Section 2. Variations in Connective Tissue

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2. Variations in Connective Tissue

There are many variations in connective tissue that occur in human and animal species. Two cautions: 1) Connective tissue variations are framed by science and medicine as “disorders.” We use the term “variation” to resist pathologizing human diversity as “disease.” However, it is important to hold in tension that many of these variations are labeled as disease/disorder because they produce pain, suffering, and other impairments that diminish wellbeing. We will proceed with the term variation while honoring the lived experience of people and animals who have variations in their connective tissues. 2) Scientists using the reductive model of science and medicine have categorized connective tissue disease into two types–genetic and acquired/autoimmune–but some acquired/autoimmune connective tissue diseases are also heritable. Moreover, genetic variants in connective tissue often have impacts on immune function that can produce autoimmunity (an immune response to one’s own tissues). This is a clue that we should be critical of the categories used to describe variations in connective tissue. The categories scientists use are socially constructed and reflect the culture and politics of the context in which scientists live and work.

2 - A: Connective Tissue Variations in Non-human Species - Cats with EDS

https://www.youtube.com/embed/2Ca1YIFnkRQ?si=YhWKF-JdDVGdAmKu

Video: https://www.youtube.com/watch?v=2Ca1YIFnkRQ

Feline Cutaneous Asthenia, Feline Dermatosparaxis, or Feline Ehlers-Danlos-like Syndrome are rare variations in collagen that can manifest as very elastic skin, joint instability, and wound healing problems in cats. In 2022, Keiner et al. found multiple variations in COL5A1 gene (collagen type 5) which may cause feline EDS. Cats with these rare variants often require expensive veterinary care, which many owners cannot afford. As such, cats with these conditions are often euthanized.

2 - B: Humans and Connective Tissue Variations

https://www.youtube.com/embed/Q3V1ItCnfas?si=QMEwA5iiHZfnfXpH

Video https://www.youtube.com/watch?v=Q3V1ItCnfas

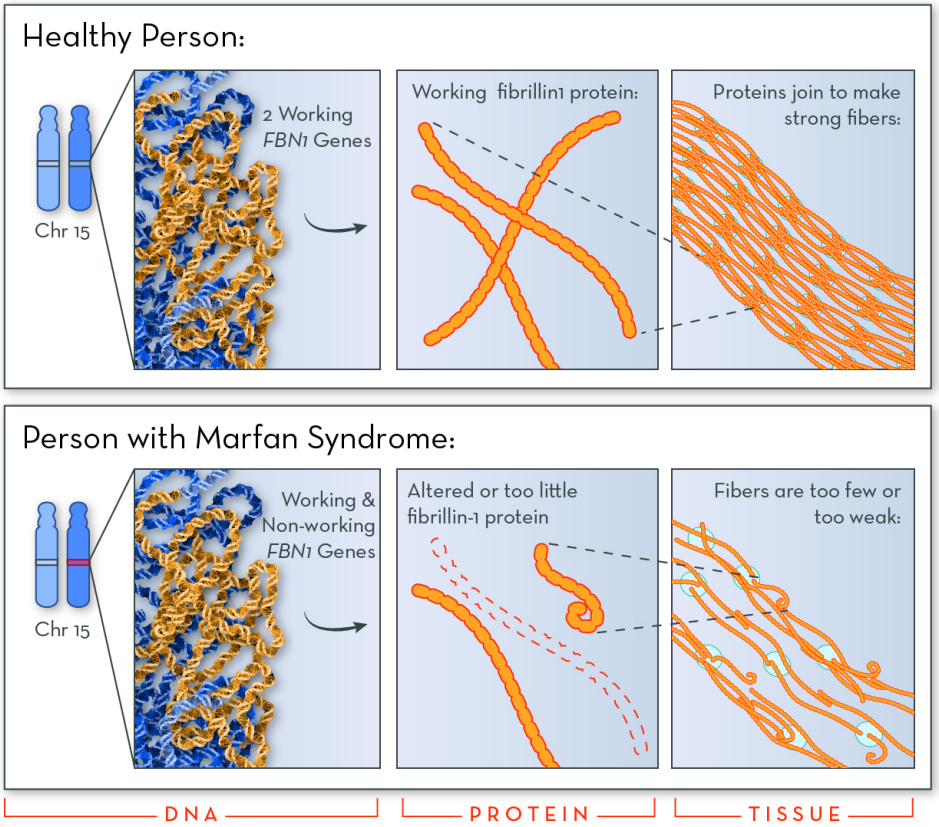
In human beings, variations in connective tissue are grouped into two categories in the current medical model: heritable (genetic) connective tissue diseases (HCTDs) and acquired connective tissue diseases. Acquired connective tissue diseases are currently understood to be autoimmune in nature. That is, they occur when the immune system mistakes various types of connective tissue in different parts of the body for bacteria or viruses that pose a threat to the body.

