Successfully Treating Embedded Infections in Chronis Inflammatory Response Syndrome (CIRS)

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Learning Objectives

1. Explain the mechanism of how infections become chronic
2. Explore how infections hide from detection and treatment
3. Identify the genetic factors which are common in chronic embedded infections
4. Consider other factors which contribute to chronic embedded infections

Acute versus Chronic Infections

ACUTE

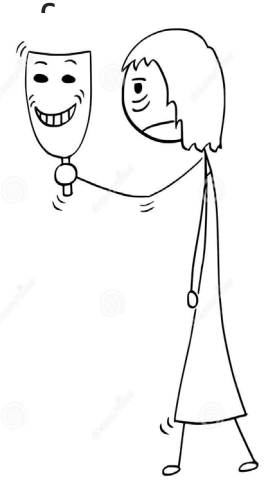
Acute illnesses generally develop suddenly and last a short time, often only a few days or weeks.

Treatment aimed at cure and expectation is that patient will fully recover.

CHRONIC

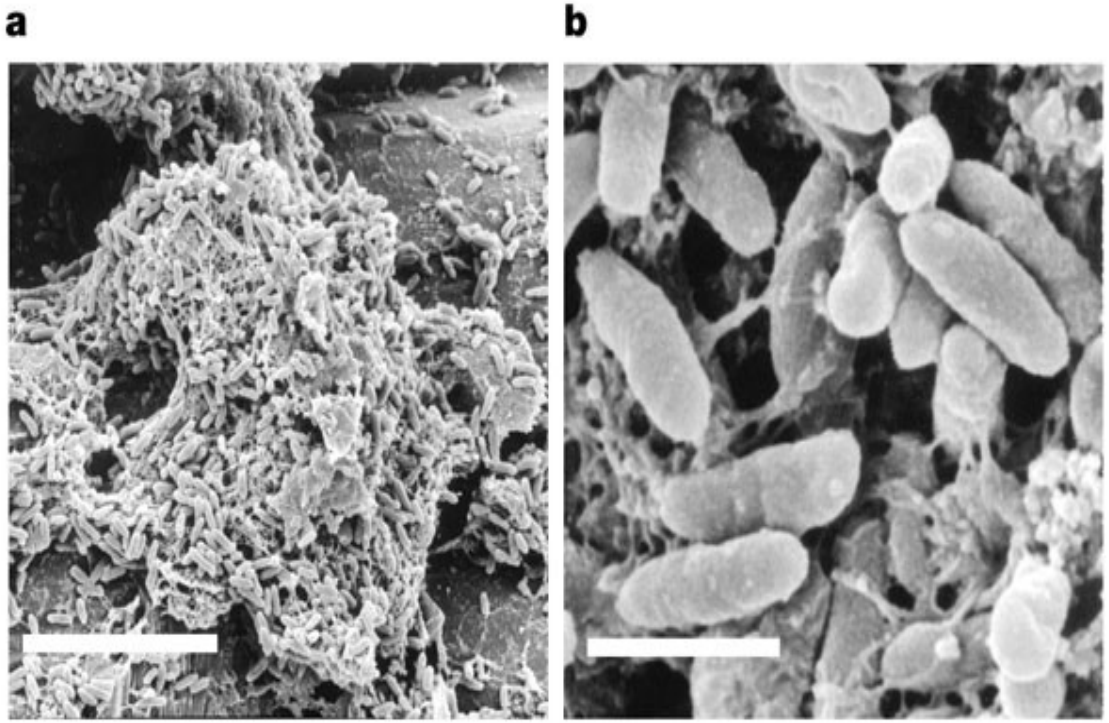
Chronic conditions develop slowly and may worsen over an extended period —months to years.

Treatment is focused on management of symptoms and quality of life without expectation patient recovery

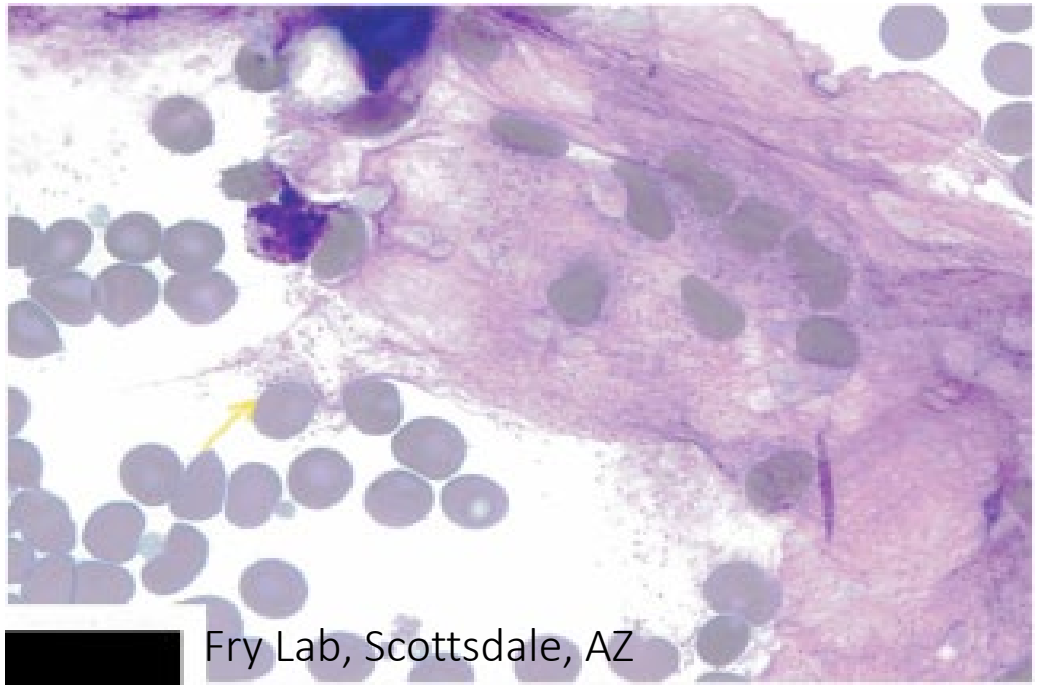


Biofilms

Produced by Bacteria Themselves -Pseudomonas [17]

