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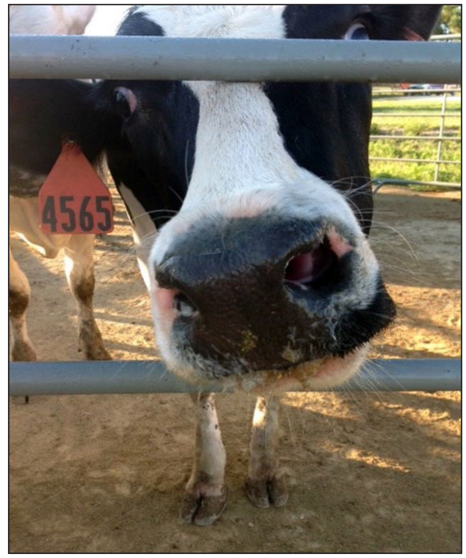

Too Hot to Trot?

The Role of Exercise in Homeostasis

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Part I – A Little Family History

It's gettin' hot in here, I'll take off all my fur.
I am gettin' so hot, I wanna take my fur off…

Oh, hay! Nelly the Holstein dairy cow here. You caught me exercisin' and a singin' my favorite song! Pardon my country grammar, this is so embarrassing…

Wait, hang on, my momma just sent me a text. Here, I'll read it to you: "Hay, girl! Turn that music down. Can't you see I have a terrible headache? And it's *way* too hot in here to be doin' all that prancing around. Plus it's undignified! Dairy cows should be calm and lying down whenever they aren't eating or being milked! How many times have you heard your grandmother and me say that?"

Wow, I'm sorry Momma ever learned to work an iPhone! She sometimes gets a little cranky when it's hot. She's also the biggest cow in the herd, so when Momma yells, even when it's via text message, everybody listens!

Anyway, now you know my little secret: I just *love* to exercise. I bet you didn't know some of us dairy cows exercised, did you? I know, I know, it's not typical, but then again, these aren't typical times we're livin' in! I mean, the Earth is gettin' hotter faster than ever, us dairy cows are gettin' bigger than ever, and the world's requirement for food has never been greater. That's caused a lot of stress and strain on us food animals, and we're important for life on this planet! Just the other day I read where scientists are projecting that by 2050 global food production will be inadequate to meet the needs of the human population (University of Minnesota, 2013). And did you know that us dairy cows produce about 10 billion gallons of milk just for cheese in the United States alone (Feinstein, 2006)?!

So why are big Holstein dairy cows like Momma so heat stressed nowadays? Let's start all the way back at the beginning. This is the earliest sketch we have of some of our family members (Figure 1). Momma says our breed started some 2,000 years ago. I've never been there, but Momma says the Netherlands has such a different climate than what we have here in the central U.S. where so many of us dairy cows now live. Momma calls the Netherlands our "native environment" and says that it has a maritime climate, which is cloudy and cool because it's influenced by the North Sea and Atlantic Ocean; in fact, the average summer temperature is 17–20 °C! Can you believe that! Why, here in Kansas where I live the average summer temperature is more like 26 to almost 30°C, and we have a lot of sunny summer days where it gets over 38°C! That's a big difference! I wonder how they stayed warm though. I mean look how small they were and how spread out the herd was in that meadow (Figure 1).

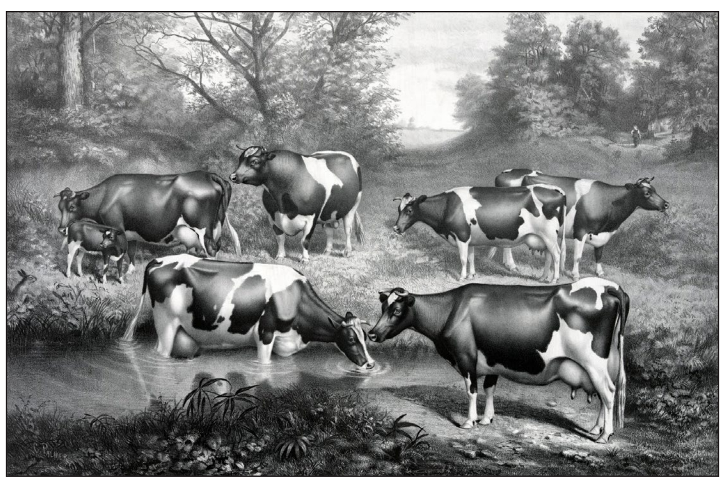


Figure 1. Holstein friesian cows. <https://www.publicdomainpictures.net/en/view-image.php?image=77271&picture=fresian-cows-in-pasture>

In 1852 our first ancestor arrived in Massachusetts. After that, our family started changing in significant ways. First of all, farmers had a plan for our family and it seemed to center upon us becoming larger and larger while still efficiently converting a small amount of feed to large amounts of milk. We excelled at this and soon the Holstein breed was very popular in the U.S. and could be found in many states. But the climate in some of these states was pretty hot and not at all similar to our native environment in the Netherlands. Even in Massachusetts, which also has a maritime climate, we found the summers to be difficult due to the heat and humidity as average daily summer temperatures ranged from 24–27°C. But this was nuthin' compared to the states we'd soon move to such as Texas, Arizona and Kansas. Momma said this became a real problem because as we were getting bigger and bigger, we were moving into climates that were hotter and sometimes more humid and eventually this impacted our milk production. In addition, we spent more time eating grain and less time eating grass because it was sometimes hard to find. Plus, we really like grain! Here are some of our family members enjoying celebration dinner together in Texas (Figure 2). Talk about hot! Average summer temperatures here can range from 33 – 38C! Sure looks hot to me.

