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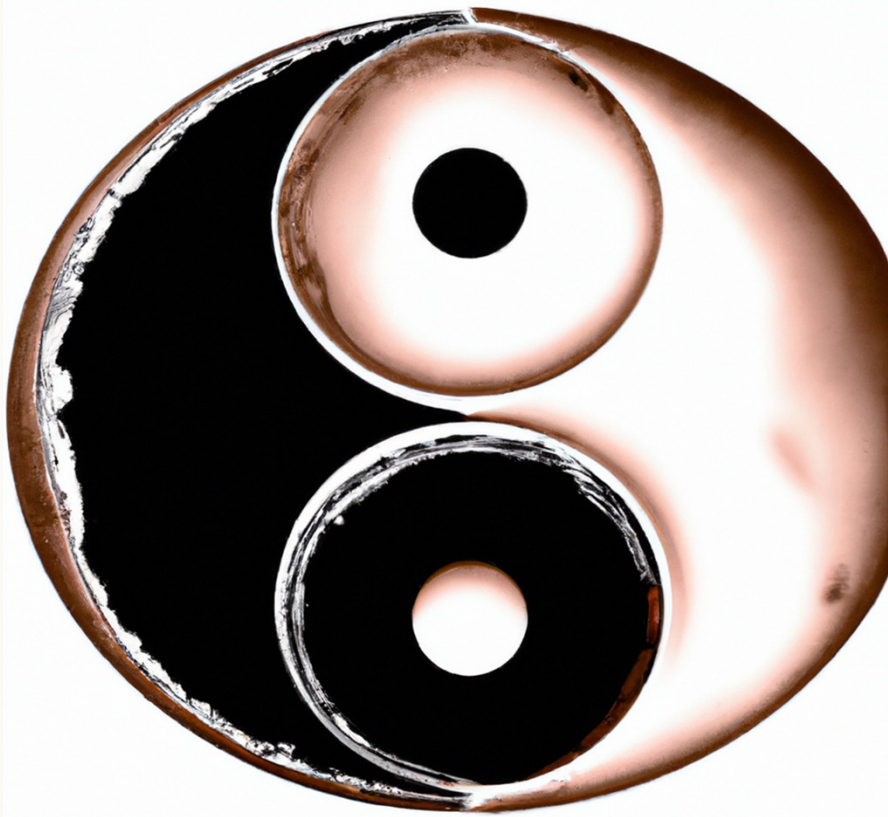
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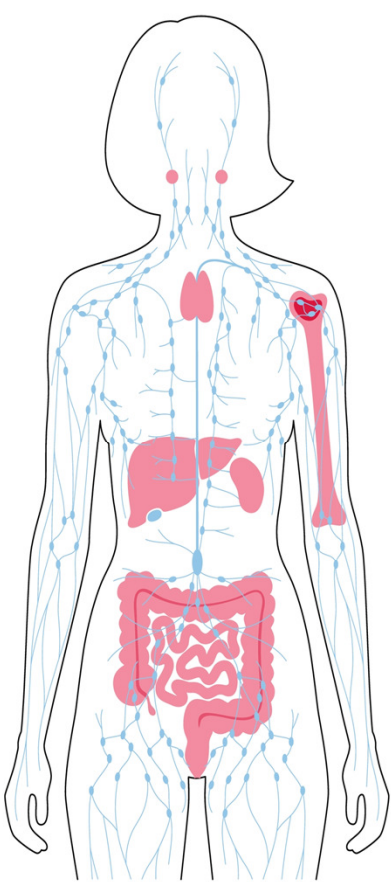
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The Yin and Yang of
Implantation: uterine
immunology and
energetics.



Supporting Fertility Patients with Dysregulated Immune Function
Written and Presented by Laura Erlich, LAc, FABORM
Healthy Seminars community talk April 15, 2024



The diagram illustrates the human immune system. A central figure of a human body shows a network of blue lymphatic vessels and nodes. Surrounding this figure are eight circular inset images, each depicting a specific organ and labeled below:

- Thymus: A cluster of blue, rounded cells.
- Tonsil: A pink, bumpy, elongated structure.
- Liver: A large, reddish-brown organ.
- Red bone marrow: A blue, porous, irregular structure.
- Lymph nodes: A network of blue, interconnected nodes.
- Spleen: A reddish, bean-shaped organ.
- Appendix: A small, pink, worm-like structure.
- Peyer's patches: A cluster of pink, rounded patches on a larger structure.