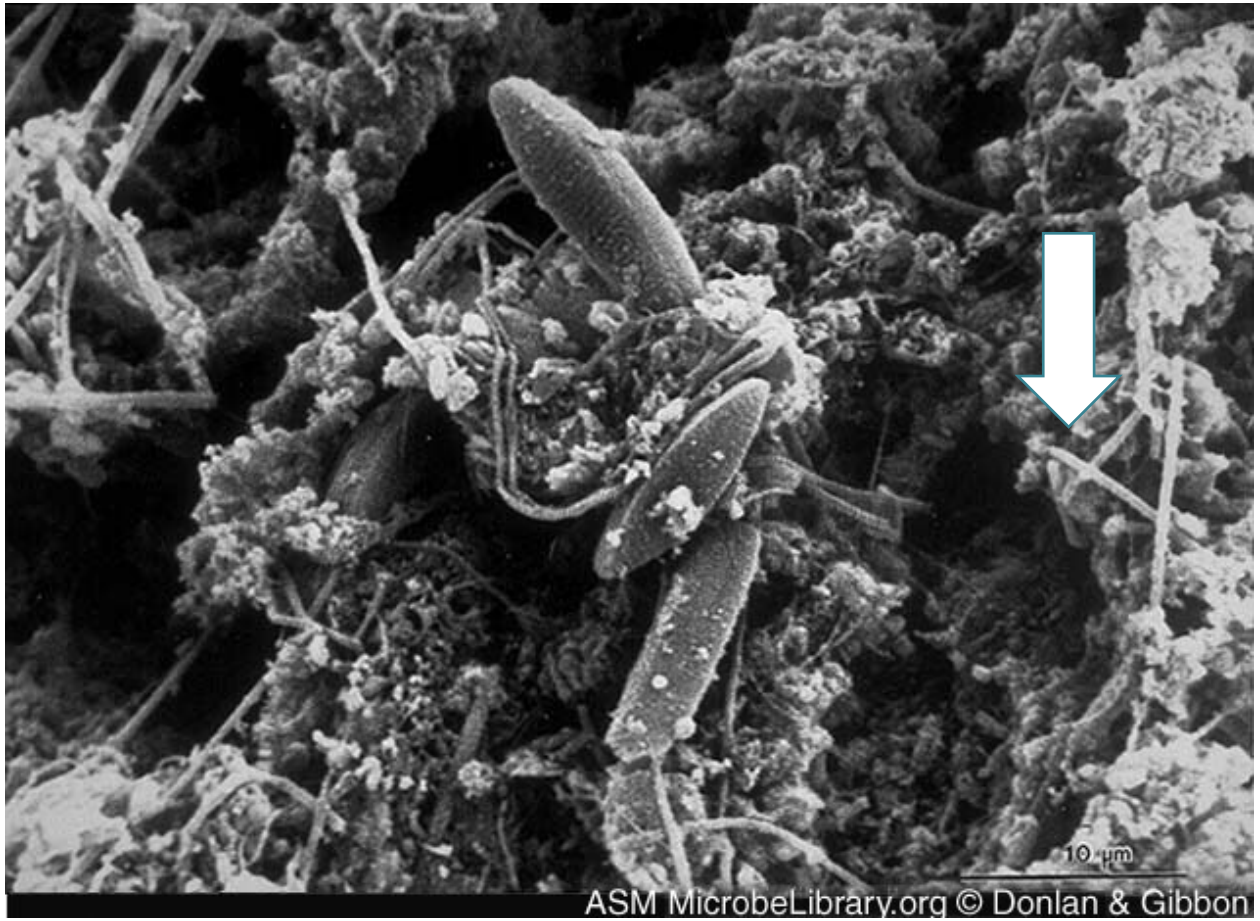


Produced by the Host – Blood Smear



Fry Lab, Scottsdale, AZ

Electron Micrograph of a Biofilm



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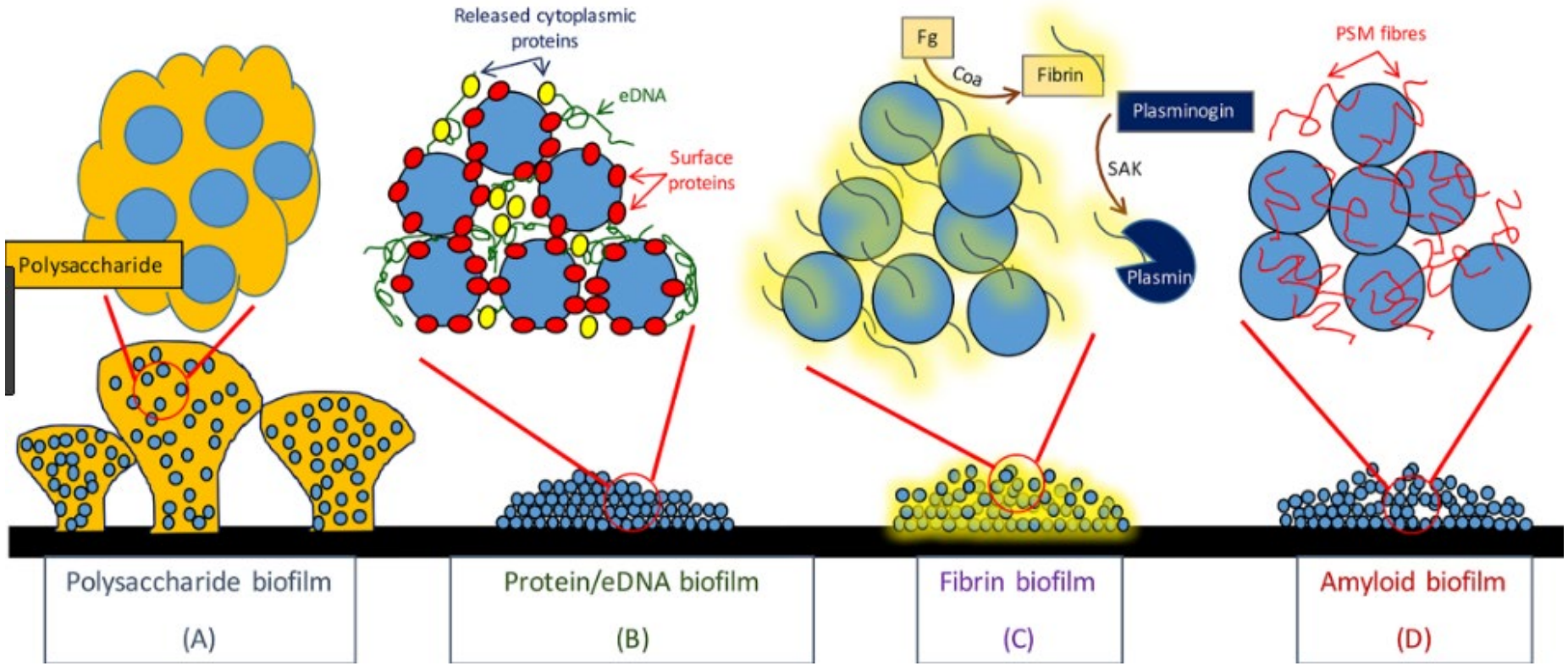
Types of Biofilm



Biofilm Diseases

RECOGNIZED

Chronic wound infection	Chronic sinusitis	Chronic urinary infection
Cystic fibrosis	Endocarditis	Middle ear infection
Kidney stones	Medical devices infections	Osteomyelitis
Periodontal disease	Prosthetic joints	Prosthetic heart valves