Some examples of HCDTs:

- Ehlers Danlos Syndromes (Classical, Vascular, and other types) - variations in collagen. People with EDS often have stretchy skin, unstable joints prone to dislocation, gastrointestinal problems, dental problems, near-sightedness, and more.
  - Note: The hypermobile type (hEDS/HSD) has historically been suspected to be related to collagen variations, however in 2024 one study suggested the condition may instead be related to degradation of fibronectin. As of Fall 2026, the genetics of hEDS/HSD have not yet been identified.
- Marfan Syndrome - variations in fibrillin. People with Marfan Syndrome are prone to aneurysm, heart valve problems, dental problems, hernia, retinal detachment, and more.
- Osteogenesis Imperfecta - variations in collagen. People with Osteogenesis Imperfecta (colloquially known as brittle bone disease) may be prone to multiple fractures, have variations in the shape of their bones, be short stature, have hearing loss, and more.
- Loey-Dietz Syndrome - variations in transforming growth factor beta. People with Loey-Dietz Syndrome may have heart valve problems, twisting/winding arteries, loose joints, scoliosis, and more.
- Lipedema - variations in adipose tissue; suspected to be genetic. People with lipedema have fat cells that accumulate in the legs and/or arms. These areas are often painful and hard. That is, the fat of people with lipedema behaves differently to fat in people without lipedema. People with lipedema often have loose joints and immune problems. Many people with lipedema have experienced intense medical fatphobia.

Figure 2 is a graphic representation of how genetic variations which alter the proteins that make up our connective tissues can produce pain and other problems. In this case we are looking at an example from Marfan Syndrome which is caused by a variant in the FBN1 gene. People with Marfan Syndrome make fibrillin fibrils that cannot lock together well, which causes them to be prone to various health issues. Please note that this graphic problematically labels the person without Marfan Syndrome as “healthy.” It is worth reflecting on how such labelling could be harmful to both people with Marfan Syndrome and people without it.