Organs of the Immune System

- Thymus
- Tonsil
- Bone Marrow
- Spleen
- Peyer's Patches
- Appendix
- Liver

**** the uterus****

Innate Immune System

- **The Innate Immune system is fully developed & present at birth**
- **Comes into play within hours of exposure to an antigen, and is activated by chemicals excreted by the antigen**
- **Response is non-specific, consisting of:**
 - **Skin (dead layers)**
 - **Mucosa**
 - **Macrophages**
 - **Dendritic cells, which will ultimately activate the adaptive immune system**

Adaptive Immune System

- Antigen-specific immunity
- Slower than the Innate response
- Antigen must first be processed (dendritic cells) and then recognized (T-helper)
 - Half go to site of injury and attack (Killer T)
 - Half go to lymph and activate B cells
- B Cells make massive amounts of antibodies
- Infection is neutralized and most cells are destroyed (apoptosis)
- A small number live on as B & T memory cells, ensuring that future exposure to this antigen will be neutralized quickly

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Autoimmune Disease

The Murphy's Law of Diseases





Autoimmunity Explained

- In order to protect our cells from immune attack, there are a multitude of checks and balances in place to ensure that immune cells are *tolerant of self*.
- On occasion, a series of unfortunate events all converge and evade this very robust system. It goes something like this:
 - An individual has a genetic predisposition
 - This human is invaded by a pathogen and the innate immune system is activated
 - The pathogen's proteins are similar in shape to proteins of the host's own tissues, or they *mimic* the shape
 - The adaptive immune system mistakenly attaches to this 'like' antigen



Autoimmunity Activated

- Once this happens, T cells will attempt to activate B cells into plasma cells, the **antibody machines**. This means that there has to be a corresponding B cell with the same intolerance. The odds are very slim, as you can see!!
- Everything that could have gone wrong, did. And now that the adaptive immune system has been activated, memory cells will ensure that antibodies are produced daily for years to come.

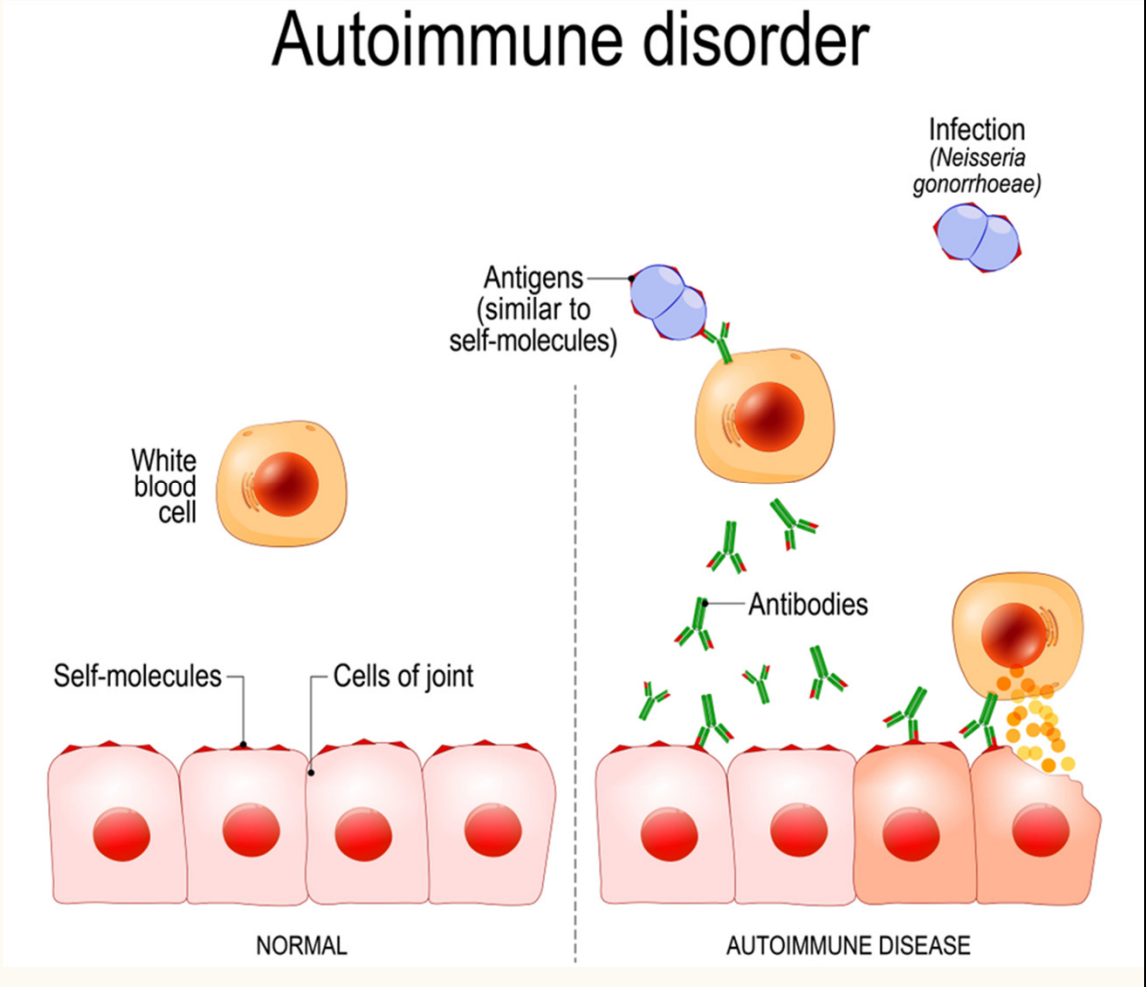
And once it's all gone wrong...

