

The Pimple (Acne) Model of Early Endometriosis

Dan C. Martin, MD

Scientific and Medical Director
Endometriosis Foundation of America

Professor Emeritus
University of Tennessee Health Science Center

Permission to Use in Education

These slides are for educational use and permission is granted for use in educational programs, presentations, articles, blogs, social media, web sites, and similar presentations. Please acknowledge that the contents are used with permission from: Dan C. Martin, MD, www.danmartinmd.com/files/pimplemodel.pdf accessed [date].

If written permission is required for publication, please send a request to danmartinmd@gmail.com or leave a message on Google Voice at +1 (901) 761-4787.

Pain, Neglect, Delay, Confusion

- Years of neglect
- Normalization of pain
- Self-normalization
- Chest pain v pelvic pain
- Normalization by family and friends
- Normalization by physicians/providers
- Situational awareness by physicians/providers
- Insensitivity / objectification
- Lack of empathy
- Generalization / homogenization
- Confusing information
- Ethnic and racial bias & inequity
- Gender diversity bias & inequity
- Cultural, income, social bias
- Emphasis on measurables
- Roadblocks
- Financial challenges
- Inadequate insurance coverage
- Ablation of deep endometriosis
- Inadequate hysterectomy results
- Productivity
- Lost jobs
- A difficult healthcare system
- Timed visits
- Hospital deserts
- Isolated islands of care
- Transportation
- Quality of life
- Isolation
- Interpersonal relationships
- Lost daily, work, school, or extracurricular activity time.
- Endo belly
- Endo brain, brain fog
- Non-menstrual symptoms
- Extrapelvic symptoms
- Silent death of a kidney or kidneys
- Sleep disturbance
- Eating disorders
- Sexual dysfunction
- Difficulties in daily leisure activities
- Loss of perspective
- Anxiety, depression
- Suicidal thoughts, attempts, suicide/death
- Being called dramatic, attention seeker, or frequent flyers
- Being diagnosed with Munchausen's syndrome
- Referral to psychiatrists
- Many other problems

Scientific and Clinical Challenges

- Age-dependency
- Genetic predispositions
- Shared genetic predispositions
- Epigenetic changes
- Epigenetic reversal
- Genetic mutations
- Retrograde menstruation
- Venous dissemination
- Lymphatic dissemination
- Surgical dissemination
- Congenital remnants & anomalies
- Window of Opportunity
- Attachment
- Implantation
- Neovascularization
- Tissue fragments
- Stem cells
- Activation
- Inflammation
- Injury and repair
- Estrogens
- Biochemistry
- Histochemistry
- Immunology
- Immunohistochemistry
- Cytokines
- Inflammatory mediators
- Fibrosis
- Window of opportunity
- Transition
- Growth
- Stabilization
- Regression
- Tunnel Vision
- Healthcare providers
- Healthcare teams
- Comprehensive centers
- Proactive approach to care
- Focused care
- Holistic approach
- Medical interventions
- Surgical interventions
- Surgeons as technicians
- Surgeons as primary care
- Surgeons in teams
- Mental health professionals
- Psychiatric support
- Psychological support
- Mental health counselling
- Supportive relationships
- Many other concerns

Focus

A focus on specific endometriosis concepts is not to detract from the suffering of those with endometriosis after years of neglect. The focus is to help prepare to provide improved care.

- *Adapted from Sawsan "Suzie" As-Sanie, University of Michigan, Society for Women's Health Research, September 12, 2023.*

Some of the Endometriosis Types

- **Never Diagnosed**
 - Scott et al. Am J Obstet Gynecol. 1953, 66(5):1082-1103
 - Evers JLH. Hum Reprod. 1994 9(12):2206-9
- **Asymptomatic, fertile women undergoing tubal ligation who are healthier than controls at 12 to 14 years.**
 - Moen and Stokstad. Fertil Steril. 2002, 78(4):773-6
- **Dysmenorrhea**
 - Knox, et al. Acta Obstet Gynecol Scand 2014, 93: 1262-1267.
- **Symptomatic Diagnosed – Suggests Access to Care**
 - Shafrir et al. 2018, doi: 10.1016/j.bpobgyn.2018.06.001
- **Symptomatic Undiagnosed**
 - Shafrir et al. 2018, doi: 10.1016/j.bpobgyn.2018.06.001
 - Access to care may add 20% or more
- **1.8 Years Delay (Subfertility)**
 - Staal et al. Gynecol Obstet Invest. 2016, 81(4):321-4
- **8.3 Years Delay (Chronic Pain)**
 - Staal et al. Gynecol Obstet Invest. 2016, 81(4):321-4
- **Long Delays, Multiple Surgeries, Multiple Surgical Specialties**
 - Nirgianakis et al. Acta Obstet Gynecol Scand 2014;93: 1262-1267

