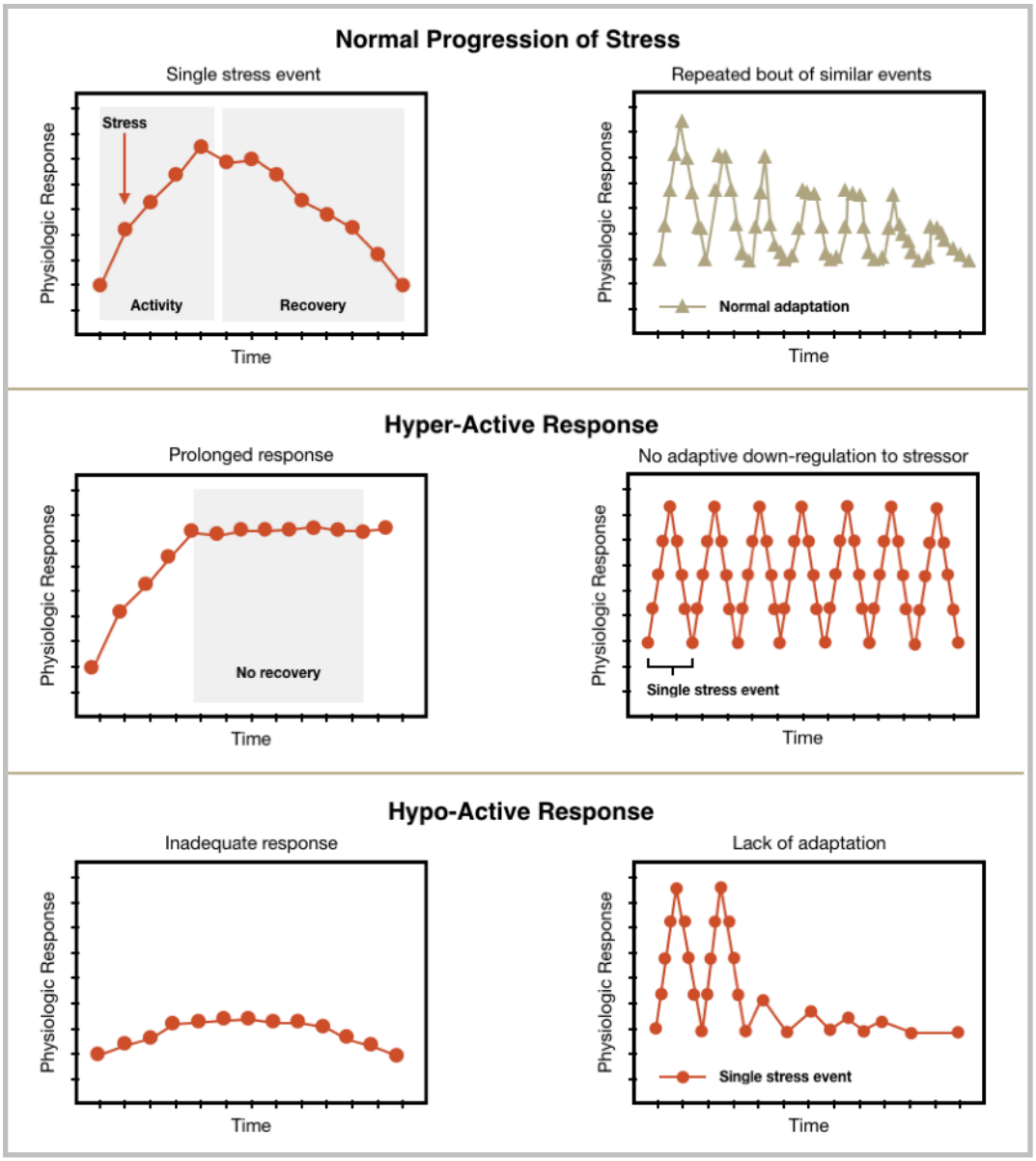
KRESSER INSTITUTE
FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