Figure 2. Feeding time. <https://www.publicdomainpictures.net/en/view-image.php?image=2759&picture=cows-feeding-time>

Momma says our family members used to be about half our size when we were back in the Netherlands and that she thinks it's a little strange that as we moved to a warmer climate we were also selected to be larger. Selection pressure by the time we got to Massachusetts resulted in us being only about halfway between our current size and that of our early ancestors in the Netherlands. Momma says being too large makes heat regulation difficult and that if you look around at some of the native mammals here in the central or southwest part of the U.S. they aren't all that big compared to their relatives found farther north. Usually in nature an adaptation to hotter climates is a smaller body size.

I think she must be right because nowadays they use an awful lot of resources trying to keep us cool. Here's a picture of some of my Arizona cousins who are kept cool using a combination of fans and misters (Figure 3). Just look at that outside temperature!

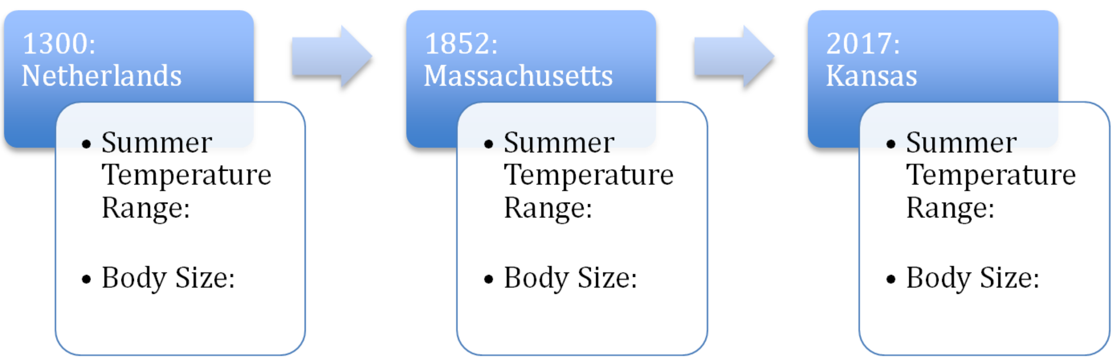
Figure 3. Hot cows. <https://www.publicdomainpictures.net/en/view-image.php?image=211506&picture=cows>

If enough water and electricity are used, my cousins can enjoy an environment that is more akin to our native environment, which helps them continue producing an impressive milk yield year after year regardless of the outside temperatures. The same is true for me and my family here in Kansas, which has a continental climate, causing temperatures to fluctuate greatly. This is much better than Arizona, but still pretty far above our native environment and the humidity can be far worse. But Momma says this reliance upon resources like electricity and water can deplete important resources and also make dairy production more expensive. The other problem is that water sprayed on us cows becomes waste water. She says we have to find new, more environmentally friendly ways to tolerate the heat. I think she's right so I'm out here exercising, trying to improve my ability to thermoregulate physiologically (Figure 4).

Figure 4. Cow exercising. Photo by authors.

Activity 1 – Impacts of Artificial Selection

Condensing the story above into a flowchart, complete the timeline within the boxes below that includes general information about the Holstein breed:



Questions

1. The general trend in your flowchart should be fairly straightforward. As Holstein cows were being raised in ________________ climates, there was also _______________________________ by humans that caused the size of the cows to become _________________________.
2. How is this different compared to general trends observed in mammals in nature?

Part II – Dairy Production in Warmer Climates Cools Production Gains

The story and flowchart above were designed to introduce you to the issues that livestock face as the climate continues to warm. For large animals such as dairy cows, many of which are maintained in climates that are already far outside of their ideal temperature zone, each additional degree of environmental heat requires them to partition additional energy to the process of thermoregulation. Because core body temperature is a tightly regulated physiological variable, it takes priority over other physiological processes deemed less important by an animal's brain such as foraging, digestion, reproduction, or lactation. This problem is frequently overlooked when artificially selecting livestock to be larger and larger so that they can produce more food or fiber. As a result, food animals must often expend a lot of energy just to maintain thermal homeostasis, ultimately decreasing the amount of energy left over for the production of muscle or milk. Thus, the genetic potential of the animal is often unrealized due to incompatible environments.

To understand the relationship between environmental temperatures and energy expenditure of an animal for regulation of body temperature, scientists often use graphs (Figure 5) which plot ambient or environmental temperatures (T_A) against metabolic rate measured in Kcals. Homeotherms like mammals and birds, which must keep a constant internal temperature, are most efficient when living in their thermal neutral zone (TNZ). In this zone, little additional energy is required to maintain body temperature because heat production caused by physiological processes such as digestion and metabolism are balanced with heat loss to the outside environment (Kingma, Frijns, Schellen, & van Marken Lichtenbelt, 2014). In fact, only small adjustments to blood distribution patterns within the body are required to maintain core body temperature (T_B) within this zone. However, once a homeotherm is placed in an environment that is outside of the thermal boundaries of their TNZ, denoted by a lower critical temperature (LCT) or upper critical temperature (UCT), energy expenditure increases dramatically and this energy expenditure can come at a great price to the animal because T_B is such a tightly regulated physiological variable (Baumgard & Rhoads, 2015).