POSSIBLE OR PROBABLE

- Atherosclerosis
- Alzheimer's disease
- Lyme disease
- PANDAS or PANS

How Biofilms Protect Bacteria

- Limitation of antibiotic diffusion through the matrix – Beta-lactams penetrate better than aminoglycosides but may trigger L-forms
- Transmission of resistance genes within the community
- Expression of efflux pumps
- Antibiotics able to diffuse can be inactivated by the pH inside biofilm.
- The presence of persister cells – dormant and not responsive to antibiotics

Genetic Variations in the Chronic Embedded Infection

HYPERCOAGULATION GENETICS

PAI-1 4G deletion – found most often (considered so rare it isn't routinely checked by hematologists)

Lp(a) – Found in the next highest numbers – most difficult patients to treat

Leiden Factor V – found least often

OTHER SNPS FOUND

Vitamin D Receptor (VDR)

Cysteine Beta Synthase (CBS) – the upregulating ones

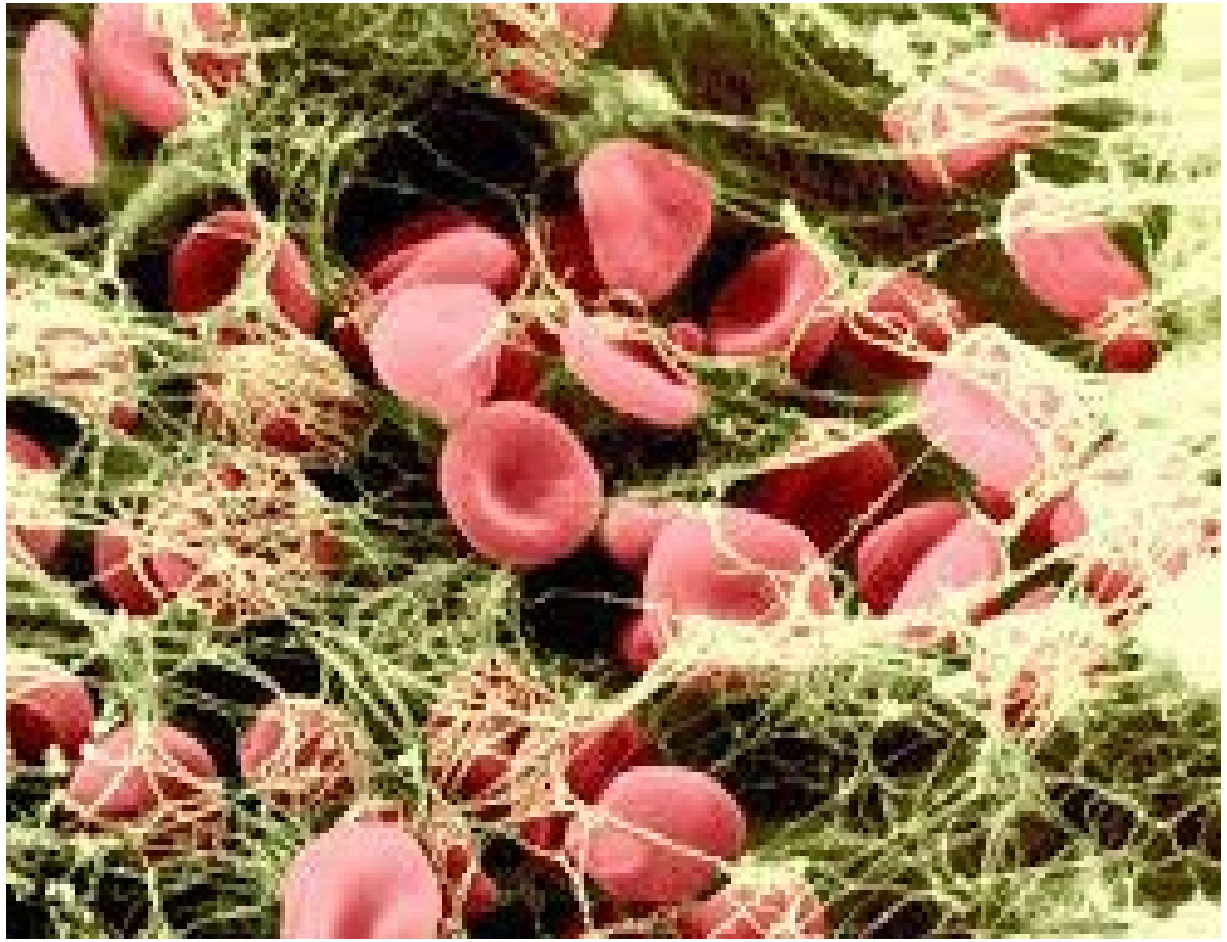
CYP450 1B1 – upregulating and associated with converting estradiol to estrone

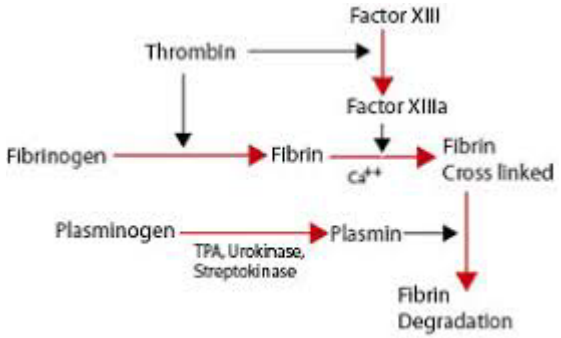
High percentage had additional SNPs contributing to high homocysteine: **MTHFR, MTR, MTRR, ACHY, SHMT, and/or ACAT in addition to CBS**

What's Fibrin Got to Do With It?

In response to infection and inflammation, the body responds with extra fibrin production. This fibrin not only contributes to atherosclerotic plaque but is utilized in making biofilms to wall off infection. These biofilms can make the bacteria undetectable by the immune system and antibiotics less able to penetrate.

What is fibrin and how is it made?