Figure 2. Fibrillin Protein Encoding in Marfan Syndrome



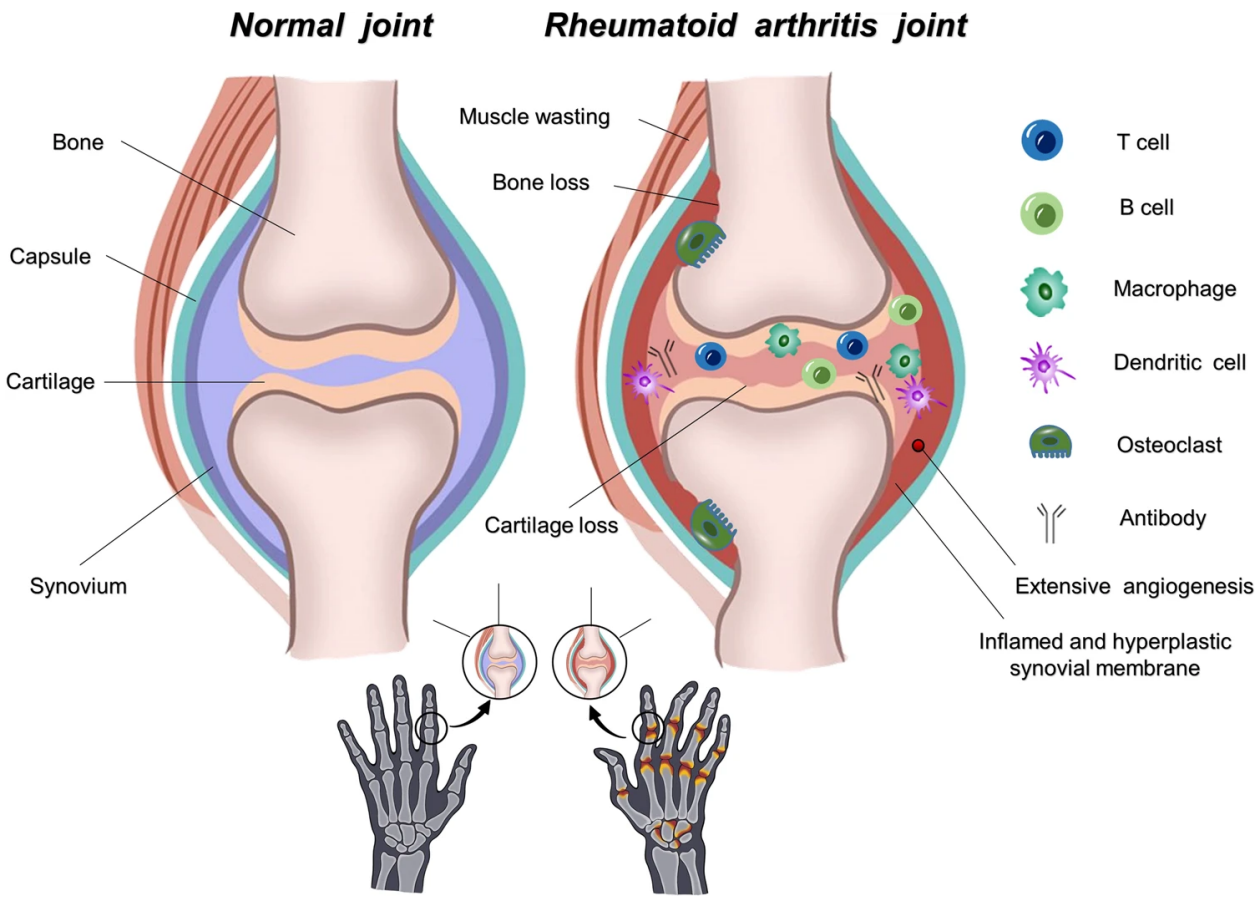
Source: https://learn-genetics.b-cdn.net/genetics/marfan/images/marfan-gene.jpg

Some examples of autoimmune connective tissue diseases:

- Rheumatoid Arthritis - immune system confuses the synovial membrane around the joints for a threat like bacteria or a virus.
- Systemic Lupus Erythematosus - immune system confuses the connective tissue in and around the organs for a threat like bacteria or a virus.
- Scleroderma - immune system creates scar tissue in small blood vessels, eyes, skin, and internal organs.

Figure 3 is a graphic representation of how the immune system affects connective tissue in Rheumatoid Arthritis causing pain and mobility problems.

Figure 3 Rheumatoid Arthritis - Immune System confuses



Source: https://media.springernature.com/full/springer-static/image/art%3A10.1038%2Fs41392-023-01331-9/MediaObjects/41392_2023_1331_Fig3_HTML.png?as=webp

Sex, Gender, Race, Size and Connective Tissue Variations

HCTDs are generally not sex-linked genetic conditions, which means they should occur at the same rate across all sexes, however HCTDs that cause joint hypermobility seem to often (but not always) manifest more severely in people assigned female. In the case of hypermobile EDS (hEDS), a type of HCTD, there is some speculation that progesterone and/or estrogen may play a role in this. After all, hormones affect not just our reproductive systems but many body systems because reproduction is connected to those other systems. For example, the hormone relaxin causes muscles and connective tissues to relax during pregnancy. This is thought to facilitate both gestation and birth, but it can lead to pelvic girdle pain during pregnancy. It should also be noted that there is some emerging evidence that hEDS has a higher prevalence among transgender, non-binary, and other gender-diverse persons.