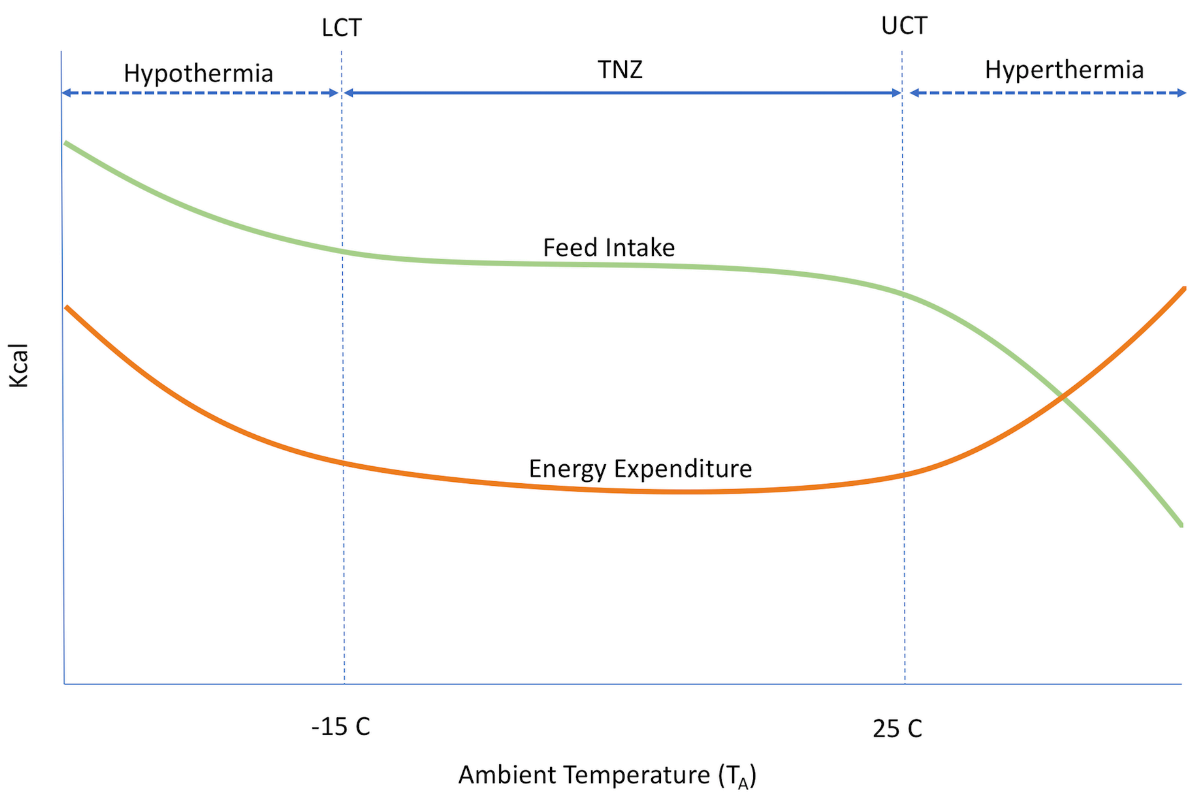


Figure 5. The thermal neutral zone of a dairy cow. The center portion of the chart, labeled "TNZ" depicts the range of temperatures at which regular homeostatic responses are capable of maintaining normal body temperatures. Energy expenditures are shown in Kcal and increase below the lower critical temperature (LCT) of around −15 °C and above the upper critical temperature (UCT) of around 25 °C. While feed intake increases below the LCT, it decreases above the UCT to reduce heat production that occurs during digestion and other chemical processes required to store or nutrients or use them immediate for ATP production.

Many physiological factors can influence a homeotherm's TNZ such as body size, adipose, size and shape of appendages, and even fur color. Of these, body size likely represents the most important factor for determining an animal's TNZ as larger animals have a larger volume to surface area ratio, which makes it more difficult to dissipate heat from the core to the outside environment. The opposite is true for smaller animals. This relationship is illustrated in Figure 6.