Measurements Acute Fibrin Production

How do you know if someone is producing high fibrin?

prothrombin time (PT)

Activated Partial Thromboplastin Clotting Time (aPPT)

Elevated Prothrombin Fragments 1+2

Upregulated Thrombin/Anti-thrombin (T/AT) Complexes - keeps clotting in check

Measurements of Chronic or old Fibrin Production

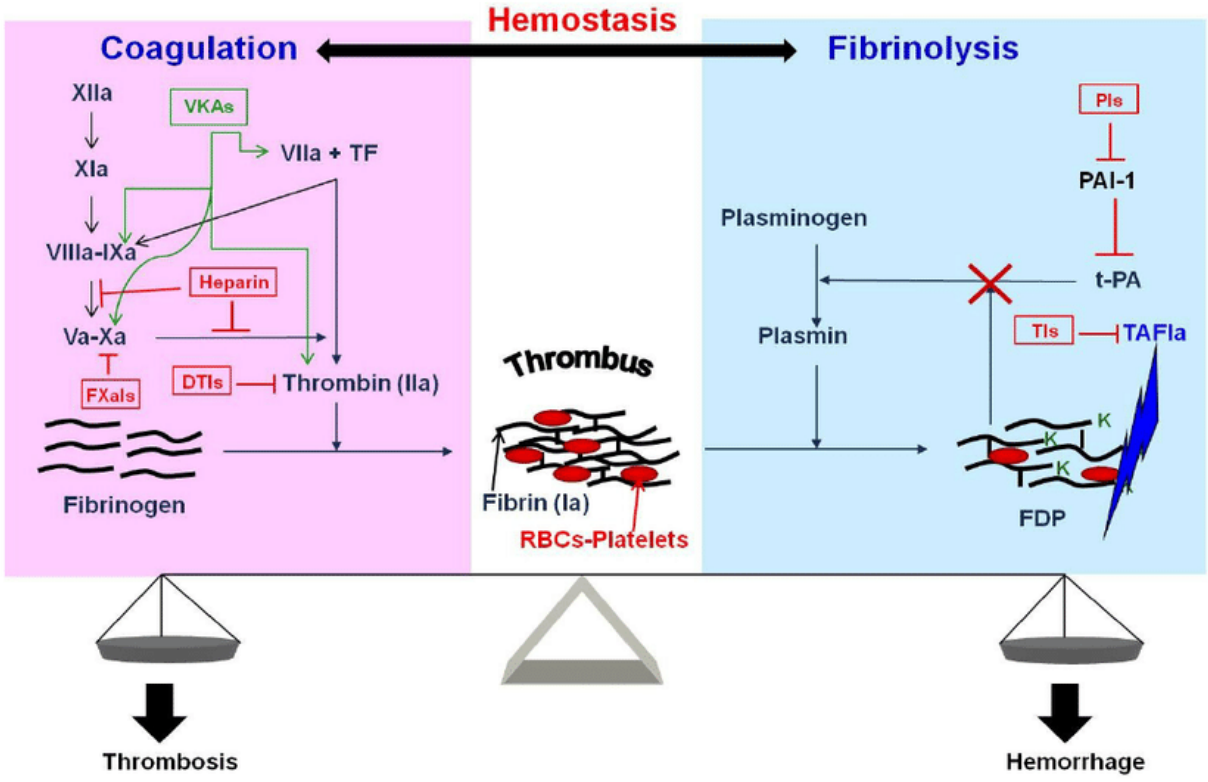
How do you know if someone has been producing fibrin in the past?

Fibrinogen Activity – reflects build up of old fibrin

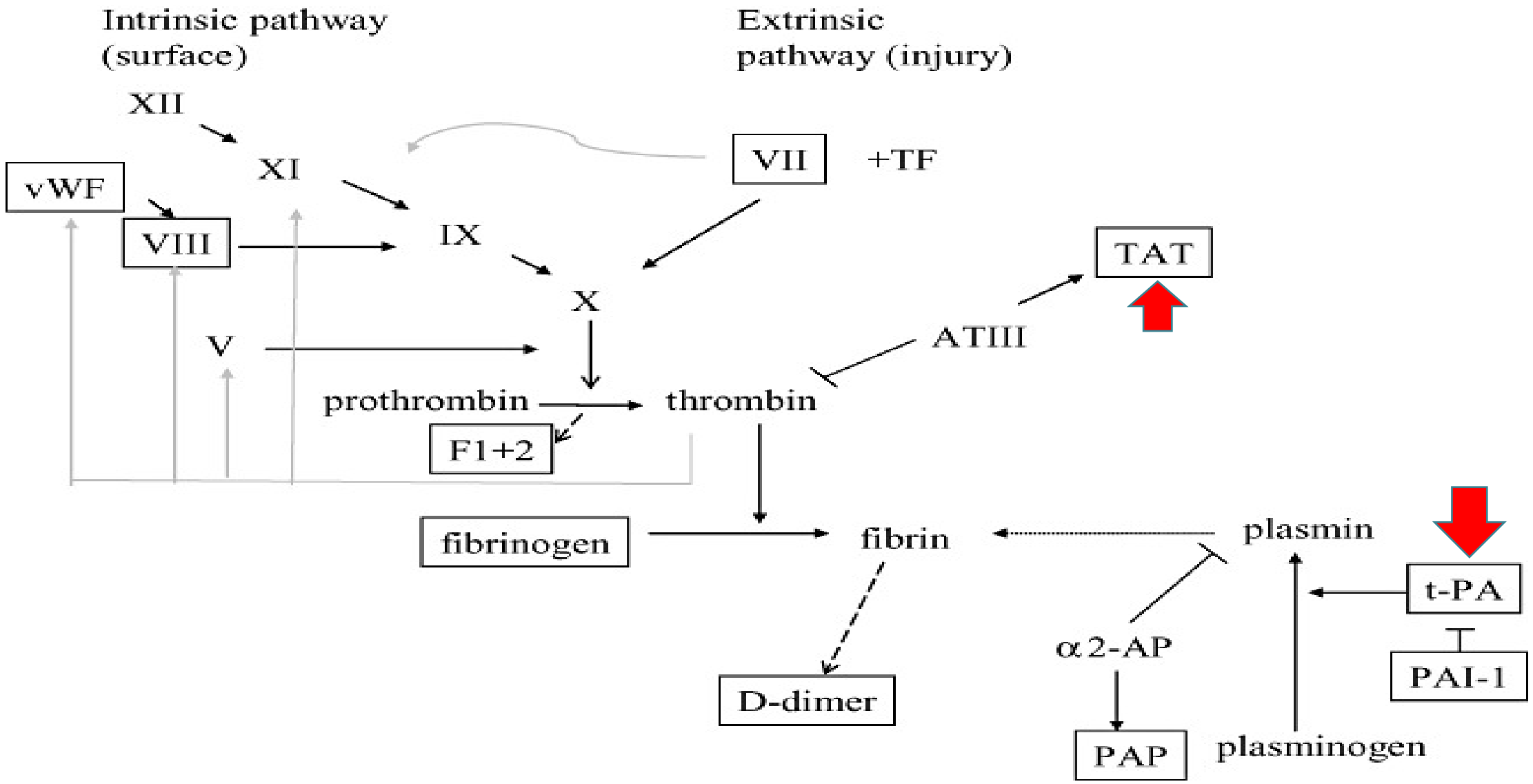
Elevated Alpha-2 Antiplasmin (prevents upregulation of T/AT Complexes)