In addition, acquired/autoimmune connective tissue diseases tend to affect people assigned female (78%) at much higher rates than those assigned male. The reasons for this are complex and have to do with interactions between genetics, the immune system, and the natural and social environment.

The difference in prevalence and severity by sex have some complicated effects for people with variations of connective tissue. In the case of HCTDs, particularly the most common type

hEDS/HSD, the assumption that the condition is milder among those assigned male can lead to dismissive attitudes about pain from doctors and others in the community towards people assigned male. Some people face attitudes like “Aren’t you man enough to tough it out?” On the other hand, medical misogyny diminishes and dismisses conditions that are perceived to affect those assigned female. This phenomenon affects both HCTDs and acquired/autoimmune connective tissue diseases. For example, in the United Kingdom the average time to diagnosis for Lupus, an acquired connective tissue variation, is 6-7 years. Researchers Harwood et al. (2025) suggest diagnostic overshadowing is responsible for much of this delay. Their data is filled with stories from people assigned female reporting being dismissed as complaining or told their symptoms are all in their heads.

Race is not genetically determined, but is instead a social construct which imbues certain biological traits (skin color, etc) with social/political meaning [link to Renae’s module] that can have very real medical consequences. Let’s return to the example of Lupus. Black women are diagnosed with Lupus at three times the rate of white women. Black women also experience higher severity of Lupus symptoms. These differences do not trace to racial differences of biology or physiology, but instead to social, economic, and environmental consequences of structural racism, such as chronic racial stress, poverty, exposure to certain environmental toxins, among many other things.

Race-based disparities are also seen among people with heritable connective tissue diseases, too. However, the problem here is underdiagnosis, which is also the result of a complex set of factors which include: the perception that people of color are more likely to be “naturally” hypermobile (more flexible/athletic) and thus less likely to be negatively impacted by these variations; racist beliefs that black people, in particular, feel pain to a lesser degree; a lack of medical documentation of the particular ways these conditions manifest in skin with higher levels of melanin; and structural factors that produce racial disparities in insurance coverage and general access to healthcare for black and indigenous people of color.

In addition, many people in larger bodies experience disparities in relation to variations of connective tissue [Link to weight science module]. Fat people with autoimmune connective tissue diseases are often dismissed by doctors and told that weight loss is the answer to their pain, despite the fact that many thin people develop these diseases too. Fat people with heritable variations of connective tissue experience similar dismissive and shaming attitudes, but also experience the misperception that only tall/thin people can have HCTDs, in part because many people with Marfan Syndrome are tall and slender. While that may be true of Marfan it is inaccurate to generalize the Marfan phenotype to all HCTDs. This is often the result of inadequate training in medical school related to HCTDs. This can lead to very long delays in diagnosis for fat people with variations of connective tissue, which can worsen health outcomes and mobility issues. It should also be noted that racism, sexism, and fatphobia are deeply interlinked and thus likely to most negatively affect fat, black, women and femmes.

Sex, race, and body size have complicated intersections with variations of connective tissue that weave together what is going on within individual bodies and what is going on in society. These issues are an excellent example of how impossible it is to disentangle the biological from the social. This is one reason the reductive model of science and medicine is problematic. More

problems with the reductive model are outlined in the next section.

2 - C: Reductive Model of Medical & Scientific Knowledge

The reductive model of medical and scientific knowledge starts by breaking down complex phenomena, like healing, into fundamental parts. While this can help us make sense of complexity, it can also lead to over-simplification which can limit a holistic understanding of the topic at hand. As medicine has shifted to become more aligned with the sciences, it too has embraced the reductive model. One way that manifests is medical specialization. Medical specialization allows doctors to become experts in a particular body system or even a particular sub-part of a system. We have doctors who treat the endocrine system, the reproductive system, the brain, the gastrointestinal system. There are even doctors who specialize in just the feet (podiatrists)!