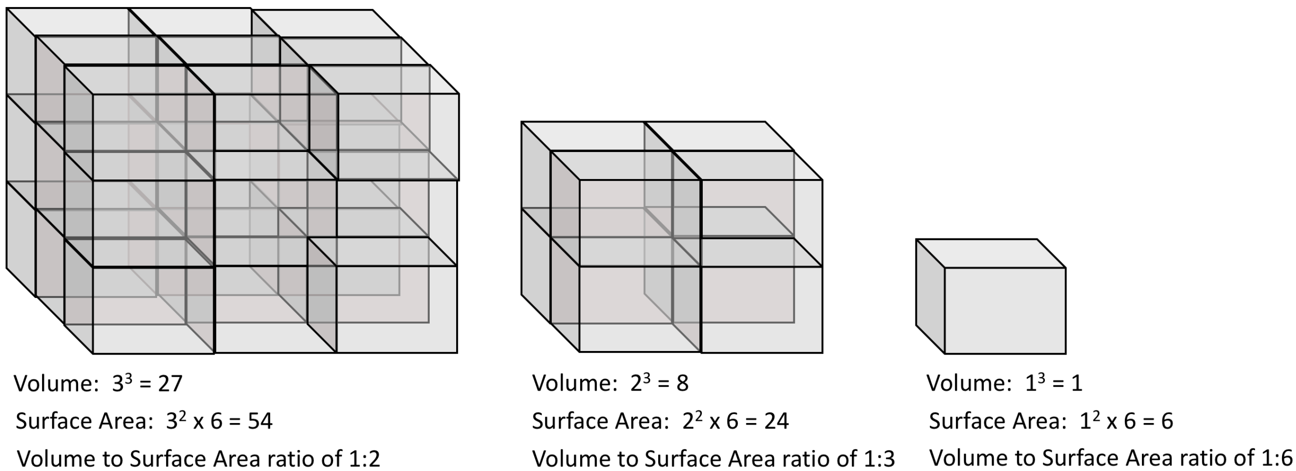
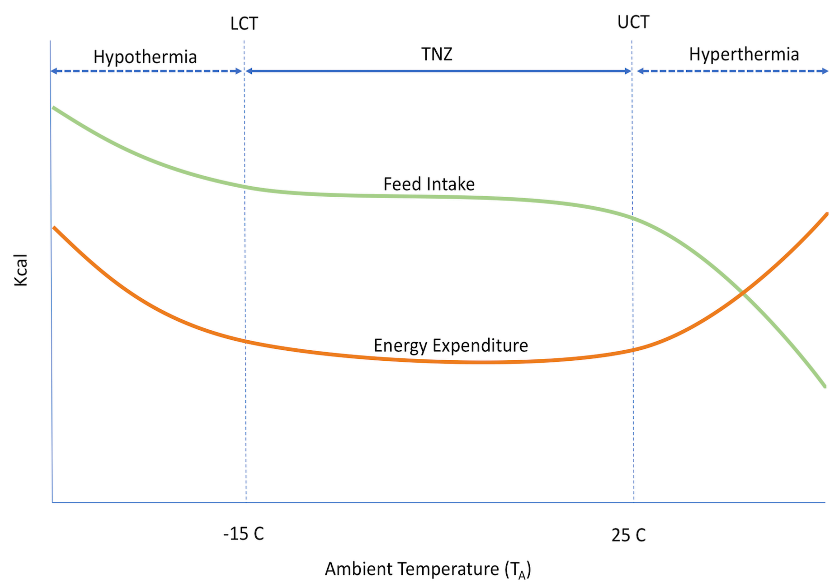


Figure 6. Relationship between volume and surface area. The majority of an animal's volume is within its core, which is also where the majority of heat is produced. Because volume increases in three dimensions but surface area only increases in two dimensions, volume can increase substantially without an equal or proportional increase in surface area. This causes an increase in heat retention because there is more tissue producing heat (volume) with relatively less surface area from which to dissipate the heat. Examine the photo below and note how these ratios might change in smaller or larger cows. Note also how the surface area to volume ratios might be different in the limbs versus in the trunk of the animals.

Activity 2 – Thermal Neutral Zones

Review the information in the flow chart you completed in Activity 1, specifically for Kansas, and add in the average summer temperature range to the TNZ chart on the right (reproduced from the previous page) for an adult dairy cow. Generally, the TNZ for smaller homeotherms is quite different than that of larger homeotherms. Using the TNZ chart for an adult dairy cow, hypothesize how the TNZ, LCT, and UCTs would change for a smaller homeotherm.



Questions

3. How might an animal's anatomical features such as exaggerated pinnae, horns or long tails impact their TNZ? Do dairy cows have any of these?
4. Given the TNZ for dairy cows and your answers to the questions above, what recommendations, including changes to genetics, housing, or feeding, would you make to livestock producers who are hoping to increase the efficiency of milk production even though they live in hot climates?

Part III – Homeostasis, Feedback, and Maintenance of Regulated Physiological Variables

Regulated physiological variables like T_B are constantly monitored by the brain and tiny adjustments are continuously made, even if the animal does not appear to be actively thermoregulating. As with any regulated physiological variable, the maintenance of T_B involves three main processes that function in a continuous homeostatic loop: sensing, interpreting, and responding if necessary. In regards to T_B maintenance, sensing begins with the activation of thermoreceptors and the triggering of an afferent action potential within sensory neurons in the periphery of the body, internal organs, spinal cord, and even within the brain itself. After receiving multiple sensory inputs, a region of the brain known as the hypothalamus interprets the information and elicits an increased "correcting" response in the form of an efferent action potential if T_B deviates further from its acceptable range. The correcting response requires the activation of motor neurons, which synapse upon and activate structures called effectors. It is the effectors that actually perform the work needed to restore T_B.

The brain finely tunes the degree of response as it continuously monitors and adjusts regulated variables using physiological feedback. These mechanisms act as forms of communication, allowing the brain to get a sense for how well effectors have done their job. For example, if a regulated variable had been outside of its acceptable range but through the action of effectors was corrected, the brain would need to know about this so that further activation of effectors does not occur. Thus there is continuous monitoring and adjustment of the physiological responses based on need. In the case of T_B maintenance, negative feedback responses initiated by an increase in T_B result in increased cooling and thus a decrease in T_B. Sensory information from thermoreceptors continuously arrives in the brain and helps it to know when to decrease activation of effectors responsible for cooling its core once an acceptable temperature has been achieved. However, until then, the effectors would continue to operate at an increased rate with the rate slowing as the regulated variable of T_B gets closer and closer to its normal physiological range.

Activity 3 – Connecting Components of Homeostatic Loops

To better understand how homeostatic loops and feedback mechanisms work together to maintain regulated physiological variables, complete Figure 7 by filling in information after each letter. Use Chart 1 for reference.