Elevated D-Dimer – degradation product

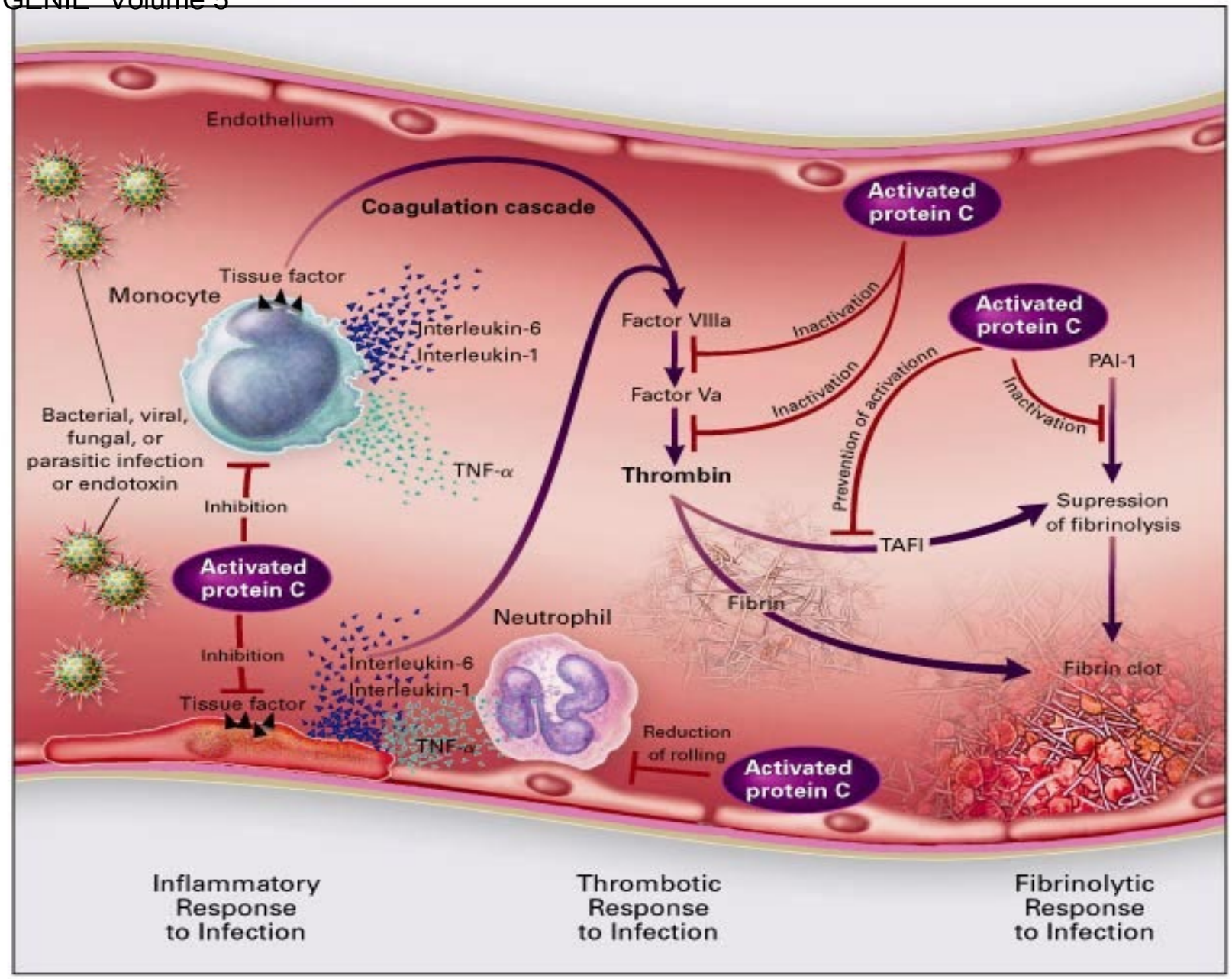
How This Works



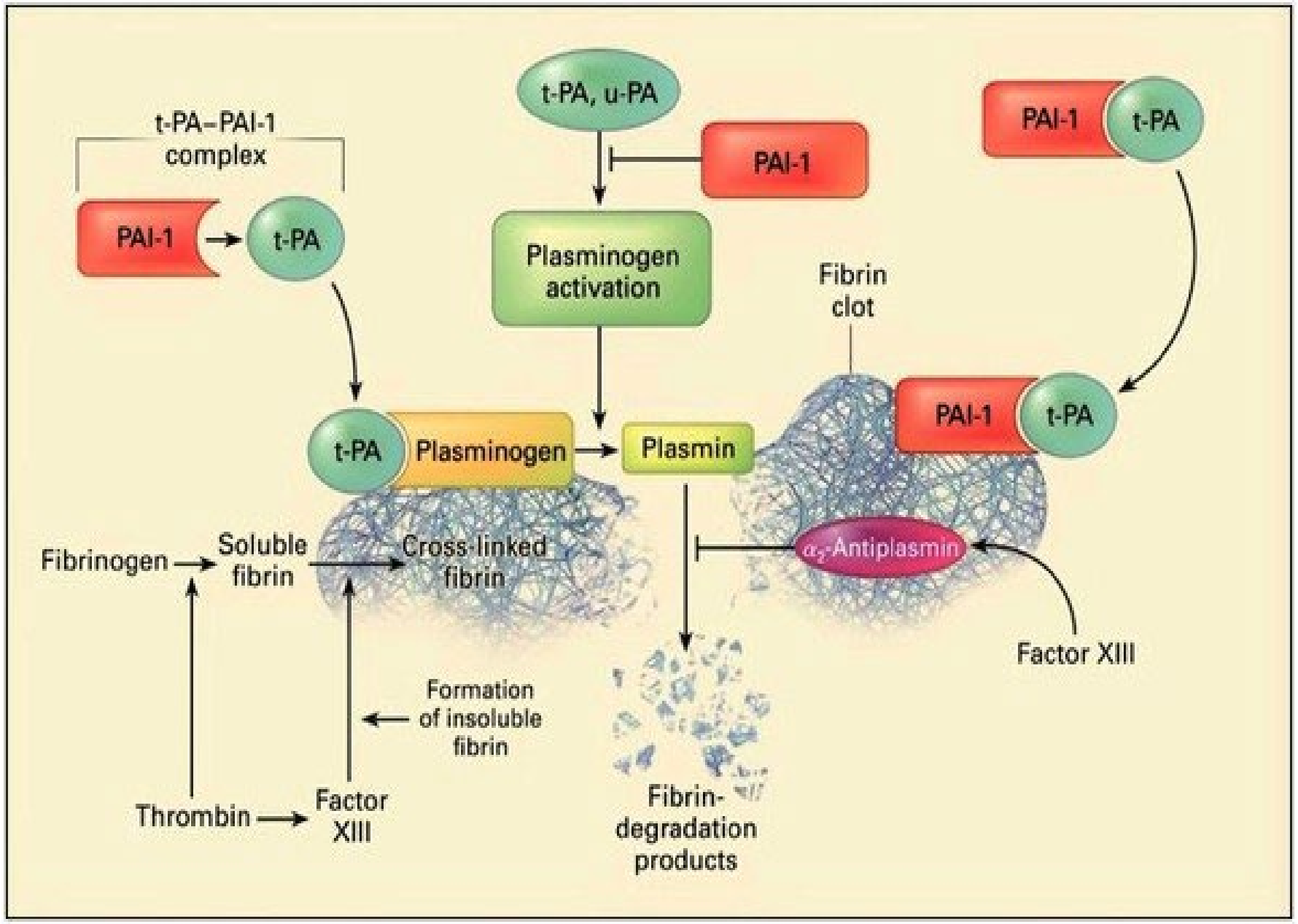
Fibrinolysis by T/ATs and t-PA



How the Players Play Leiden Factor V (APCR) 33



How the Players Play PAI-1 [33]



Lipoprotein(a)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Those with Lp(a) elevations are generally thin and may be on the tall side.