Prevalence

- 10% - Symptomatic diagnosed
 - 3.4% to 6.3% - Infertility with no pain
 - 3.7% to 6.6% - Pain with or without infertility
 - Shafirir et al. 2018, doi: 10.1016/j.bpobgyn.2018.06.001
 - Koninckx et al. 1991 & 2019, doi: 10.1016/s0015-0282(16)54244-7 & 10.1016/j.fertnstert.2018.10.01
 - Almquist 2017, doi: 10.1016/j.fertnstert.2017.09.017
- 2% (2% to 3.7%) - Symptomatic undiagnosed
 - Shafirir et al. 2018, doi: 10.1016/j.bpobgyn.2018.06.001
 - Ferrero et al. 2010, doi: 10.1016/j.ijgo. 2010.03.039
 - NIH 2021, <https://www.ncbi.nlm.nih.gov/books/NBK578537/>
- 5.7% (2 to 43%) - Women undergoing tubal ligation
 - Fuentes et al. 2016, doi: 10.4067/S0034-98872014000100003
 - Shafirir et al. 2018, doi: 10.1016/j.bpobgyn.2018.06.001
- 20% - Asymptomatic, fertile women undergoing tubal ligation who are healthier than controls at 12 to 14 years.
 - Moen and Stokstad. Fertil Steril. 2002, 78(4):773-6
- 100% - Transient in all women? / Was it symptomatic and missed?
 - Evers 1994, Evers 2013
- 0.1% to 1% - Long delays, multiple surgeries, multiple surgical specialties
This represents up to 1.6 million USA or 39 million worldwide women.
 - Koninckx et al. Fertil Steril 1991, 55(4):759-765, doi: 10.1016/s0015-0282(16)54244-7
 - Koninckx et al. Fertil Steril 2019, 111:327-40. doi: 10.1016/j.fertnstert.2018.10.01
 - Nirgianakis et al. Acta Obstet Gynecol Scand 2014;93: 1262-1267
 - Shafirir et al. 2018, doi: 10.1016/j.bpobgyn.2018.06.001
 - Staal et al. Gynecol Obstet Invest. 2016, 81(4):321-4

Focus

Early Endometriosis

- Medical therapy and supportive care are reasonable, safer than surgery, and work for many adolescents and women.
- The pimple model complements the literature on later stages of endometriosis, gastrointestinal concerns, immunologic diseases, cancers, and other health concerns which are the more common focus of publications.

Compare and Contrast

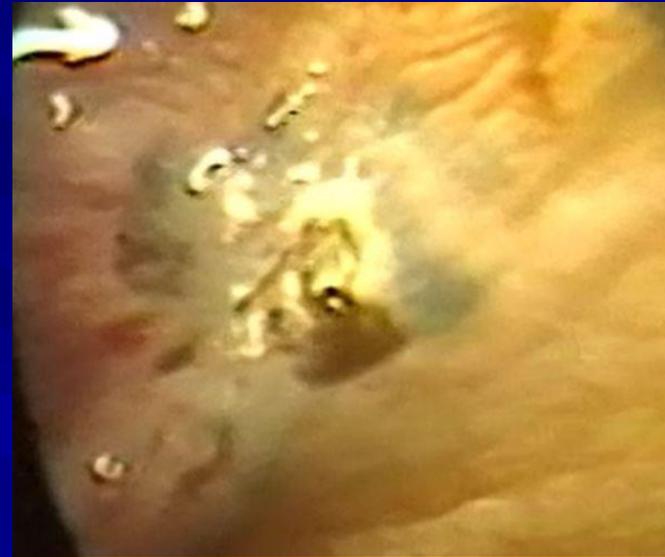
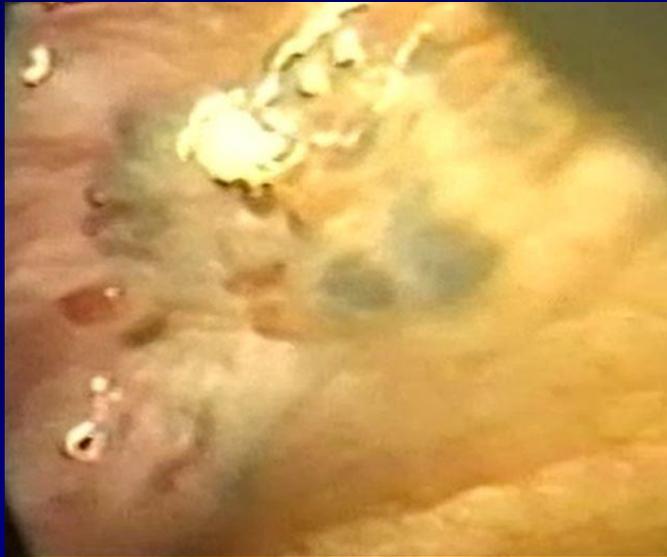
Pimples and Early Endometriosis

- Window of Opportunity
- Appearances
- Treatment
- Progression or Regression

“The study of endometriosis is like nailing Jell-O to a tree.”

