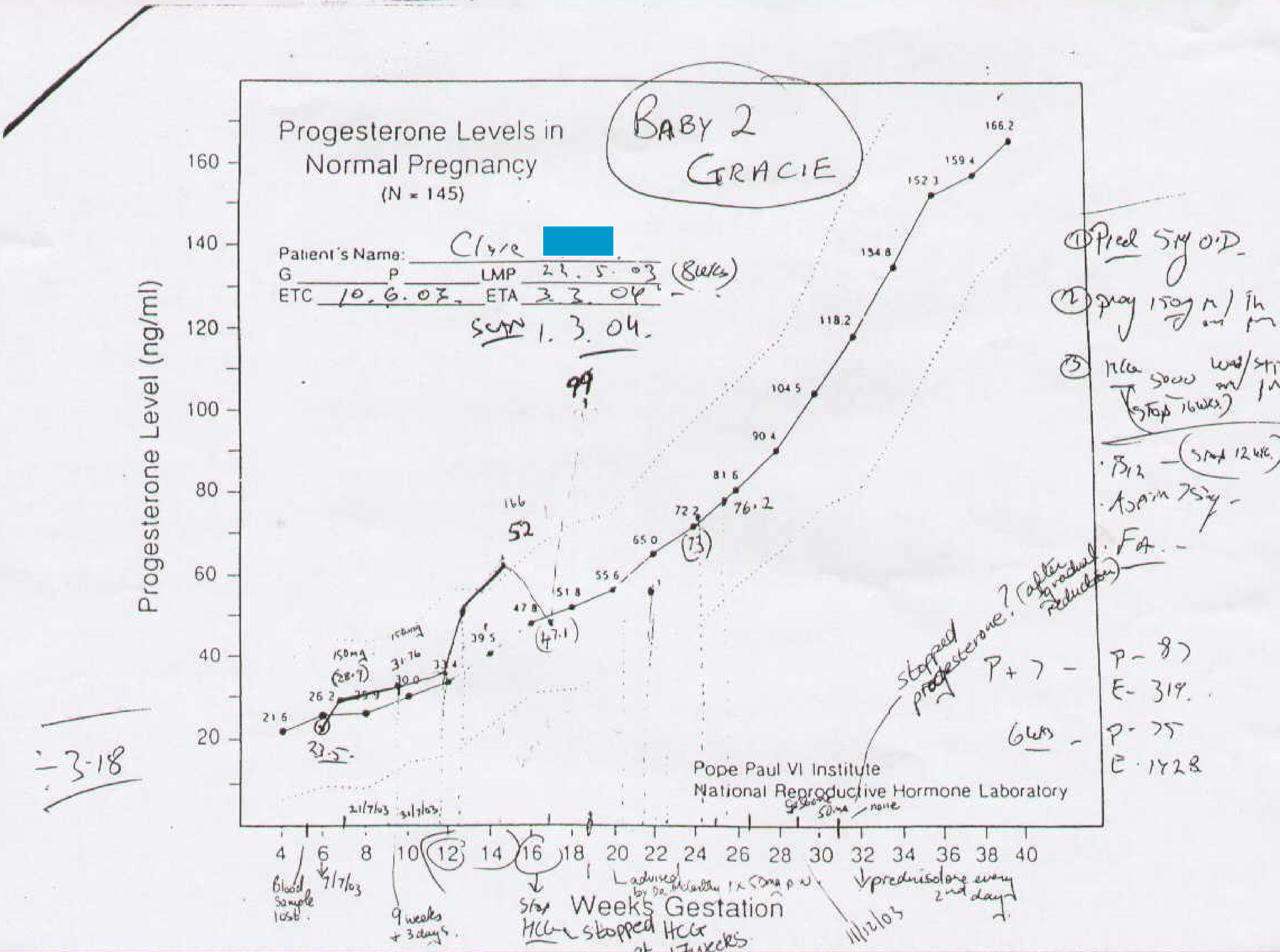
- I explain "LDN is experimental….but safe if you want to give it a try!"
- Feb 06
  - Persistent fatigue, tired all the time
  - Sleep Disturbance
  - Tail end Brown Bleeding
  - Depression
  - Male anti-sperm antibodies

Case Presentations - LDN

- Clare

- Recurrent Miscarriages –
  ? immune disorder


Progesterone Levels in Normal Pregnancy
(N = 145)
BABY 1
OLIVIA
Patient's Name: Clare
G P LMP
ETC 30.3.01 ETA 23.12.01
Add Prednisolone 5mg
Progesterone Level (ng/ml)
Weeks Gestation
Pope Paul VI Institute
National Reproductive Hormone Laboratory
Average
Low
High
Stop Gestone



Progesterone Levels in Normal Pregnancy
(N = 145)
BABY 2 GRACIE
Patient's Name: Clare [redacted]
G P LMP 23. 5. 03 (8wks)
ETC 10. 6. 03. ETA 3. 3. 04
Scan 1. 3. 04.
Progesterone Level (ng/ml)
160
140
120
100
80
60
40
20
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
40
Weeks Gestation
21.6
26.2
150mg
(28.7)
29.9
31.76
30.0
33.4
39.5
52
47.8
(47.1)
51.8
55.6
65.0
72.2
(73)
76.2
81.6
90.4
104.5
118.2
134.8
152.3
159.4
166.2
Pope Paul VI Institute
National Reproductive Hormone Laboratory
(1) Pred 5mg O.D.
(3) HCG 5000 (stop 16wks)
B12 (stop 12 wks)
Aspirin 75mg
FA
stopped progesterone? (after gradual reduction)
P + 7 - P - 87
E - 319.
6wks - P - 75
E - 1428
9 weeks + 3 days.
Stop HCG stopped HCG
prednisolone every 2nd day
11/12/03

Clare - LDN

- Developed Lupus rash
- Resistant to clomid now and trying for 3rd baby!
- Added LDN – ovulating normally with much less hormonal treatment

FertilityCare

Low Dose Naltrexone
LDN