Associated with coronary disease – Lipoprotein (a) binds to tPA, inhibiting fibrinolysis.

Elevations contribute to significant % of LDL on lipid panel, but because Lp(a) isn't lowered by diet, exercise, or statin drugs, you won't significantly reduce cardiac risk by simply lowering total LDL.

October, 2018 – own ICD 10 code assigned: E78.41 (screening code is Z13.220)

Problems Associated with these Mutations

Recurrent miscarriages,
PCOS, endometriosis [34, 35]

Fibromyalgia [36]

DVT and PE
(post surgical and prolonged sitting) [37, 38]

Other chronic infections – sinusitis, prostatitis, ear infections in children

Other possible problems caused my hypercoagulation - PANDAs?, Raynaud's?

Chronic Inflammatory Response Syndrome

What does this have to do with embedded infections?

MODEL:

Coagulation defects - Leiden Factor V, PAI-1, and Lp(a) + Pathogens =

Fibrin Generation =

Biofilms =

Chronic infection

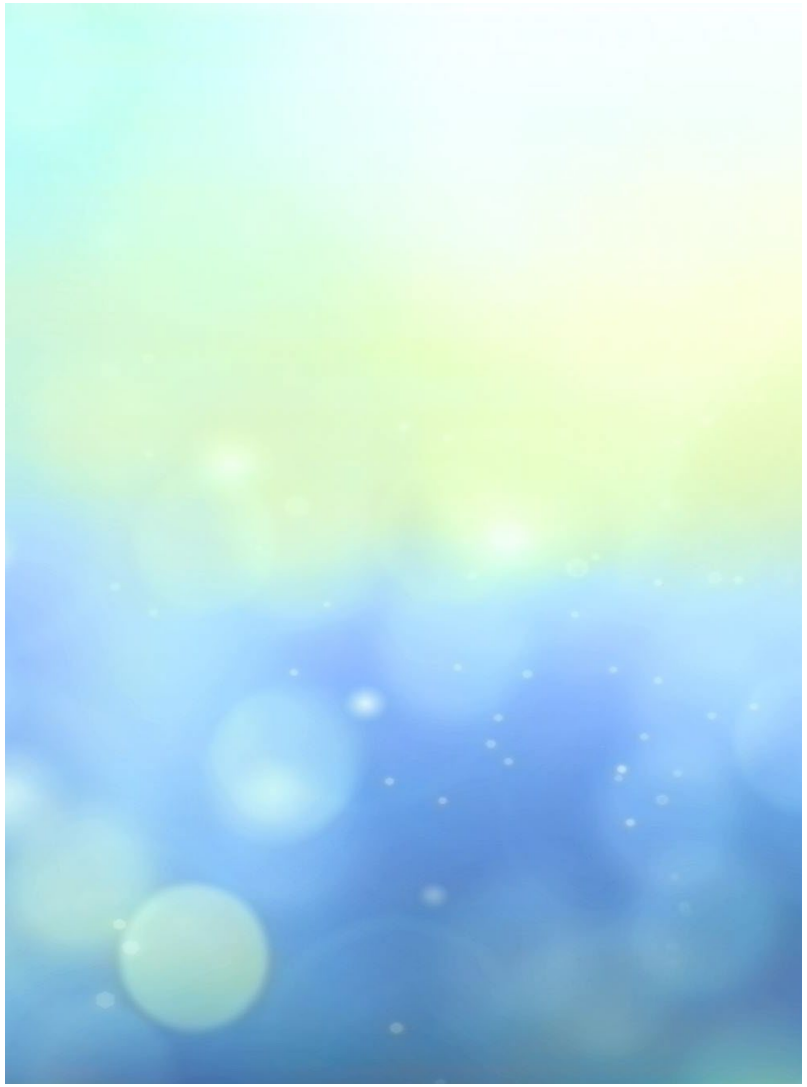
Vitamin D

It's more than

It's more than sunshine!

Vitamin D Receptor Mutation

- 100% of my patients who did genetic testing had a VDR mutation
- These patients make vitamin D as well as others, but they can't hold onto it as well – they will always need to supplement
- All of them who weren't supplementing, had levels in the low 30's or lower, even at the end of summer.
- The optimum range should be above 50 since the reference range didn't exclude those with a VDR mutation and the reference is skewed to the low end
- Vitamin D is the precursor of 17-OH progesterone, needed for cortisol and progesterone synthesis