HPA-D: Pathology – Part 1

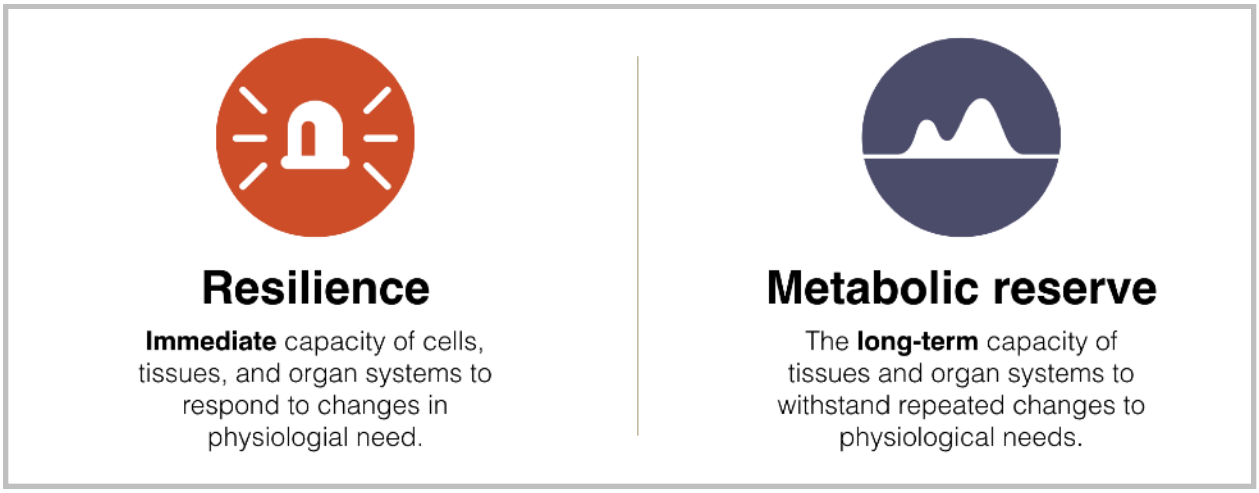
Hey, everybody, in this short presentation we're going to talk about the pathology of the HPA axis. I briefly introduced the concept of allostatic load in the basic physiology presentation. Allostatic load is the wear and tear produced by imbalances and the mediators of allostasis. Put in simpler terms, allostatic load refers to the price the body pays for being forced to adapt to adverse psychological or physical situations, and it represents either the presence of too much stress or the inefficient operation of the stress hormone response system, which must be turned on and then turned off again after the stressful situation is over.



We'll be talking about more specific patterns of dysfunction in the diagnosis unit, but the figure on this slide illustrates some of the more general categories of dysfunction caused by allostatic load, and this is based on Bruce McKuen's model that shows a general response to both single and repeated allostatic loads. So on the top row, we have what you'd expect to see with normal progression of stress. So at the top left, you have a normal response to a single stress event, so you see the stress response increases during that event, and then it declines over time after the stressful event has passed. And then on the upper right, you see what should happen with a repeated bout of similar events. At first, the stress response is higher, because remember, the NUTS framework for determining how stressful an event will be, we talked about that earlier in this unit. N stands for novelty, and U stands for unpredictable, so if an event is novel and unpredictable, it'll be more stressful, but if we have repeated bouts of the same event, you would expect the stress caused by that event to be lower, and that's what's pictured in that figure on the upper right.

In the second row, we have a hyperactive stress response, and on the left, we see a prolonged response to a single stressor, and this can happen in PTSD type of scenarios, where there's an intensely stressful event, and instead of seeing a decline in the stress response after the event has passed, we just see a persistently elevated stress response. The figure on the right in the middle column shows no adaptive downregulation to the stressor, so we have a single stress event and then a repeated bout of similar events, but instead of seeing the healthy normal adaptation as the novelty and unpredictability declines, we just see repeated activation that's similar to the first time that we experienced the event, and that's not expected and it's pathological.

Then on the bottom row, we have hypoactive response, so on the bottom left we see an inadequate response to a single stressor, and this often happens when the HPA axis has become downregulated, like let's say in PTSD, and then the patient is unable to mount an effective response to future stressors. And then on the right, we have lack of adaptation to a repeated bout of similar events, and this is also similar, so if someone has a condition like PTSD, then the whole HPA axis gets downregulated and they're not able to mount a successful stress response to these repeated events. So these are just a number of ways that HPA axis dysfunction can manifest.