– Donna Vogel, NIH 2002

The Pimple Model *(1983)*



Old trapped blood erupts as the fibrotic surface of dark scarred endometriosis is vaporized with a CO₂ laser.

Window of Opportunity

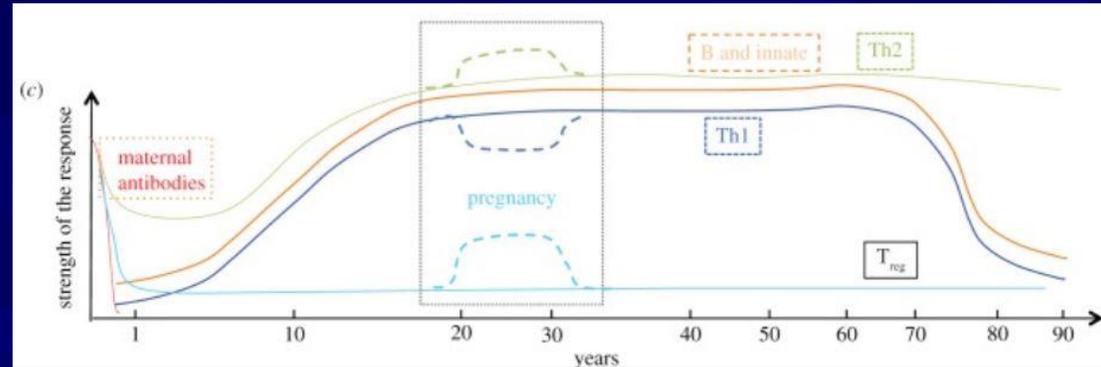
Acne

- Adolescents and young adults
- Later stressors may activate.
- Neuroimmune maturation may play a role.
- Hormones introduce the window by stimulating oil glands.
- Hormonal fluctuations become less pronounced in adults.

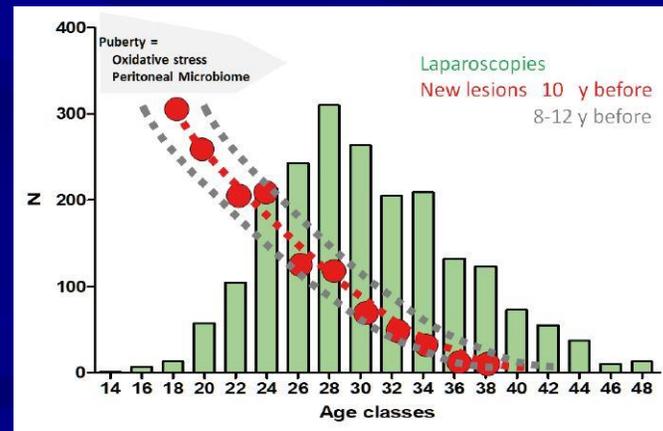
Endometriosis

- Adolescents and young adults
- Later stressors may activate.
- Neuroimmune maturation may play a role.
- The onset and irregularity of FSH and estrogen activates growth and possibly receptivity of peritoneal secondary mullerian system.
- Hormonal and FSH fluctuations become less pronounced in adults.