Medical specialization can be beneficial because the body is so complex no one can be an expert in the whole of it. But, medical specialization has some major downsides. First, it can leave body systems on the boundaries between specializations without a clear specialist. The jaw is one example. If you have jaw pain, is that a medical or dental problem? The jaw is involved in chewing, so you might think a dentist would treat jaw (mandibular joint) pain. But it would depend on that dentist's training and their evaluation of whether the root cause of your pain is dental or medical. The mandibular joint is also right next to the ear. Problems with that joint can even cause ear pain, so you might think an Ear, Nose, Throat (ENT) specialist would treat it. Some do, but most do not. The jaw is also close to the brain and has major nerves that run through it, so you might think a neurologist should treat it, but most do not. Rheumatologists deal with the joints, so you might consider seeing one about jaw pain, but unless your pain was due to arthritis or an autoimmune disease, they would likely refer you back to a dentist. The jaw turns out to sit right at the boundaries of a number of medical specialities. Some people may find care for jaw pain within mainstream medicine, but many people do not.

Another effect of the reductive model is that specialists tend to view problems through the lens of their specialty. When a biologist tells the story of connective tissue (as above), they start with healing. That is, connective tissue is understood as a part of the immune system. In the case of feline Ehlers-Danlos-like syndrome, the veterinary naming of genetic connective tissue variations refers to the effects of connective tissue on skin rather than the immune system. Cutaneous asthenia means ‘weak skin’ while dermatosparaxis refers to skin that tears easily. However, in the video, the first difference Cappy’s humans noticed was that he had wound healing problems. While collagen (an important protein that makes up some types of connective tissue) does affect the skin, it also plays a role in immune function (healing). In the case of humans, when HCTDs are viewed from the perspective of an orthopedist or a rheumatologist, connective tissue variations are

understood to cause joint and/bone problems. The reductive model can make it difficult to understand the ways that connective tissues affect the whole body because reductiveness runs the risk of compartmentalizing the body and treating each part/system in isolation. Under this model many doctors just don't know that much about connective tissue diseases precisely because variations in connective tissue affect virtually every part of the body–the skin, the joints, the immune system, and much much more.

When connective tissue variations like hEDS or Marfan or rheumatoid arthritis are compartmentalized there is an effect on both medical research and medical care. The funding for medical research often drives medical specializations. For example, the weightloss industry and pharmaceutical industry have created the specialization of "Obesity Medicine" (link to Weight Science Module). So, research, not just doctors, can be hyper-focused, too. Again, there are some advantages to this. Researchers develop deep expertise. But research questions can get overly specialized and neglect the wellbeing of people with connective tissue variations. For example, researchers have spent many years focused on isolating the genetics of hypermobile Ehlers Danlos Syndrome – one of the most common heritable connective tissue diseases – while comparatively little research is done on improving care and quality of life for people with hEDS. While isolating the genes responsible may help with diagnosis, it does little to help people manage their conditions, minimize suffering, or reduce pain. Moreover, the focus of this research on genetics may not actually lead to easier diagnosis as genetic testing is extremely expensive and out of reach of many people. Worse, the identification of genes opens the door to eugenics via gene editing technologies.

People with variations of connective tissue that affect the whole body, frequently have trouble accessing medical care that deals with all of the elements of their condition. An orthopedist might help with a person's joint instability, but they may not be thinking about the impacts to the immune system. A dermatologist might be able to help with skin fragility, but they may not be aware of the gastro-intestinal effects of the condition. People with connective tissue variations may experience the opposite of what is described in the example of the jaw. Rather than existing at the margins of medical specialties, they exist across almost all of the medical specialities. That means, in order to get comprehensive care, they may need to see a dozen or more specialists–something that is difficult in even the best healthcare systems in the world. However, in many places, including in the USA, accessing that many doctors is virtually impossible. Of course, people with connective tissue variations, can also have specific issues like jaw pain or other issues that exist in between medical specialties, like fatigue, that make it difficult to get any care at all.