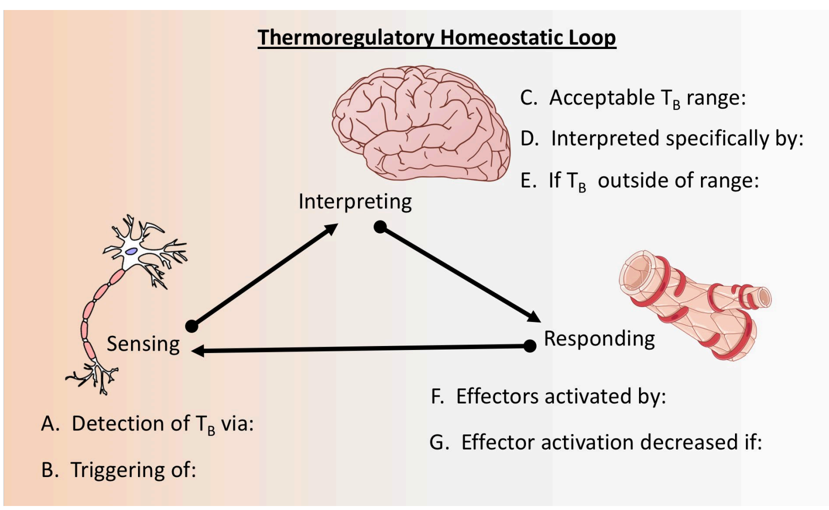


Figure 7. Thermoregulatory homeostatic loop. Relationship between sensors, interpreters and effectors to maintain homeostasis of the regulated variable, T_B. Temperature sensitive neurons send information to the brain, which then interprets the information and causes a response by effectors such as blood vessels in the dermis.

Chart 1. Resting Dairy Cow Vitals	
T_B	38–39.3 °C
Heart Rate	48–84 beats per min
Respiratory Rate	26–50 breaths per min
Source: Merck Veterinary Manual, <http://www.merckvetmanual.com/appendixes/reference-guides>	

Question

5. Suppose you are taking the vitals of a very sick cow and notice that her T_B is 43 °C yet none of her effectors have been activated to initiate cooling and her other vitals are within their normal range. Which components of the homeostatic loop you completed above might be different as compared to a healthy cow?

Part IV – Thermoregulation in Rising Ambient Temperatures

For dairy cows, maintenance of T_B in temperatures above their TNZ can quickly become energetically expensive because cows do not sweat as efficiently as horses and humans. Instead, as ambient temperatures increase and approach or surpass the UCT, cows rely heavily on blood vessel dilation within the dermis, driven by increased blood pressure and resulting in increased blood flow through capillaries of the dermis. Assuming the ambient temperature is not too far from the UCT, this mechanism can be effective for cooling because blood moves heat. In other words, increased blood shunting from the core to the skin brings hotter blood closer to a cooler outside environment, exposing a temperature gradient which causes heat transfer. As a result, heat is transferred in one of three ways: radiation, conduction or convection. These are defined and examples given in the chart below.

Chart 2: Mechanisms of Heat Transfer Between Animal and Environment			
Form	*Definition*	*Heat Loss Examples*	*Heat Gain Examples*
Radiation	Transfer of heat via electromagnetic radiation	Hot cow on a cool day	Skin absorbing UV rays
Conduction	Transfer of heat through physical contact	Lying on cool surface	Contact with herd mates
Convection	Transfer of heat through moving fluid or air	Cool air from a fan	Hot moving air above T_B

However, if the ambient temperature or that of the substrate on which the cows are lying is hotter than their skin temperature and above the UCT, loss of heat via these mechanisms will not occur. In fact, if the environment is hotter than the cows it is possible that heat could actually be gained from the environment, not lost. Should this occur, cows begin employing active and more energetically expensive mechanisms for thermoregulation as their only additional option is evaporative cooling. But remember, cows do not produce a lot of sweat so evaporative cooling for them mostly occurs via panting.

For large animals, panting is rarely an efficient mechanism for thermoregulation. Part of the issue stems from their large volume to surface area ratio; cows that originated in Northern Europe are just built to hold heat because they evolved in cool climates. Additionally, the available surface area for evaporative cooling is small and is generally confined to their respiratory tract where droplets evaporate during inhalation and exhalation. To increase evaporative heat loss, cows can increase their respiratory rate. However, many skeletal muscles are needed to create and sustain an increased respiratory rate, and an increased heart rate is required to supply oxygen to rapidly contracting skeletal muscles. Thus, panting can actually add to an animal's heat load. Furthermore, if humidity levels in the ambient environment are high, evaporative cooling via panting will be less efficient, leaving the animals little to no additional cooling mechanisms. At this point, the animal will likely require outside intervention by humans or risk death due to heat stroke.

Activity 4 – Heat Transfer Between Animal and Environment

Using the information in the text above, complete Figure 8 on the following page.

Questions

6. Blood flow to the dermis increases linearly as T_B increases but enhanced flow will eventually reach a limit and plateau. Why can't dermal blood flow increase linearly with T_B indefinitely?
7. If enhanced blood flow to the skin corrects the issue of increased T_B, how will the brain "know" and what should the brain do as a result?