What remains is a persistent condition that must be managed

Because "self" cells are everywhere, the likelihood of reactivation is extremely high

The only way to deal with this situation is by minimizing the immune system's triggers though protective measures

Autoimmune disorder



The Immuno- reproductive System



Anatomy

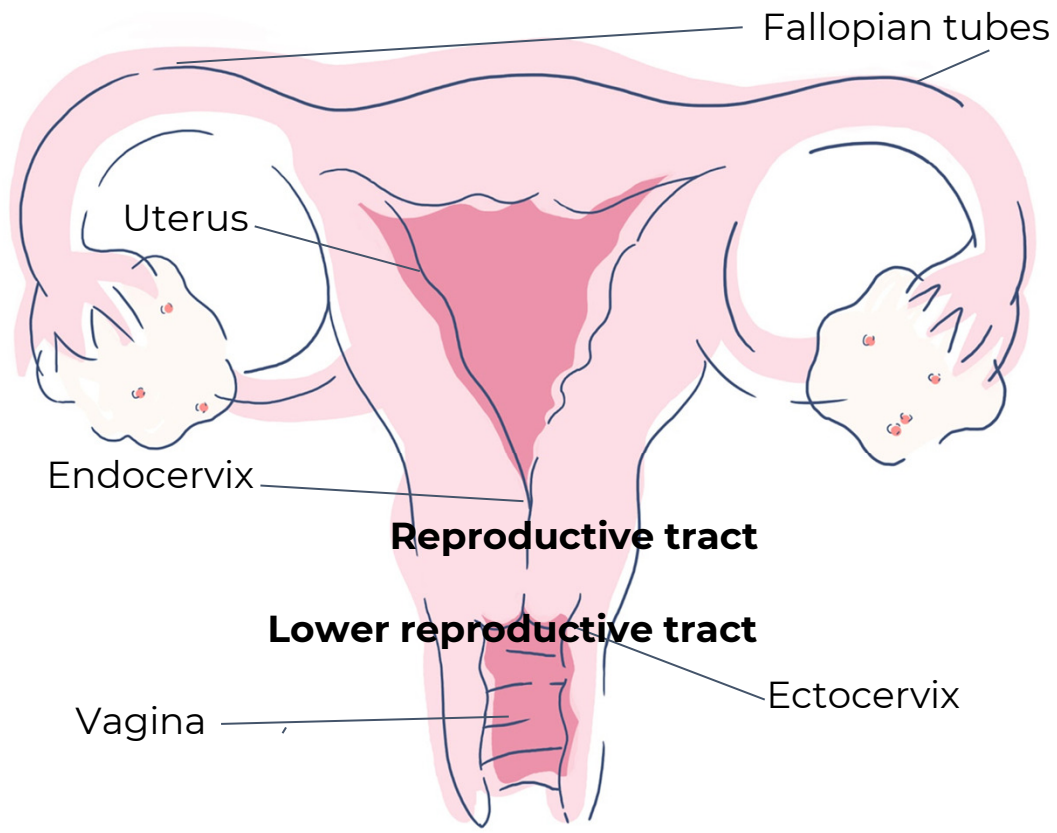
The female reproductive tracts two main functions are to **protect itself** from microbes and to **sustain a pregnancy** to term.

The upper reproductive tract is comprised of the **endocervix, uterus and fallopian tubes**

The lower reproductive tract is comprised of the **ectocervix and the vagina**

The role of immune cells in the **upper** reproductive tract are to create **immune tolerance** for an implanting blastocyst through **downregulation** of inflammation.

The role of **immune cells** in the **lower** reproductive tract are to block **microbial invasion**



Curious, isn't it??

Decidualization

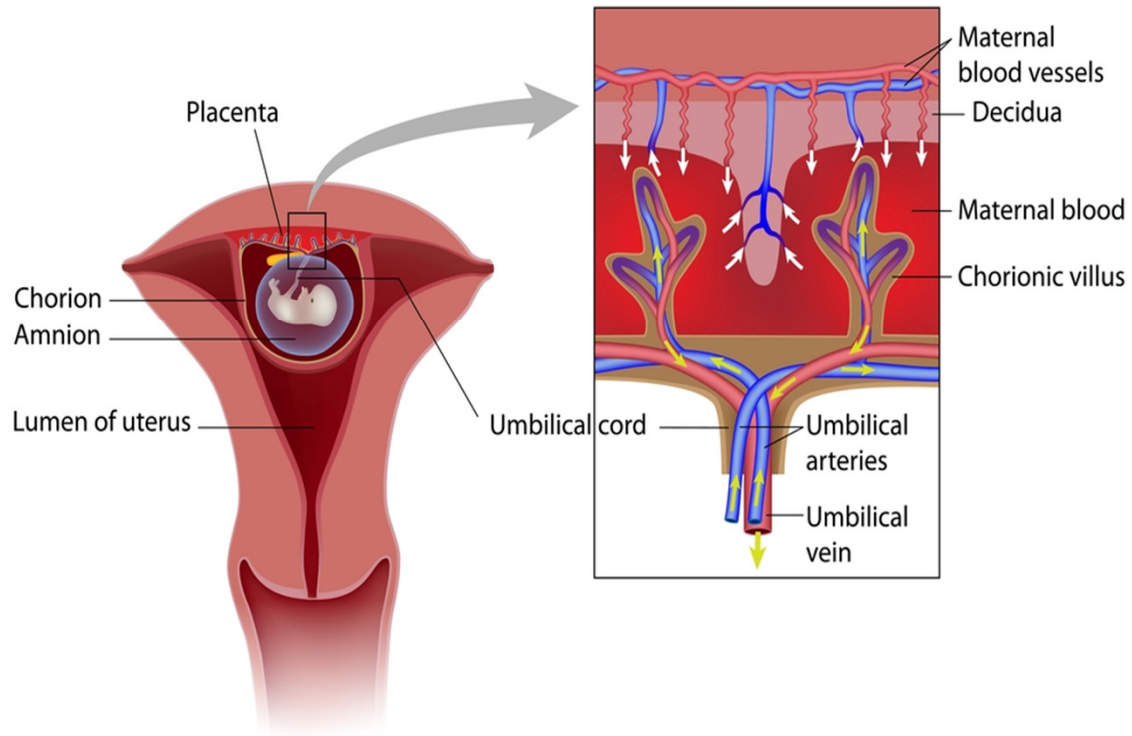
In order for implantation to occur, a complex interplay of hormones and immune cells must undergo cyclic changes in order to maintain balance between the maternal immune system and the invasive trophoblast