There are two additional key concepts related to allostatic load. I believe we covered before as well, and these are resilience and metabolic reserve. These are defined succinctly by Dr. Guilliams in his book. Resilience is the immediate capacity of cells, tissues, and organ systems to respond to changes in physiological need, which would be induced by stress. And the metabolic reserve is the long-term capacity of tissues and organ systems to withstand repeated changes to physiological needs. Put in more simple terms, metabolic reserve is the stored-up reserve that's available for each metabolic and organ system to maintain and rebuild its physiological resilience.

Now, just like any other reserve, metabolic reserve can be depleted, and it can also be replenished and strengthened, and this is an absolutely crucial concept for you and your patients to understand, and it's the core of the relationship between stress and disease, and it explains why the HPA axis assessment and treatment must be done with any patient with any chronic disease. As you'll recall from the basic physiology presentation, the goal of the stress response is to keep us alive through physiological challenges and threats. The problem is, it does so in a way that adversely affects the systems required for maintaining optimal health and preventing disease.

Fight or flight response

Heart rate and blood pressure increase.

Pupils dilate to take in as much light as possible.

Veins in skin constrict.

Blood glucose level increases.

Muscles tense up.

Smooth muscle relaxes.

Nonessential systems shut down.

Trouble focusing on small tasks.

In the fight-or-flight response, the sympathetic nervous system is activated, and the body diverts vital resources to systems that allow for the best chance of survival in the short term. The overall effect of this is the body tensing up, speeding up, and becoming very alert. To get a sense of this, just think of a time that you were scared or threatened. Physiologically, a whole cascade of reactions is occurring; heart rate and blood pressure increase to prepare for action, the pupils dilate to take in as much light as possible, the veins in the skin constrict to send more blood to major muscle groups, and as a side note, cold hands and feet are not always thyroid-related—they can often be related to HPA axis dysfunction because of this mechanism. Blood sugar levels increase to provide energy for cells, muscles tense up, they're energized by adrenaline and glucose. The smooth muscles relax in order to allow more oxygen into the lungs. Non-essential systems like digestion, immune function, endocrine system, reproductive health shut down, because there's no need to digest your next meal or prepare for having a baby if you don't survive the next five minutes, and of course this is why stress is such a big player with digestive conditions and infertility and weakened immune function. Then you'd also have trouble focusing on small tasks or keeping your mind focused because the brain is directed to focus only on the big picture in order to determine where the threat is coming from, and so this of course explains the relationship between stress and all kinds of cognitive and mental health disorders.

Rest and digest response

Heart rate and blood pressure decrease.

Saliva and digestive enzymes increased.

Bronchial tubes in lungs contrict.

Muscles relax.

Pupils in eyes constrict.

Blood flow to GI tract and endocrine organs increased.

Immune function restored.

Once the threat has passed, the parasympathetic nervous system is activated, and the body starts using resources for activities that promote long-term survival again. So it's kind of the mirror image of the sympathetic fight-or-flight response: heart rate and blood pressure decrease; saliva and digestive enzymes, which support long-term digestive health, increase; bronchial tubes in the lungs constrict; muscles relax; pupils in the eyes constrict; blood flow to the GI tract and endocrine organs is increased; the reproductive system would kick back into gear; and immune function is restored.

Getting our patients to spend more time in this rest-and-digest response is an absolutely crucial part of the treatment protocol, and unfortunately most people in the modern world, if they're not paying attention to this and making active changes in their life to induce a parasympathetic rest-and-digest response, are probably spending the majority of their time in some kind of fight-or-flight response, and I really do believe, and I think the research supports this, that this is the elephant in the room when it comes to chronic disease and chronic disease management, is if most of our patients are in a nearly continual fight-or-flight response, the body was never designed for that, and as you can see now, all of these things that happen in the fight-or-flight response will directly contribute to chronic inflammatory disease and all of the symptoms that our patients experience.