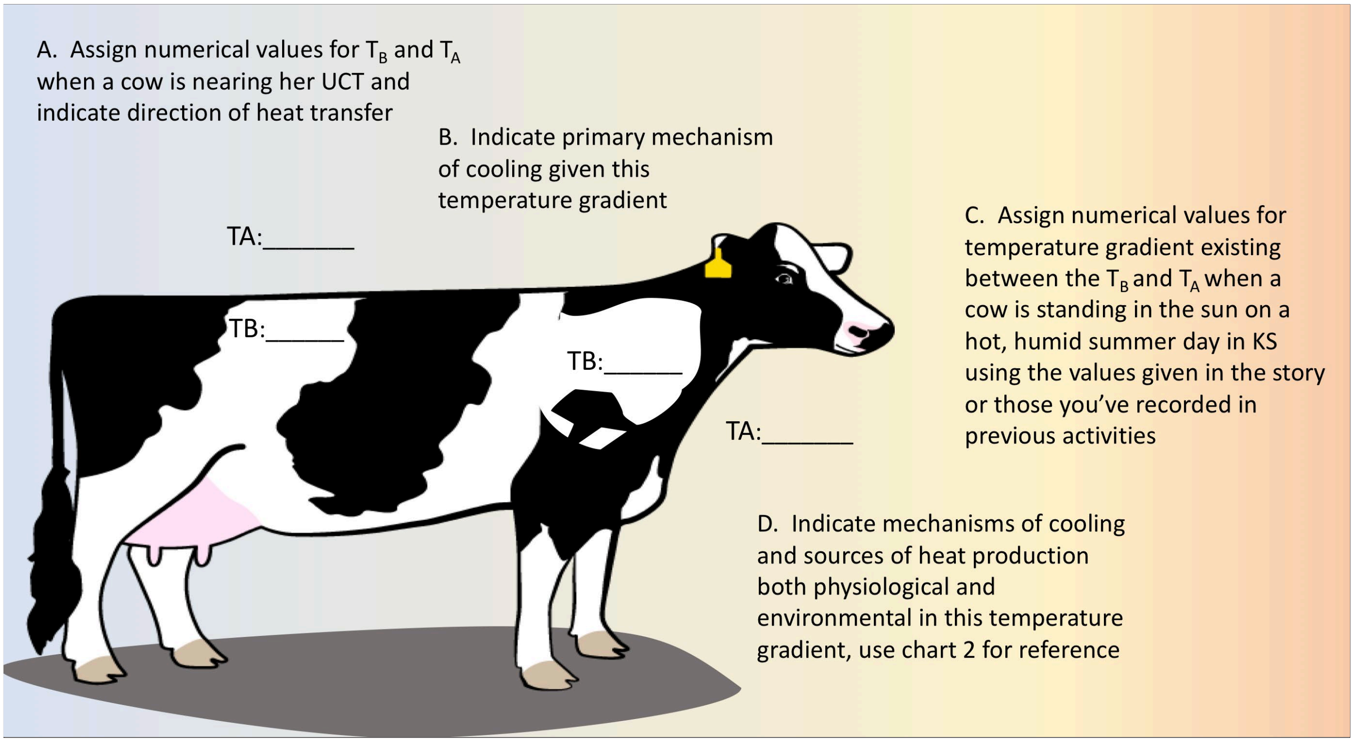


Figure 8. Relationship of heat gradients to thermoregulation. Heat transfer occurs because of thermal gradients in which heat moves from an area of higher "heat concentration" to an area of lower "heat concentration." The larger the difference, or gradient, the faster the heat will move.

Cows can efficiently thermoregulate if, and only if, their T_B is higher than the T_A and the thermal gradient that is required for transfer of heat can be maintained (Figure 8). But what happens when cows live in an environment where temperatures are typically far above their UCT, even at night? As mentioned previously in the story told by Nelly, many dairy cows are kept cool with the use of fans and water misters, but this comes at an environmental cost and given the predicted shortage of water in some regions, these methods may eventually become unavailable as options. But what if there was a more economical and environmentally friendly way to help these large mammals avoid severe homeostatic disruptions due to increased temperatures? What if cows could be managed in such a way that they became better acclimatized to the heat?

What if Nelly has the right idea about exercise as a mechanism for reducing heat stress?

Part V – Acclimatizing to Rising Ambient Temperatures

When sedentary animals begin a regimented exercise program, disruptions to homeostasis occur due to exercise-related stressors such as reduced blood oxygen levels, defined as hypoxia, and increased T_B, defined as hyperthermia. After sensing, interpreting, and responding to these disruptions, physiological changes occur that will cause the animal to eventually become more fit. Being fit provides long-term benefits that are not only useful during subsequent bouts of exercise, but also for coping with other physiologically demanding challenges such as living or working in hotter ambient temperatures. But how can acclimatizing (or adjusting) to one physiological challenge, like exercise, help ameliorate issues caused by other, seemingly unrelated physiological challenges? The answer begins with a homeostatic loop, similar to the one in Activity 3, but this time is specifically initiated by acute exercise-related stressors. We'll use hyperthermia as our example.

Activity 5 – Homeostasis and Exercise-Related Stress: Mitigating Acute Hyperthermia

Starting at letter A in Figure 9, label the condensed homeostatic loop. Starting with letter D in Figure 9, include information related to feedback mechanisms.