During the follicular phase, granulosa cells in the ovaries make estrogen, leading the thickening of the endometrial lining

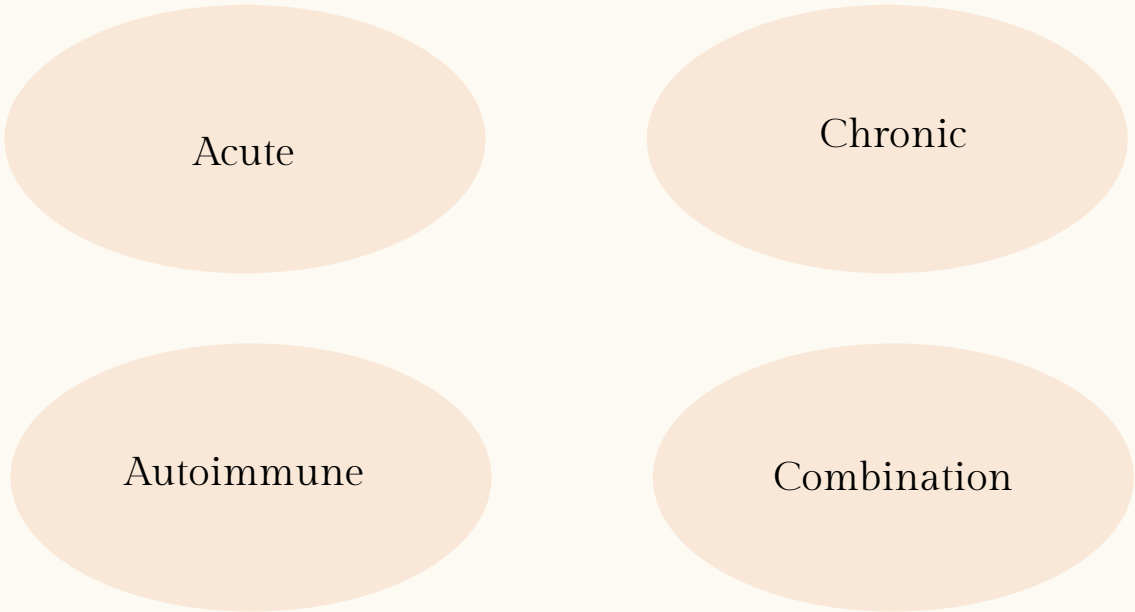
After ovulation, and under the influence of progesterone, the lining undergoes decidual transformation, creating an environment of receptivity for a blastocyst to implant

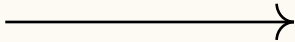
Between days 19- 23 (5-9 DPO), the decidua is formed, which will become the maternal side of the placenta in event of conception. Cellular changes allow decidual immune cells to downregulate & moderate immune response to allow for trophoblastic invasion. Immune dysregulation can lead lead to infertility due to dysregulation of the decidual immune system.