Window of Opportunity

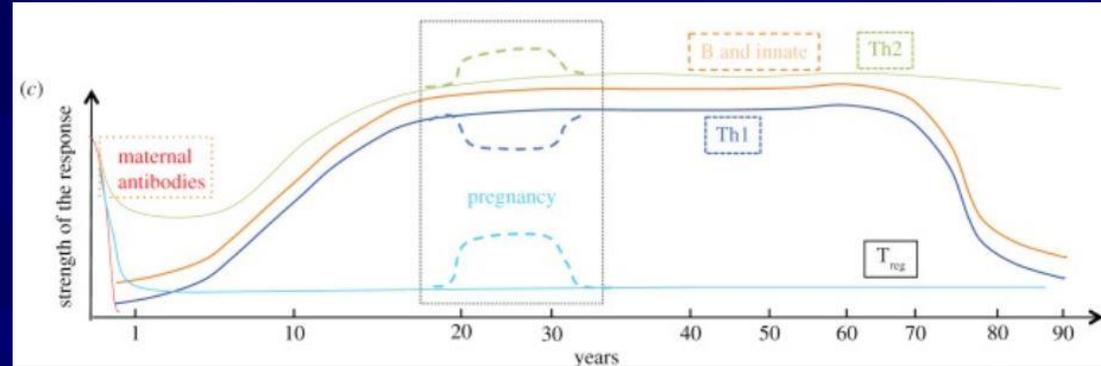


Neuroimmune maturation Simon et al. PMID: 26702035; PMCID: PMC4707740

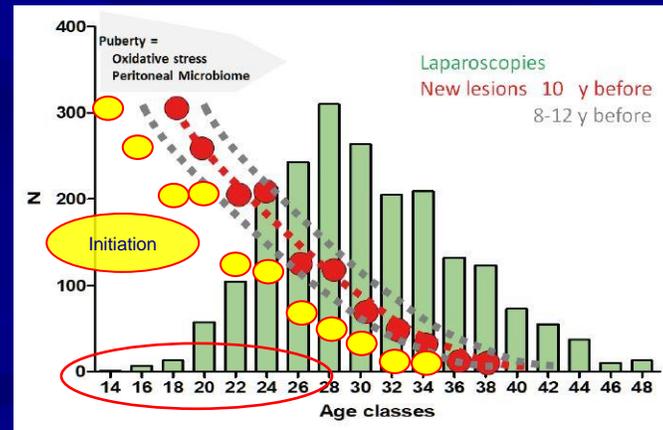


Natural history endo. Koninckx et al. PMID: 34555875; PMCID: PMC8823267

Window of Opportunity



Neuroimmune maturation Simon et al. PMID: 26702035; PMCID: PMC4707740



Age 14 to 26

Natural history endo. Koninckx et al. PMID: 34555875; PMCID: PMC8823267

Appearance

Acne

- There are multiple appearances that change over time
- You can see what looks ugly.
- You cannot see what causes pain.
- You cannot see immunologic, epigenetic, or genetic changes
- You cannot predict what will scar.

Endometriosis

- There are multiple appearances that change over time.
- You can see what looks ugly.
- You cannot see what causes pain.
- You cannot see immunologic, epigenetic, or genetic changes
- You cannot predict what will scar.

Treatment

Acne

- Most (many?) do not need treatment.
- Some respond to tetracycline probably as an anti-inflammatory medication rather than an antibiotic.
- Some respond to hormones (estrogens or anti-androgens)
- Some require surgery (dermabrasion)

Endometriosis

- Some (many?) do not need treatment.
- Some pain responds to NSAIDs as an anti-inflammatory and analgesic medication.
- Some respond to hormones (progestins or GnRH α)
- Some require surgery (excision, cystectomy, adhesiolysis...)

Progression or Regression

Acne

- Pimples come and go.
- Most pimples get better.
- Some pimples get worse.
- Hormones (androgens) make some worse.
- Hormones (estrogens) make some better.

Endometriosis

- Endometriosis comes and goes.
- Some endometriosis gets better.
- Some endometriosis gets worse.
- Hormones (estrogens) make some worse.
- Hormones (progestins, GnRHa) make some better.

Concerns

- Delayed Diagnosis
- What is the chance of progression?
- What surveillance is needed?
- Avoidable Surgery
- Age-Associated Concerns
- How much endometriosis is asymptomatic?

Proactive Management of Dysmenorrhea

Seventy-four adolescents seen for dysmenorrhea in a tertiary pediatric and adolescent gynaecology practice were followed-up at an average of 10.2 years.

- 13 (18.6%) were diagnosed with endometriosis.
- All cases of endometriosis were minimal/mild, i.e., none had moderate or severe endometriosis.

Regression or Progression

Summary of seven articles with 130 women.

- 42% Spontaneous regression
- 29% Stable disease
- 29% Progression

Age

- If an adolescent starts menstruation at age 12, she has seven years for development of deep endometriosis by age 19.
- Three cm rectovaginal nodule at age 21
 - Habib N. Intestinal deep infiltrating endometriosis at young age. EC Gynaecology. 2018

Age-Associated Stages

Adolescents Studies

≤ Age 19 – 5% Stage IV

≤ Age 21 – 25% Stage IV

NOTE: Staging is based on anatomic appearance and does not consider age-associated changes, immunology, inflammation, biochemistry, epigenetics, or genetics.

“The study of endometriosis is like nailing Jell-O to a tree.”

– Donna Vogel, NIH, 2002