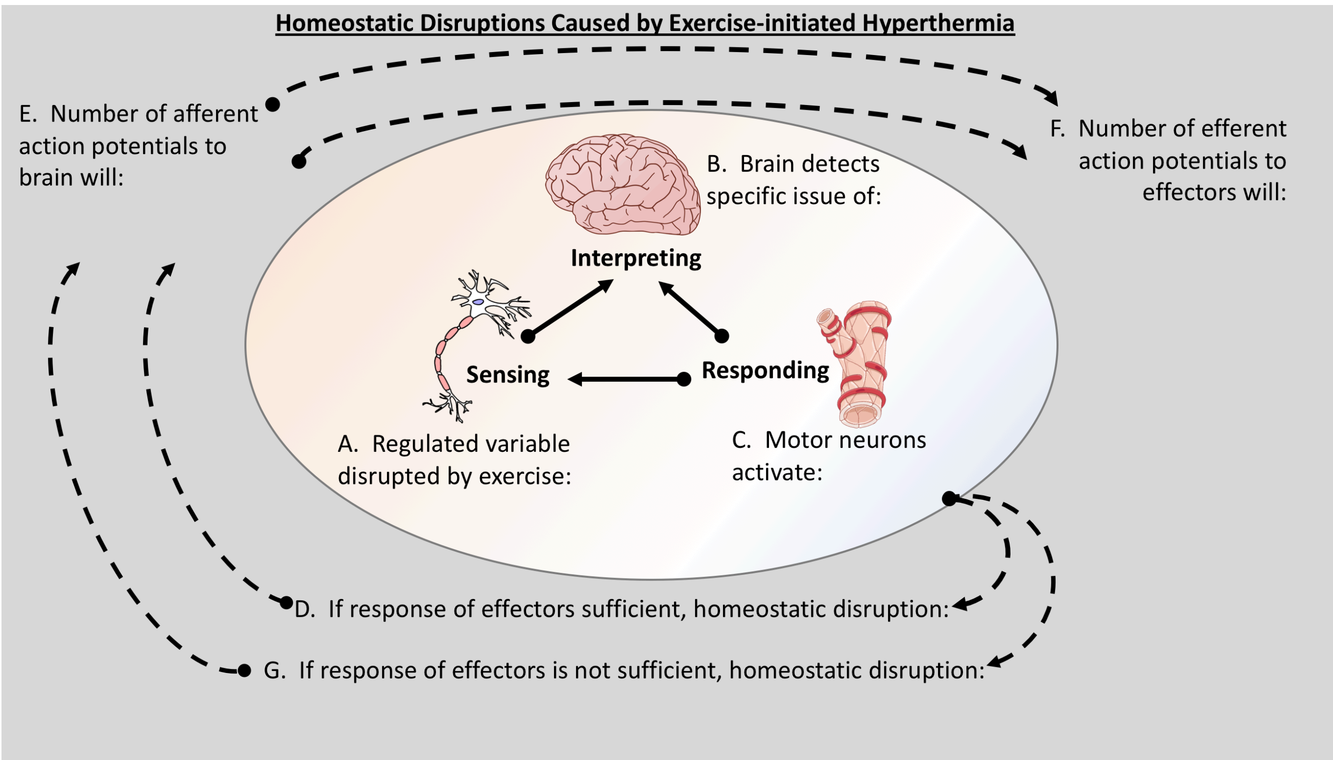


Figure 9. Disruptions of homeostasis caused by exercise. Feedback responses should continue until regulated variables such as body temperature are returned to their normal physiological range.

Questions

8. In regards to your answer to letter D above in the activity, what kind of feedback would occur?
9. Thinking about your response to letter G above in the activity, what would happen to T_B?

Part VI – Vasculogenesis and Angiogenesis

In many instances, the homeostatic loop occurring in response to an acute stressor is not sufficient and the disruption remains. When this happens, an acute problem becomes a chronic problem requiring a more complex response if real and lasting improvements are to be made and the animal is to acclimatize to the new challenge. Simple feedback loops are just not enough as the response of effectors does not correct the issue. For example, increased blood shunting through the skin via existing blood vessels can only provide so much cooling. To substantially improve cooling efficiency, additional blood vessels would be required. Interestingly, it is hypothesized that this is exactly what happens as a result of chronic exercise-related hyperthermia. Additional blood vessels are created via two processes: vasculogenesis and angiogenesis.

Vasculogenesis refers to the initial construction of brand new blood vessels while angiogenesis refers to the refinement and rearrangement of these vessels, resulting in smoother blood flow. Together these two processes—vasculogenesis followed by angiogenesis—result in the formation of a network of narrow, functional capillaries that enhance blood flow to or through particular tissues (Krock, Skuli, & Simon, 2011; Silvestre, Smadja, & Levy, 2013; Weidemann & Johnson, 2008). Thus, more blood flow to the skin is possible and initial exercise-induced stressors like hyperthermia that triggered the homeostatic loop you completed in Activity 5 are blunted, making homeostasis easier to maintain when T_B increases, whether from exercise or as a result of increased T_A.

Despite what is known about the benefits provided by vasculogenesis and angiogenesis, less is known about what causes them to occur in certain tissues like the skin. Currently it is believed that the initial stimulus for increasing capillary density in the skin, specifically within the dermis, is chronic hyperthermia coupled with chronic increases in blood shunting to the skin. Referred to as hyperemia, this increased blood flow to the skin causes shearing stress within the walls of the vessels and in turn causes the vessels to remain dilated for longer periods of time as the body attempts to dissipate heat to the outside environment (Padilla, 2011). In turn, chronic dilation of blood vessels likely stimulates the release of a compound called nitric oxide from the endothelial cells that comprise the walls of the blood vessels themselves (Padilla, 2011; Simmons, 2011). Nitric oxide plays a key role in regulation of vascular functions including vasodilation, stimulation of angiogenesis and regulation of blood flow (Simmons, 2011; Yang, 2016). But nitric oxide also initiates a cascade of events that likely causes endothelial cells to produce another compound called vascular endothelial growth factor (VEGF) (Kane *et al.*, 2001; Kimura & Esumi, 2003; Ziche *et al.*, 1993; Ziche *et al.*, 1997), which has long been recognized as the key regulator of vascular development in health and disease (Eichmann & Simons, 2012; Lee *et al.*, 2007). In skin, VEGF is potentially the major factor instigating vasculogenesis and subsequent angiogenesis (Detmar, 2000; Neufeld *et al.,* 1999). With time, the formation of new, fully functional capillaries ultimately increases capillary density within the skin (Figure 10). In the end, maintenance of T_B becomes more efficient as increased capillary density permits larger volumes of blood to be shunted to the surface, allowing for a more efficient transfer of heat, even in higher ambient temperatures.