Placenta and Umbilical Cord



Types of Immune-infertility





Acute vs Chronic: inflammation and infertility



Acute vs Chronic inflammation

Acute

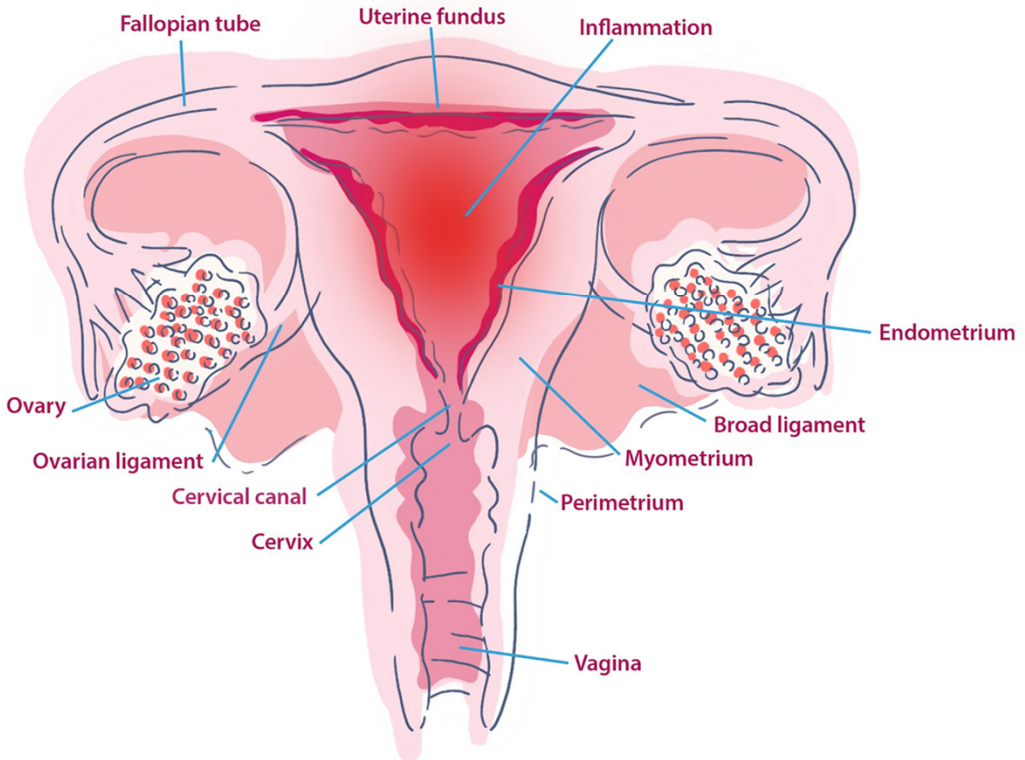
- Sudden onset of redness, swelling heat or pain
- May be accompanied by high fever
- Common with flu, injury, infection such as tonsillitis. ingrown toenail
- A gynecologic example is septic abortion

Chronic

- Low level inflammation that persists over time
- May lead to tissue damage
- Inflammation may persist in spite of no ongoing pathogen
- Primary cause of unexplained infertility

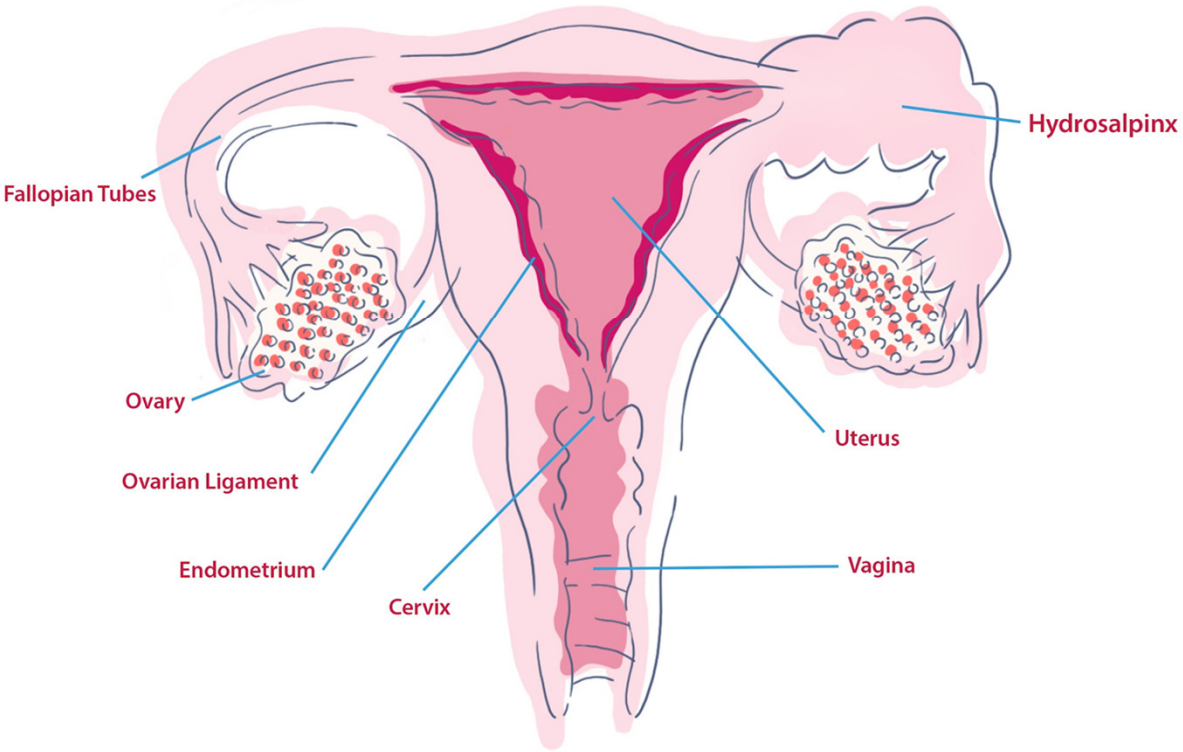
- Endometritis is an infection of the uterine lining (endometrium)
- Most common following abortion, miscarriage, c-section or very long labor
- Can be caused by STDs, tuberculosis
- Symptoms include fever, abdominal pain, discharge and/or bleeding
- Divided into acute and chronic:
 - Acute: infection from one of the above procedures
 - Chronic pelvic inflammatory disease, may be due to STDs or other low grade infection.
 - Both conditions typically treated successfully with antibiotics