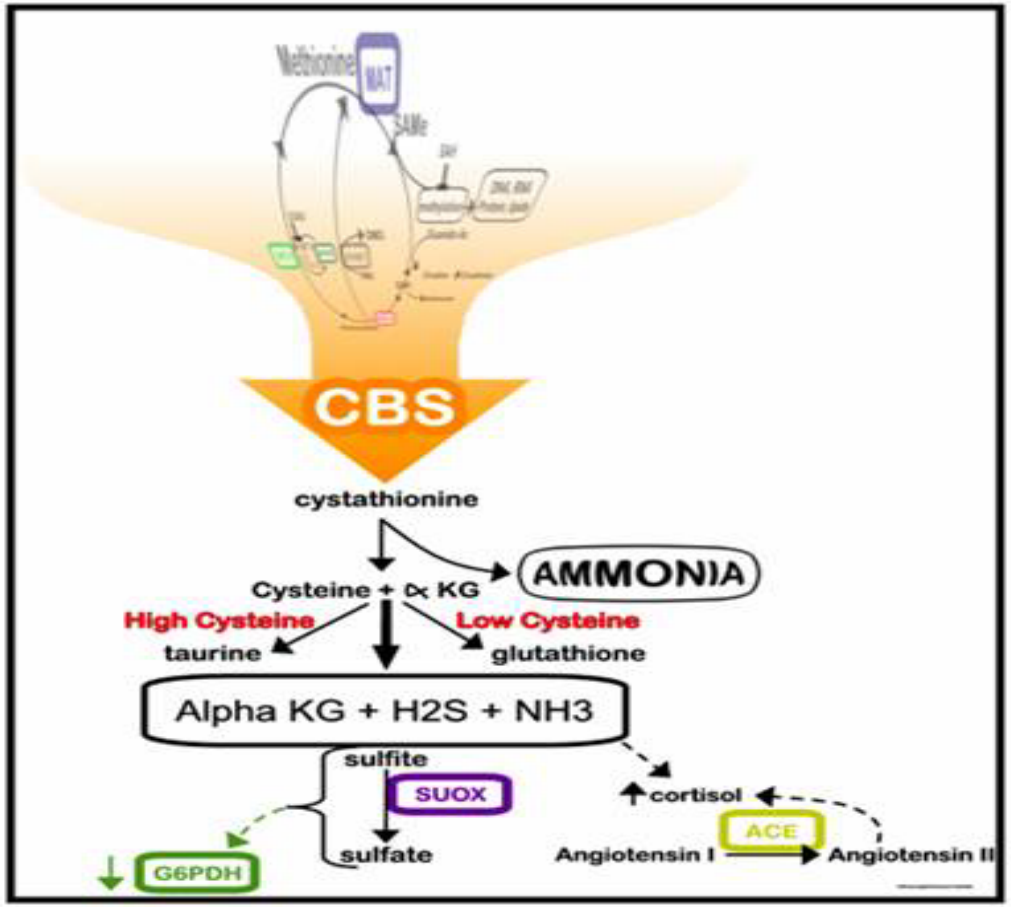


CBS (Cystathionine Beta Synthase)

If there is an upregulating CBS mutation, converting homocysteine to cystathionine

Often homocysteine and cystathionine convert too quickly to taurine, leaving not enough glutathione for the body.

Glutathione deficit is a reason that those with chronic illness suffer from recurrent bacterial, viral, parasitic, and fungal infections, cancers, and toxic metal sensitivities



METHYLATION MAP

courtesy of

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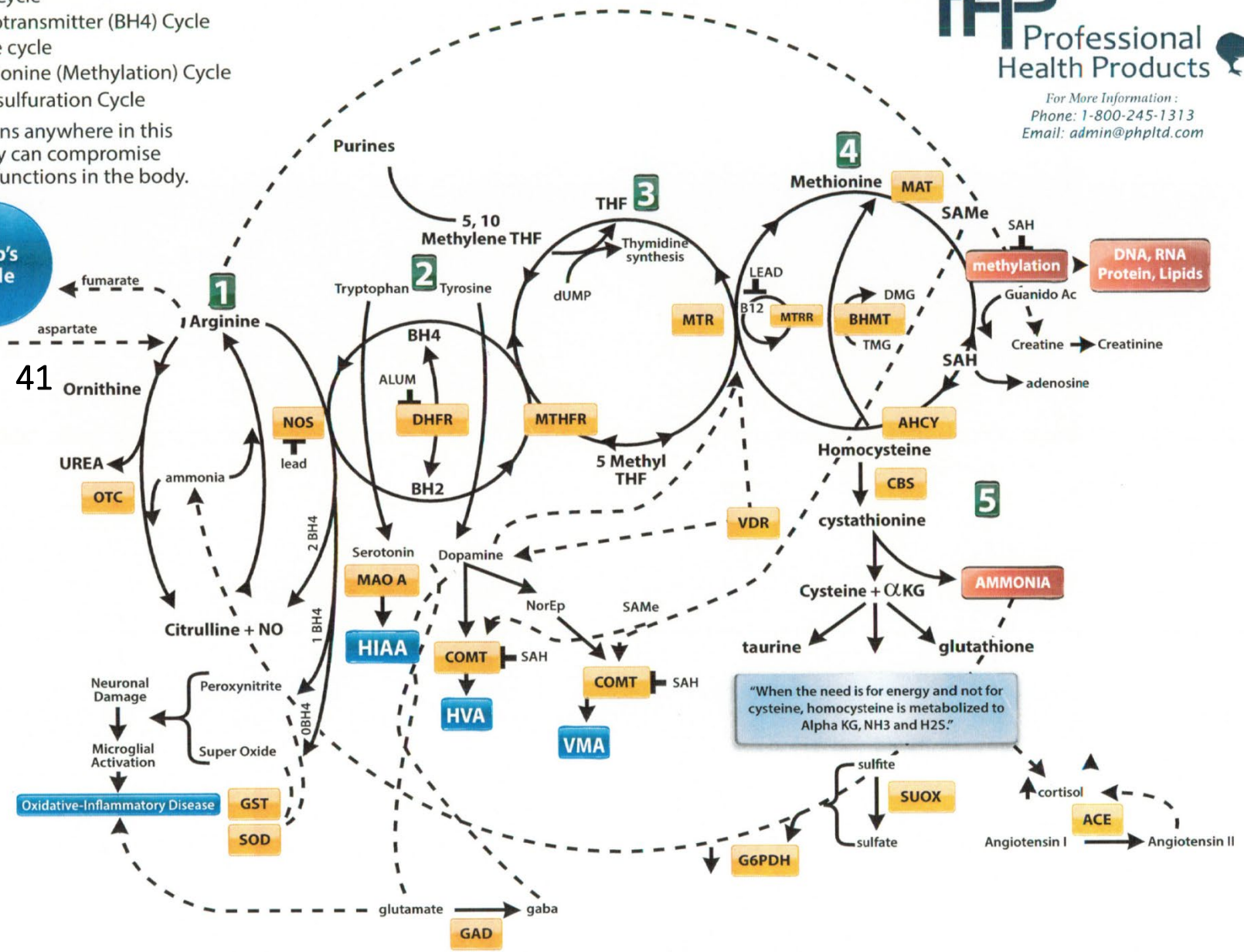
1 Urea Cycle
2 Neurotransmitter (BH4) Cycle
3 Folate cycle
4 Methionine (Methylation) Cycle
5 Transsulfuration Cycle

Mutations anywhere in this pathway can compromise critical functions in the body.



SurvivingMold / CIRSx "I Dream of GENIE" Volume 5
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Expanding the Clinical Toolbox

Diagnostics:

GENIE testing

Vitamin D 25-OH (stored form)

HNK 1 (CD57) panel – if <100, consider CIRS contributing to inadequate immune function

Hypercoagulation testing – LabCorp panel 504723 – will need to enter manually – checks for fibrin generation, ability to break down fibrin with T/ATs, and screens for Leiden Factor V and PAI-1 with reflex to genetic testing as well as elevations in Lp(a) and homocysteine (should be <10)

Additional testing as indicated by history and symptoms – mold, Lyme and co-infections, thyroid, adrenals (Vitamin D precursor of 17-OH, used for cortisol and progesterone synthesis), and hormones (all patients tested with 23 and Me had CYP 1B1 mutation as well – estradiol converts to estrone contributing to estrogen dominance, especially with low progesterone production due to low vitamin D.