Activity 6 – Structure of Skin is Dynamic, Changes Aid Thermoregulation

For letters A–I, finish the flowchart (Figure 10, next page) by using the given descriptions of processes or compounds to identify the correct physiological term or substance. The first one has been done for you. Once you have completed the flowchart, illustrate the information in the graphic directly below by adding detail or labeling the changes occurring in the blood vessels provided.

Questions

10. What impact would angiogenesis in the dermis have on the process of heat dissipation? Be specific using terms found in Chart 2 (Part IV above).
11. If exercise increases angiogenesis in the dermis, how would this shift a cow's TNZ? What specific mechanisms of heat transfer might become more efficient?

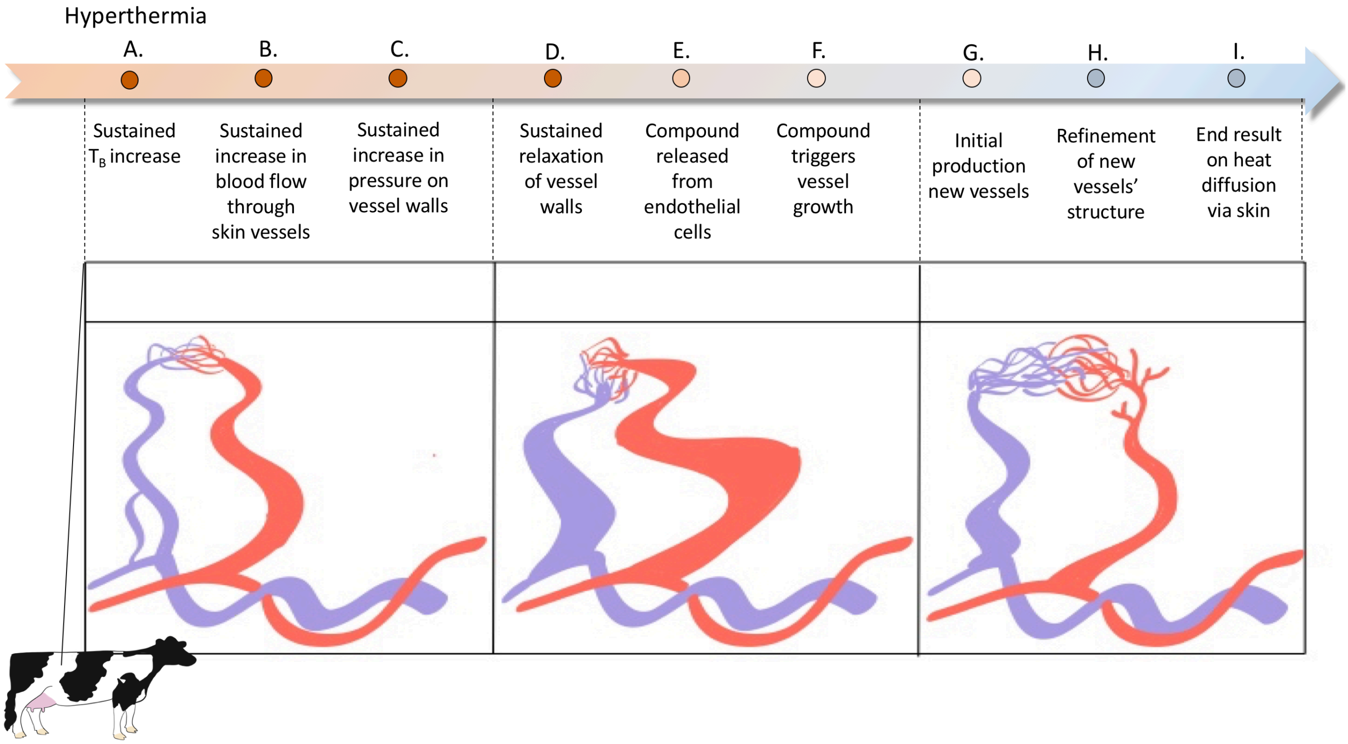


Figure 10. Changes in dermal blood flow in response to deviations above normal body temperature. Note the progressive changes from left to right in structures of blood vessels within the dermis of the skin in response to hyperthermia, as shown in the lower panels. Letters A through I in the upper panel and along the arrow refer to specific physiological changes that occur during acclimation to hyperthermia within the skin.

Part VII – Conclusion

Is it getting hot for Nelly? Yes, but she doesn't have to take off her fur. Given the physiological changes brought about by exercise, it is possible that more fit animals like Nelly will have an easier time maintaining their T_B, even when they are living in climates that are far warmer than their native environment. Because heat moooooves from hotter to cooler areas, it is critically important to get as much heat into the skin as possible in order to create a large thermal gradient that can be remoooooved via radiation, conduction or convection. The physiological changes that occur as a result of acclimatizing to challenges such as those presented by exercise could be just the thing that all the cool cows will be doing as our climate continues to warm.

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