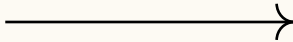
ENDOMETRITIS is inflammation of the endometrium



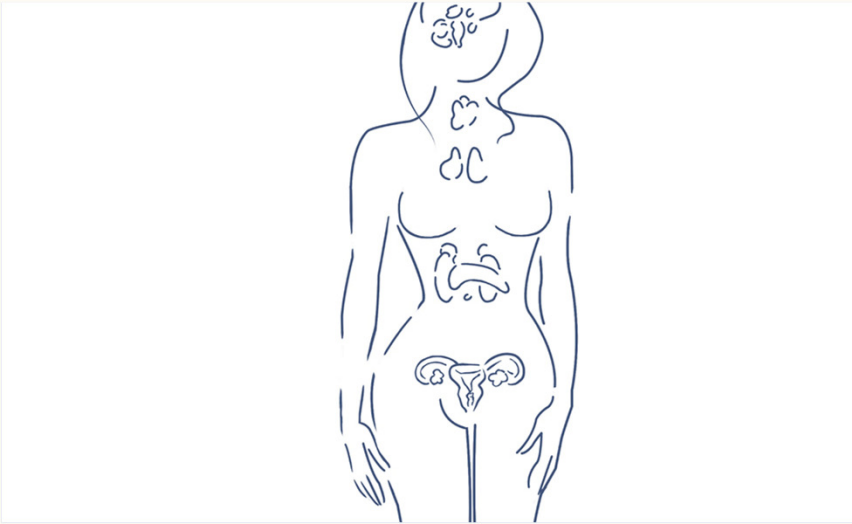
HYDROSALPINX

- A hydrosalpinx occurs when one or both fallopian tubes are filled with immunologically active fluid
- Can be associated with STD's that were improperly treated
- The fluid can 'reflux' into the uterus around implantation and prevent it
- Often requires surgical removal of affected tube(s)



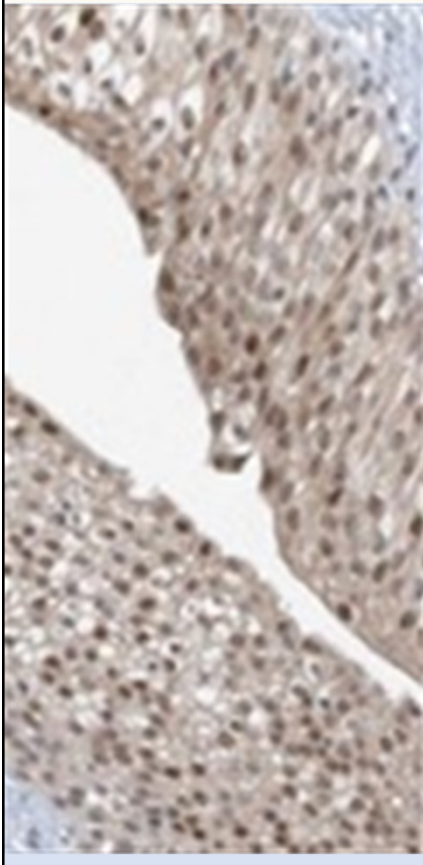


Autoimmune Infertility



Autoimmune Disease and Implantation Failure

- Implantation is a highly complex process that involves inflammation as well as the downregulation of the decidual immune system. For all intents and purposes, implantation is a mini-organ transplant, because it is allogenic & the body must tolerate the “non-self” half of the embryo.
- As long as the immune system works normally, the decidual immune system will be *tolerant* of the invading trophoblast. The maternal immune system “trips a switch,” that temporarily reprograms itself to accept something it would otherwise reject.
- Once the immune system has auto-antibodies, the ability to trip the switch is inhibited, leading to increased rates of implantation failure and miscarriage.
- Autoimmune disease may be asymptomatic, or have a *sub-clinical* presentation. This differential does not reduce the impact on implantation or miscarriage.



The role of Treg cells in immune infertility

- T cells are ever-present white blood cells that reside throughout the body, including in the ovaries.
- T-cells are matured in the thymus where they undergo exposure to antigens, teaching them to learn the difference between 'self' and 'non-self' antigens (tolerance)
- T-cells have 3 subgroups which make up essential elements of the innate immune system:
 - Helper
 - **Regulatory (Tregs)**
 - Cytotoxic
- Tregs play a central role in fertility through mediation of the maternal (decidual) immune system in implantation of an allogenic pregnancy by downregulating efforts to attack the non-self (male) aspect of the blastocyst.
- Dysregulation of Tregs are also most likely implicated in the onset and progression of autoimmune diseases and immunologic infertility

Autoimmune Diseases and Unexplained Infertility

(UI)

SLE (Lupus)

Immune system attacks tissues systemically leading to tissue damage chronic inflammation

- UI
- Preterm birth
- Pre-eclampsia
- Associated with antiphospholipid antibody syndrome

Autoimmune Thyroid Disease

The TOA (thyroid ovarian axis) is in continuous communication, esp. before and during pregnancy

Elevated Thyroid antibodies are associated with:

- Miscarriage
- Premature birth
- Fetal morbidities (metabolic, neuro, etc.)