How are these patients treated differently?

- Chronic infection treatment utilized vs repeated acute infection protocols
- Vitamin D 25-OH kept between 50 and 100
- Biofilms addressed based on genetics
- Preventative protocols for those prone to chronic infections

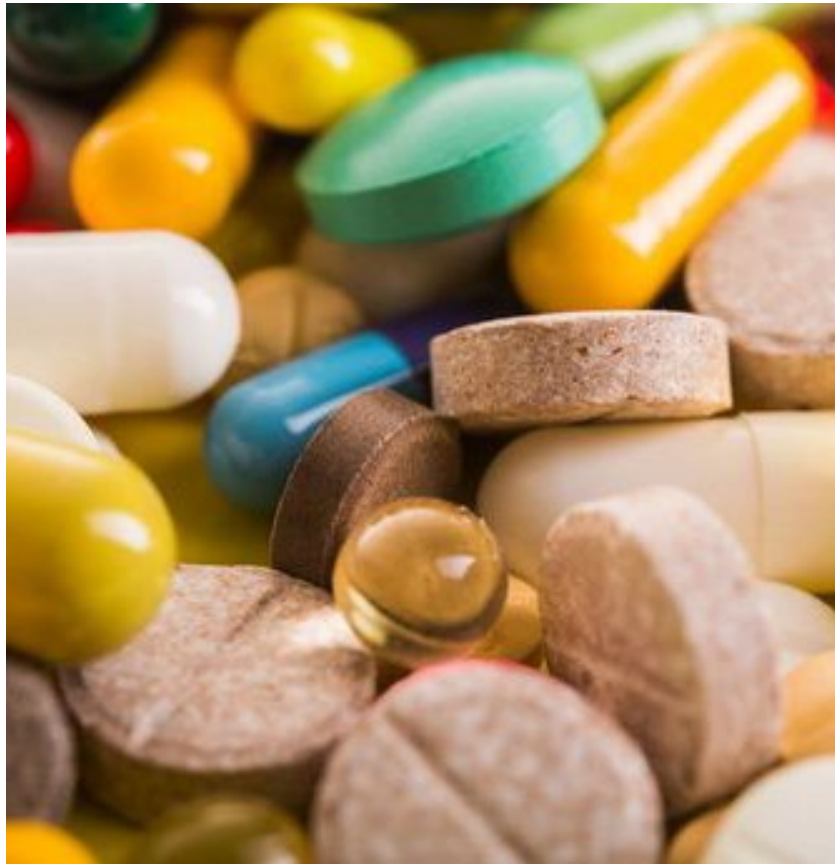
Helpful Supplements:

Vitamin D – 100% of my patients needed 5,000 u/day. If not coming up check RBC Magnesium – may do better with transdermal patches (Patch MD)

Ornithine – binds ammonia – take a bedtime but can dose tid if brain fog related to high ammonia

NRF2 –

- Helps prevent bacteria from embedding in bladder wall [42]
- Downregulates NF-kB that contributes to kidney damage from mold toxins [43, 44]



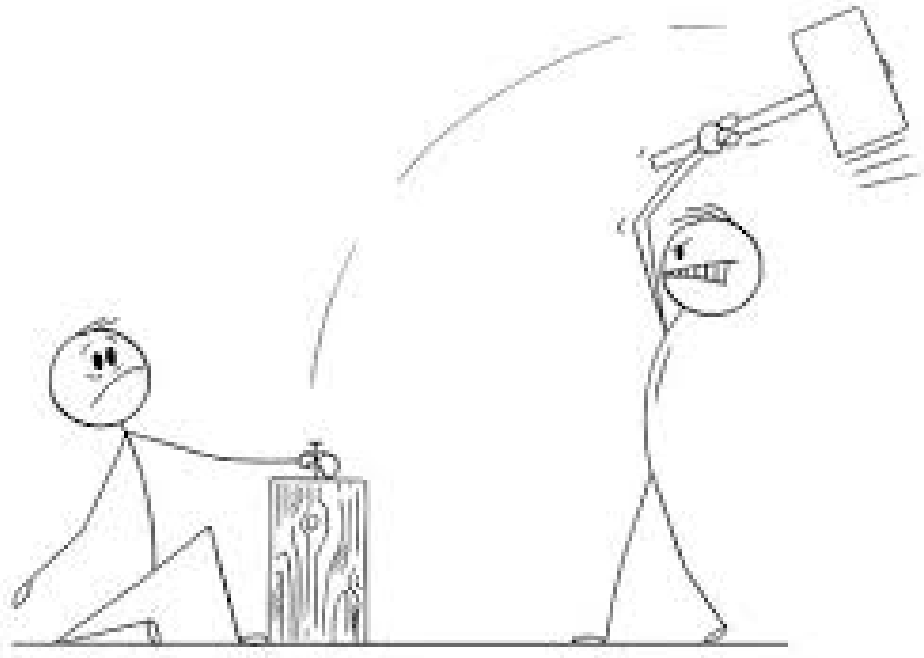
Biofilm Disrupters

Kirkman Biofilm Defense – helpful to start 5 days before first urine collection – 1 po bid

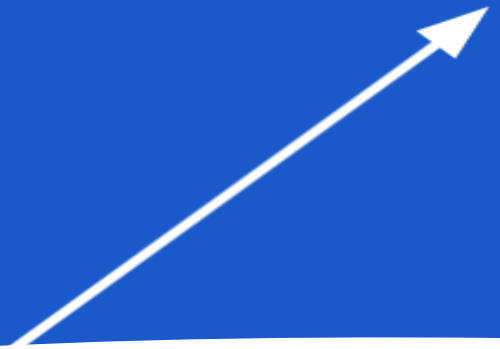
Biofilm phase 2, Advanced by Priority One if Klebsiella or pseudomonas found with testing – good studies on effectiveness of bismuth on these biofilms produced by these pathogens

Boluoke (lumbrokinase) – everyone with Leiden Factor V, PAI-1 4G deletion, or elevated Lp(a). Dose based on Alpha-2 Antiplasmin(A2AP) level.

Niacin if elevated Lp(a) – lower dosages will be needed if Boluoke also used (Build slowly with lower dosages)



Expectation



Reality

Multi-factorial - need to identify and address as many contributing factors as possible – not just treating with the “right” antibiotic

This is a process – repeated urine testing and treating needed as biofilms are broken down and more infection(s) come out. May take 1-2 years depending upon genetics and length of time infection(s) have been embedded

Progress will NOT be steady – it’s like a dance – 2 steps forward and 1 step back and sometimes 1 step forward and 2 steps back – compare current symptoms to 3 months or 6 months prior

THANK YOU!

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