People with connective tissue variations have an "everywhere" and "nowhere" problem in accessing healthcare as a result of the reductive model of medical research and practice. Their medical issues exist across all medical specialties, and so they are claimed by no single specialty rendering them invisible within the healthcare system. As a result, many people with hEDS report experiencing what researchers have termed "clinician associated trauma" while seeking care. In the most extreme cases, the reductive model of science and medicine can contribute to suicide as people living in extreme daily pain and experiencing medical neglect can become hopeless about ever feeling better.

2 - D: Case Study 2 - I woke up like this

I woke up one morning and immediately noticed a deep and intense pain in my left knee. As I rolled out of bed and put my feet on the ground, the pain spiked. I mentally checked where I was on the pain scale. An eight, right? Yes, an eight. My wife was out of town so I was on my own to figure out what to do next. I hobbled to the edge of the stairs and managed to sit and then slide down, stair-by-stair, to the main level of my house.

I grabbed my good quad-footed cane to take as much weight off as I could–I have hypermobile Ehlers Danlos Syndrome, so I'm prepared for these moments. I hobbled to the couch and sat down with my leg up. Now to start googling: Left inner knee pain. The internet suggested an MCL tear or torn meniscus. I had to think carefully now. Do I call a ride and go to urgent care? If I do, what will be the next step? They will take an X-ray and nothing will show up, because though it is dense, this type of connective tissue doesn't show up on an X-ray. If the physician is a little more savvy they might check the function of the knee to see if it is an MCL tear. But even that will be hard for them to determine. So, I will likely be referred to an orthopedic surgeon. Been there, done that. The surgeon probably won't know anything about my connective tissue disease. Or maybe they won't believe that I could have torn my meniscus in my sleep. Most people tear their meniscus doing sports; I just woke up like this. In anycase, they will probably recommend physical therapy. And, if that doesn't work, maybe they will consider surgery. But probably not in my case, because I'm fat [link to weight stigma module]. Physical Therapy is my best bet. And, I already see a PT regularly.

So, I checked my calendar. My next appointment is in two weeks. Can I wait until then and just work with my regular PT? I swallow as much ibuprofen as is recommended and cancel my meetings for the day, figuring it is probably best to wait it out. I know how to manage pain. The next day, the pain is a little better, but still severe. And the day after that, the same. When I finally see my physical therapist, I'm still using the cane, still in severe pain. The PT evaluates my knee and gives his best guess: torn meniscus. He agrees to help me, and agrees that seeing an orthopedic surgeon probably won't get me anything other than a referral to see … him. But he cautions it will take upwards of six months to heal before we can begin rehabilitation exercises. I've got hEDS. I've torn cartilage before, unfortunately. A podiatrist treated the broken cartilage in my toe a number of years before I got diagnosed with hEDS. I know it takes a long time to heal. Here we go again!

2 - E: Discussion/Reflection Questions

Reflection on Healing

- Building from Case Study 2, and what you know about healing, why might it take so long for cartilage to heal?

- Think back to the healing dream above, what is happening inside the knee after the meniscus is torn and the healing process begins?

- What about in the case of Cappy, the cat with Feline EDS: What healing processes are disrupted by his connective tissue variation?

Reflection on Biopolitics

- How does the narrative Case Study 2 reflect the way this person feels disconnected from medicine?
  - How are disconnections in science and medicine contributing to this person's disconnection from medicine?
  - Could that lead to disconnection from other people, friends, family, etc?
- What about her past experience led her to decide to skip going to the doctor? What are the pros and cons of that decision?

- How would better scientific knowledge about connective tissue help improve her wellbeing?

- How would a more holistic understanding of connective tissue help in this case?

- What would need to change socially, politically, economically to ensure that people and pets (don't forget Cappy!) with variations of connective tissue get better care?