Rheumatoid Arthritis

Chronic inflammation due the immune system attacking joints

May lead to impaired ovarian function

Women with RA are more often nulliparous/ UI

RA medications are often contraindicated in pregnancy

Flares may be cyclic

Anti Ovarian Antibodies

Antibodies against granulosa, zona pellucida and theca interna cells of ovarian follicles

Present in high numbers in patients with unexplained infertility diagnosis

Associated with premature ovarian failure, infertility and IVF failure

Western Approaches to Immunologic Infertility

IVIg or Intralipid
Infusion

Reduces uterine & systemic NK cells (natural killer cells) when immunologic infertility is implicated in RPL (downregulation of maternal immune system)

Corticosteroids

Lowers inflammation for immune modulation (downregulating maternal immune system)

Antibiotics

For the treatment of endometritis and other PID diagnosis

Blood Thinners

Baby Aspirin
Heparin
Lovenox
Used in the treatment of thromblysis (ie Antiphospholipid antibody syndrome)

Integrative Considerations for Immunologic Infertility

Acupuncture

Regulation of the neuro-immuno-endocrine system can be achieved with acupuncture.

Utilizing the Eight Extra's and the Divergent Meridians can help bring AI into latency

Herbs

Phasic formulas:

Follicular:

- Reduce inflammation
- Nourish yin/ clear xu heat

Luteal

- Nourish Spleen
- Warm Yang
- Smooth flow of qi/ calm shen

Nutrition

Focus on nourishing the spleen

Assess for leaky gut syndrome and treat

Autoimmune Paleo dietary approach (or similar)

Low glycemic index foods

Diet high in methyl donors

Supplements

Antioxidants, esp follicular phase

Antifungals

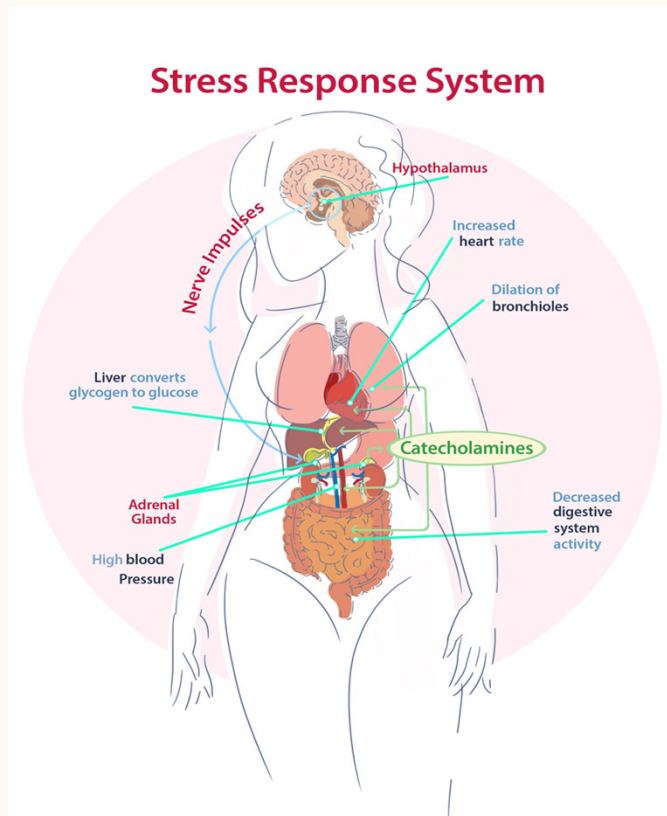
Probiotics

NAC

D*A*K

Curcumin

NAD

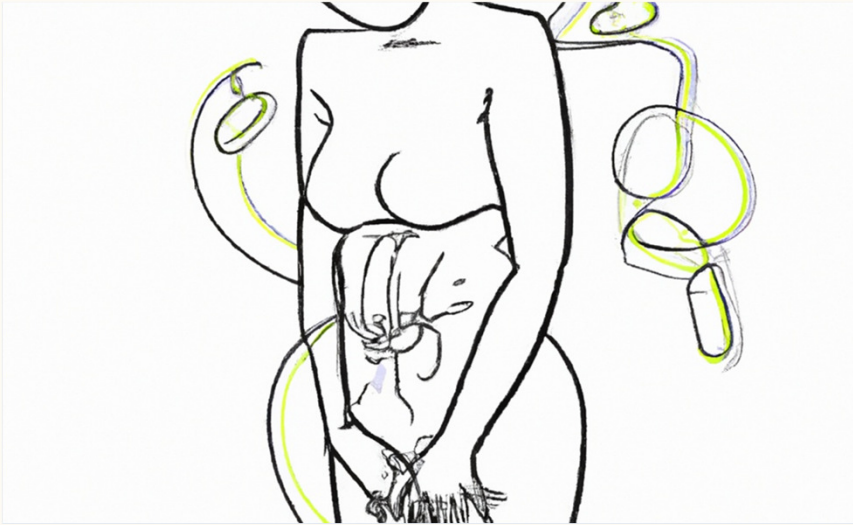


Immune health and the Spleen

The Spleen craves physical and emotional **routine** in order to thrive:

- Meal times: predictable, seated and mindful eating- balanced blood sugar levels, cultured foods
- Movement: consistent, moderate
- Rest: 11 PM or earlier bedtime, 7.5-8 hours, sleep hygiene routines .
- Meditation/ Mindfulness to manage worry and anxiety
- Regular elimination
- *Baseline* Hormone balance

—————→ Mixed Presentation Immunologic Infertility



Endometriosis

Acute

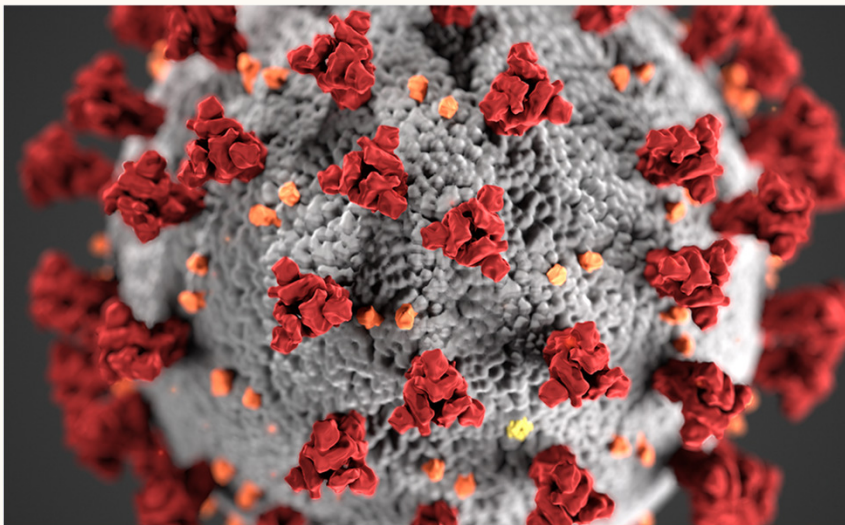
- Dysmenorrhea
- Acute inflammatory response to internal bleeding of pigmented lesions
- Joint Pain (transient)
- Acute GI issues (during menses)

Chronic

- Chronic inflammation
- Chronic pain
- Chronic hormone dysregulation
- Scar tissue disfigurement
- Mental Health Issues
- Chronic digestive issues

SARS-CoV-2 and infertility

The virus, not the vaccine
(don't even try me)



- SARS-COV-2 infection is associated with increased rates of miscarriage, preterm birth and stillbirth likely due to upregulation of the decidual immune system in pregnancy
- SARS-COV-2 likely enters the testicles and may harm male fertility
- SARS-COV-2 can attack the thyroid, leading to thyroid related fertility issues
- Much is still to be learned, though we can infer that the consequences of long Covid can lead to chronic, long term illness and inflammation

Should we “boost”the immune system? Which immune cells should we “strengthen?”

Macrophages and
Neutrophils

Do you want increased inflammation? Higher fevers? A BIG immune response to every small pathogen you encounter?

NK Cells

These little psychos will be happy to kill cancer cells but left unchecked may also kill You!

Dendritic Cells
Or T&B's??

More of these guys would lead to more frequent activation of adaptive immune system and potentially increase the risk for AID,, not to mention exhausting resources

Mast Cells?

Yes! Let's crank up that allergic reaction!

Key Takeaways



- Your Innate Immune System came fully assembled at birth
- Your adaptive immune system has a myriad of checks and balances to prevent it from attacking 'self'
- Sometimes that goes wrong and results in autoimmune disease
- The decidual immune system is impeded in its ability to downregulate in the presence of immune activity (auto or otherwise)
- Deliberate exposure to pathogens DOES NOT make your immune system stronger. Play in the dirt instead, but please don't be cavalier about viruses.
- Exposure to pathogens increases the risk of molecular mimicry and autoimmune disease, and the worse the disease, the greater the risk.

Healthy Seminars

Mentorship Program
The Integrative Fertility and Reproductive Medicine



Laura Erlich

www.HealthySeminars.com

Program Starts
April 30



SCAN ME

What can you expect?

- Participants will gain confidence and deep insight into both eastern and western approaches to the treatment of infertility
- With an emphasis on integrating holistic and allopathic modalities
- Practitioners will come away with a deeper understanding of all aspects of reproductive medicine and will be well prepared to sit for the ABORM exam if desired
- ABORM study groups will be created as desired, and group tutoring sessions for the exam may be arranged
- Participate in live webinars, Q&A sessions, interactive expert interviews, office hours, and private tutoring (one session is included in the program)

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LAURA ERLICH, LAc, FABORM



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